PROVIDER*ALERT*

AmeriHealth Caritas Louisiana

To: **AmeriHealth Caritas Louisiana Providers**

Date: **September 12, 2024**

Subject: **LDH Approved Clinical Policies Effective October 11, 2024**

Summary: Guidelines for Electrical Muscle Stimulation; Gastroparesis Evaluations; Lung Transplants; Pancreas Transplantation; Sacral Nerve Modulation Stimulation, and Speech Therapy.

AmeriHealth Caritas Louisiana would like to inform you of seven new policies that have been approved by the Louisiana Department of Health in accordance with La. R.S. 46:460.54. The guidelines are effective on **October 11, 2024** and will be posted at the following link on our website under Clinical Policies: https://www.amerihealthcaritasla.com/provider/resources/clinical/policies.aspx.

1. Electrical Muscle Stimulation
2. Gastroparesis Evaluations
3. Lung Transplants
4. Pancreas Transplantation
5. Phototherapy Photochemotherapy Skin Conditions
6. Sacral Nerve Modulation Stimulation
7. Speech Therapy

Reminder: If your practice is not registered with our website portal-NaviNet, we highly recommend registering.
To register, please visit www.navinet.net to sign up or contact your Provider Account Executive for details.

Questions: Thank you for your continued support and commitment to the care of our members. If you have questions about this communication, please contact AmeriHealth Caritas Louisiana Provider Services at 1-888-922-0007 or your Provider Network Management Account Executive.

Missed an alert? You can find a complete listing of provider alerts on the Provider Newsletters and Updates page of our website.

Need to update your provider information? Send full details to network@amerihealthcaritasla.com.

AmeriHealth Caritas Louisiana

Electrical muscle stimulation

Clinical Policy ID: CCP.1377

Recent review date: 4/2024

Next review date: 8/2025

Policy contains: Functional electrical stimulation; neuromuscular electrical stimulation; physical rehabilitation

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Electrical muscle stimulation (also referred to as neuromuscular electrical stimulation) is clinically proven and, therefore, medically necessary when used in accordance with U.S. Food and Drug Administration labeling instructions for each device for the following indications:

- Correcting foot drop of central neurological origin when an ankle-foot orthosis is not tolerated (Moll, 2017; National Institute for Health and Care Excellence, 2009; Prenton, 2018).
- Attenuating muscle disuse atrophy in immobilized lower limbs following a non-neurological injury or surgery with intact nerve supply (Conley, 2021; Hauger, 2018; Wylde, 2018).
- Correcting or preventing glenohumeral subluxation after an acute or subacute stroke (Lee, 2017; Winstein, 2016).
- Restoring upper limb function after an acute or subacute stroke or spinal cord injury with minimal volitional movement, combined with task-specific training (de Freitas, 2018; Fehlings, 2017; Mirkowski, 2019; Monte-Silva, 2019; National Institute for Health and Care Excellence, 2023).
- To enable independent ambulation using Parastep 1® for those with spinal cord injury who meet criteria including:
    - Intact lower motor units from L1 down.
    - Stability for weight bearing with balance/trunk control.

- Responsive muscles and sensation to stimulation
- Independent transfers and standing three plus minutes.
- Motivation/ability to use device long term.
- Finger function to operate controls.
- Six plus months post-injury/surgery.
- No hip/knee degeneration or osteoporotic fractures.

Limitations

All other uses of electrical muscle stimulation are not medically necessary, as the safety and effectiveness has not been established. These include, but are not limited to:

- Muscle disuse atrophy in members with spinal cord injury.
- Pain control.
- Non-medical uses (e.g., exercise).
- Oropharyngeal dysphagia (Almeida, 2020; Alamer, 2020; Diéguez-Pérez, 2020; López-Liria, 2020).
- Edema reduction (Burgess, 2019).
- Knee osteoarthritis in a non-surgical member (Novak, 2020).

Alternative covered services

- Occupational therapy.
- Physical therapy.
- Speech therapy.
- Specialist consultation.
- Hip-knee-ankle-foot orthoses.

Background

Electrical stimulation is one of many interventions employed to restore body movement critical for daily function and quality of life. Available in many forms, electrical stimulation facilitates changes in either bioelectrical or biochemical communication among cellular components to effect muscle action, pain modulation, and performance. Electrodes may be positioned transcutaneously, percutaneously, or subcutaneously. Small portable units with modifiable capabilities are the most popular, because they allow providers to set parameters and design custom programs that patients can use in the clinic or at home (Doucet, 2012).

Transcutaneous methods such as transcutaneous electrical nerve stimulation and interferential current work at lower frequencies (0.5 to 100 Hz) in the bioelectric range to alter pain signals that travel to the brain, thereby decreasing acute and chronic pain without any discernable muscle contraction. Other benefits may be improved circulation, lymphatic flow, swelling, and muscle function. Similarly, higher-frequency electrical stimulation is used to decrease pain, improve circulation, and speed wound healing (Doucet, 2012).

Electrical muscle stimulation, also referred to as neuromuscular electrical stimulation or e-stim, typically delivers higher frequencies (20 – 50 Hz) to produce muscle tetany and contraction. It has two main purposes: 1) to treat muscle atrophy during temporary extremity immobilization; and 2) to pair the stimulation simultaneously or intermittently with a functional task in neurologically impaired individuals (commonly referred to as functional electrical stimulation). Electrical muscle stimulation was first applied clinically to correct foot drop in paraplegics and has become an integral part of modern rehabilitation programs (Doucet, 2012).

Electroceutical therapy, also referred to as bioelectric nerve block, uses even higher electrical frequencies (ranging

from 1 to 20,000 Hz) to mimic the human bioelectric system. An example of this is the Hako-Med PRO ElecDT 2000. This device employs a proprietary concept called Horizontal® Therapy into its product, which the manufacturer claims can treat both bioelectrical and biochemical cellular communication components in one treatment session by holding the bioelectric intensity constant while changing the frequency. Due to safety concerns, it may only be prescribed and administered under the supervision of a health care provider experienced in this method of treatment.

Regulation

The U.S. Food and Drug Administration regulates neuromuscular electrical stimulators for clinical use either through the 510(k) process or the premarket approval process. Devices required to go through the more rigorous premarket approval process have additional issues of safety and efficacy. Several devices have been approved for a range of indications that often overlap with other transcutaneous methods (U.S. Food and Drug Administration, 2023a, 2023b):

- Stroke rehabilitation by muscle re-education.
- Relaxation of muscle spasm.
- Attenuation of disuse atrophy.
- Increasing local blood circulation.
- Muscle re-education for other conditions.
- Maintaining or increasing range of motion.
- Prevention of deep vein thrombosis following surgery.
-

Unlike neuromuscular electrical stimulators (product codes IPF, GZI, and MKD), approved uses for transcutaneous methods, such as interferential current therapy, typically include control of pain. As such, these devices are regulated as transcutaneous electrical nerve stimulators (product code LIH).

Findings

The evidence from several systematic reviews, meta-analyses, and guidelines suggests electrical muscle stimulation is safe and efficacious when used in accordance with established rehabilitation protocols requiring supervision or in unattended settings (Fehlings, 2017; Gatewood, 2017; Ho, 2014; Lee, 2017; Moll, 2017; National Institute for Health and Care Excellence, 2009, 2013; Prenton, 2016; Winstein, 2016). The strongest evidence for neuromuscular electrical stimulation based on systematic reviews and meta-analyses supports its use for improving swallowing function and limb strength in stroke patients, as well as strengthening muscles in patients with knee surgery, chronic kidney disease, and advanced diseases like respiratory failure, heart failure, and cancer. Potential benefits are also seen for enhancing rehabilitation and gross motor function in cerebral palsy, postural control in spastic diplegia, and respiratory function in spinal cord injury.

Professional Clinical Guidelines

Neuromuscular electrical stimulation is reasonably recommended in several circumstances for stroke rehabilitation based on generally strong levels of evidence, according to joint guidelines issued by the American Heart Association/American Stroke Association (Winstein, 2016). It can be considered as an alternative to an ankle foot orthosis for treating foot drop, supported by strong Level B evidence. Neuromuscular electrical stimulation is also reasonably recommended for individuals in the first few month's post-stroke who have minimal voluntary movement, in order to facilitate improvement, backed by strong Level A evidence. Managing increased muscle tone temporarily with neuromuscular electrical stimulation as an adjunct to rehabilitation therapy is a reasonable option with moderate Level A evidence. Finally, neuromuscular electrical stimulation is reasonably recommended

for treating shoulder instability, with the strongest Level A evidence (Winstein, 2016).

The National Institute for Health and Care Excellence has issued two guidelines related to electrical muscle stimulation. The first issued in 2009 noted that evidence supports the safety and efficacy of the treatment for improving gait in patients with drop foot caused by upper motor neuron lesions from conditions like stroke, cerebral palsy, multiple sclerosis, or spinal cord injury (National Institute for Health and Care Excellence, 2009). A supplemental guideline issued in 2023 notes that electrical stimulation is not recommended for routine use in the rehabilitation of the hand or arm after stroke. However, a trial of electrical stimulation therapy is suggested as part of a comprehensive rehabilitation program for individuals who exhibit evidence of muscle contraction post-stroke but cannot move their arm against resistance. The continuation of this therapy is advised if it leads to improvements in the person's strength and their ability to practice functional tasks, such as maintaining range of motion or enhancing grasp and release (National Institute for Health and Care Excellence, 2023).

Neuromuscular electrical stimulation

In an immobilized extremity, neuromuscular electrical stimulation can control edema, increase local blood circulation, maintain muscle tone, or delay the development of disuse atrophy (Doucet, 2012). It has been proposed as treatment for muscle atrophy in conditions such as cerebral palsy, congestive heart failure, progressive neuromuscular diseases, chronic obstructive pulmonary disease, and upper extremity hemiplegia. In these populations, the rationale for use is to enhance the effects of rehabilitation or provide an alternative for patients with muscle weakness who have difficulty engaging with traditional rehabilitation services.

Post-Stroke Dysphagia and Motor Impairment

Several systematic reviews have found that neuromuscular electrical stimulation improves swallowing function and limb strength in stroke patients. Alamer (2020) analyzed 11 randomized controlled trials with 784 patients and found moderate to high quality evidence that neuromuscular electrical stimulation combined with swallowing therapy was more effective than swallowing therapy alone for improving dysphagia post-stroke. Chiang (2019) compared different stimulation techniques in 19 randomized controlled trials with 691 stroke patients and found neuromuscular electrical stimulation significantly improved swallowing function versus placebo. Wang (2021) meta-analyzed 20 studies totaling 914 stroke patients and found neuromuscular electrical stimulation groups had significantly better dysphagia outcomes than control groups. For limb function, Yang (2019) reviewed 48 randomized controlled trials with 1712 stroke patients and found neuromuscular electrical stimulation significantly improved arm function and strength compared to placebo. Monte (2019) meta-analyzed 26 randomized controlled trials with 782 patients and found a robust short-term effect of electromyography-triggered neuromuscular electrical stimulation on upper limb motor impairment, especially in chronic stroke.

Muscle Strengthening in Other Populations

Quadriceps strength after knee surgery: Gatewood (2017) reviewed 7 studies with over 300 patients and found neuromuscular electrical stimulation improved post-operative quadriceps strength and function. Conley (2021) identified optimal neuromuscular electrical stimulation parameters from 8 randomized controlled trials with 559 patients.

Chronic kidney disease: Schardong (2020) meta-analyzed 10 studies with 242 hemodialysis patients and found neuromuscular electrical stimulation significantly improved quadriceps strength, upper limb strength, and functional capacity. Valenzuela (2020) reviewed 8 trials with 221 patients and found neuromuscular electrical stimulation during dialysis improved walk distance, cycling workload, and limb strength.

Advanced disease: A Cochrane review by Jones (2016) of 18 randomized controlled trials with 933 participants found neuromuscular electrical stimulation improved quadriceps strength and muscle mass in patients with

respiratory disease, heart failure, and cancer.

Spinal cord injury: de Freitas (2018) analyzed 5 studies with 170 patients but found insufficient evidence that neuromuscular electrical stimulation was superior to other treatments for improving strength.

Rehabilitation and Functional Outcomes

Beyond strength, neuromuscular electrical stimulation may enhance rehabilitation and physical function in certain populations. Chen (2023) meta-analyzed 14 randomized controlled trials with 421 children with cerebral palsy and found neuromuscular electrical stimulation significantly improved walking speed and gross motor scores compared to conventional therapy alone. McCaughey (2016) reviewed 14 studies in 129 spinal cord injury patients and found abdominal functional electrical stimulation acutely improved cough and chronically increased vital capacity and peak expiratory flow. Dewar (2015) concluded level II evidence from 2 studies supported functional stimulation combined with rehabilitation for improving postural alignment in children with spastic diplegia, but called for more research.

Edema and Pain Management

A few reviews suggest potential benefits of neuromuscular electrical stimulation for managing edema and pain, though the evidence is limited. Burgess (2019) found 6 of 7 studies totaling over 200 patients showed neuromuscular electrical stimulation effectively reduced edema in various conditions. Novak (2020) reviewed 9 randomized controlled trials and recommended neuromuscular electrical stimulation combined with strengthening exercises for reducing pain in knee osteoarthritis. However, Zayed (2020) meta-analyzed 6 randomized controlled trials with 718 critically ill patients and found no significant effect of neuromuscular electrical stimulation on ICU outcomes. Martimbianco (2017) found very low quality evidence from up to 4 trials with 118 participants that neuromuscular electrical stimulation plus exercise slightly reduced patellofemoral pain compared to exercise alone.

Specialty Populations

A few systematic reviews examined neuromuscular electrical stimulation in specialty populations with mixed findings:

Dysphonia: Almeida (2020) reviewed 11 studies with 382 patients and found while neuromuscular electrical stimulation showed some improvements in laryngeal function and vocal quality, heterogeneity in designs prevented determinations of overall effectiveness for treating dysphonia.

Parkinson's dysphagia: López-Liria (2020) found 2 studies with 199 Parkinson's patients where neuromuscular electrical stimulation did not significantly improve dysphagia compared to traditional therapy alone.

Chronic Obstructive Pulmonary Disease: A statement by Maltais noted neuromuscular electrical stimulation is emerging as a useful modality for muscle dysfunction in severe chronic obstructive pulmonary disease and exacerbations but did not quantify the evidence or make a formal recommendation. Orthopedic Applications Regarding orthopedic uses, evidence is lacking to support neuromuscular electrical stimulation, especially long-term. McAlindon's guidelines reviewed one systematic review and two randomized controlled trials with 107 patients and determined neuromuscular electrical stimulation was "not appropriate" for treating knee osteoarthritis. Wylde (2018) reviewed 17 randomized controlled trials with 2485 participants and found no interventions, including 1 neuromuscular electrical stimulation trial, reduced chronic pain beyond 3 months after total knee replacement.

Adverse Events and Limitations

Across the reviewed studies, no serious adverse events related to neuromuscular electrical stimulation were reported. However, several reviews noted limitations in the current evidence base, including small sample sizes, heterogeneous designs and outcome measures, lack of long-term follow-up, and overall low quality of many included studies. Newberry (2017) concluded evidence was insufficient to evaluate neuromuscular electrical stimulation effectiveness, largely due to poor quality and heterogeneous study design.

Functional electrical stimulation

In the lower extremities, functional electrical (muscle) stimulation has been used to perform stationary exercise and assist with standing and walking. For persons with upper extremity paralysis caused by injury or disease of the central nervous system, it has been used to improve hand function and range of motion and correct or prevent glenohumeral subluxation in stroke. Devices used to augment stationary exercise are considered exercise equipment and not necessarily for medical use.

Functional Electrical Stimulation for Stroke

Several studies have investigated the impact of functional electrical stimulation on walking and upper extremity function in stroke patients. A systematic review and meta-analysis by Prenton (2016) synthesized 7 randomized controlled trials with a total of 815 stroke participants. The analysis found that functional electrical stimulation and ankle foot orthoses produced comparable improvements in walking speed, functional exercise capacity, timed up-and-go, and perceived mobility. The authors concluded that ankle foot orthoses have equally positive combined-orthotic effects as functional electrical stimulation on key walking measures for foot-drop caused by stroke.

In a systematic review and meta-analysis, Lee JH (2017) examined 11 randomized controlled trials with a total of 432 participants (216 receiving functional electrical stimulation plus conventional therapy, 216 receiving conventional therapy alone) to assess the effectiveness of functional electrical stimulation for managing shoulder subluxation post-stroke. The studies included participants with acute stroke who were 2.0±2.2 months (intervention) and 1.6±1.7 months (control) post-stroke, and those with chronic stroke who were 9.4±4.1 months (intervention) and 9.1±3.9 months (control) post-stroke.

Functional Electrical Stimulation for Spinal Cord Injury

The use of functional electrical stimulation for restoring functions in individuals with spinal cord injury has been reviewed in several studies. Fehlings (2017) reviewed two randomized controlled trials involving a total of 89 patients with acute and subacute cervical spinal cord injury. One study found that compared to occupational therapy alone, functional electrical stimulation combined with occupational therapy resulted in significantly greater improvements on the Functional Independence Measure Motor subscore (15.0 vs 4.1 points), Functional Independence Measure Self-Care subscore (20.1 vs 10 points), and Spinal Cord Independence Measure Self-Care subscore (10.2 vs 3.1 points). The other study found no significant differences between functional electrical stimulation, biofeedback, combined functional electrical stimulation/biofeedback, and conventional strengthening for recovering tenodesis grasp. Based on this low-quality evidence, the guideline suggests offering functional electrical stimulation to improve hand and upper extremity function in individuals with acute and subacute cervical spinal cord injury.

Ho (2014) systematically reviewed functional electrical stimulation applications for various functions in spinal cord injury patients. The largest clinical trial of an upper extremity functional electrical stimulation neuroprosthesis (the Freehand trial) included 28 participants, all of whom improved independence in at least one task. A second generation implanted functional electrical stimulation system (IST-12) has been implanted in 12 spinal cord injury subjects, with each demonstrating improvement in at least 2 activities. For lower extremity function, functional electrical stimulation neuroprosthesis recipients exhibited mean and median standing times of 10 and 3 minutes

respectively, with some recipients in a Phase II trial standing over 20 minutes.

Functional Electrical Stimulation for Cerebral Palsy

Moll (2017) conducted a systematic review assessing the effect of functional electrical stimulation on ankle dorsiflexors in children and adolescents with spastic cerebral palsy during walking. The review included 14 articles (11 studies) with a total of 127 patients aged 5 to 19 years with Gross Motor Function Classification System levels I to III receiving functional electrical stimulation. Only five articles (three studies) were of level I to III evidence. Ankle dorsiflexion angle was the most frequently investigated outcome. Adverse events included skin irritation, poor tolerance, and acceptation issues. The review found some evidence supporting functional electrical stimulation use in children with spastic cerebral palsy for improving ankle and gait biomechanics, but more high-quality research is needed. In 2024, condensed and reorganized findings section clearly noting affirmative guidelines, and synthesizing commonalties across studies reviewed. No new studied were added and no policy changes are warranted.

In 2024, condensed and reorganized findings section clearly noting affirmative guidelines, and synthesizing commonalties across studies reviewed. No new studied were added and no policy changes are warranted.

References

On April 3, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “speech deficit,” ”speech fluency,” “Feeding and Eating Disorders of Childhood/therapy" (MAJR), “Feeding behavior/therapy” (MeSH), “deglutition disorders” (MeSH), “dysphagia,” and “speech therapy” (MeSH). We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Alamer A, Melese H, Nigussie F. Effectiveness of neuromuscular electrical stimulation on post-stroke dysphagia: A systematic review of randomized controlled trials. *Clin Interv Aging.* 2020;15:1521-1531. Doi: 10.2147/cia.s262596.
Almeida ANS, Cunha DAD, Ferreira SLS, et al. Effect of electrical stimulation on the treatment of dysphonia: A systematic review. *J Voice.* 2020. Doi: 10.1016/j.jvoice.2020.08.002.

Bath PM, Lee HS, Everton LF. Swallowing therapy for dysphagia in acute and subacute stroke. *Cochrane Database Syst Rev*. 2018;10(10):CD000323. Doi: 10.1002/14651858.CD000323.pub3.

Bistolfi A, Zanovello J, Ferracini R, et al. Evaluation of the effectiveness of neuromuscular electrical stimulation after total knee arthroplasty: A meta-analysis. *Am J Phys Med Rehabil.* 2018;97(2):123-130. Doi: 10.1097/phm.0000000000000847.

Burge AT, Cox NS, Abramson MJ, Holland AE. Interventions for promoting physical activity in people with chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev.* 2020;4(4):Cd012626. Doi: 10.1002/14651858.CD012626.pub2.

Burgess LC, Immins T, Swain I, Wainwright TW. Effectiveness of neuromuscular electrical stimulation for reducing oedema: A systematic review. *J Rehab Med.* 2019;51(4):237-243. Doi: 10.2340/16501977-2529.

Centers for Medicare & Medicaid Services. Local Coverage Determination L34565 Home health-surface electrical stimulation in the treatment of dysphagia. https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Effective October 31, 2019 (a).

Centers for Medicare & Medicaid Services. Local Coverage Determination L34578 Surface electrical stimulation in the treatment of dysphagia. https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Effective November 21, 2019 (b).

Centers for Medicare & Medicaid Services. National Coverage Determination 160.12 Neuromuscular Electrical Stimulation (NMES). https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Effective October 2, 2006.

Centers for Medicare & Medicaid Services. National Coverage Determination 160.13 Supplies used in the delivery of transcutaneous electrical nerve stimulation (TENS) and neuromuscular electrical stimulation (NMES). https://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Effective July 14, 1988.

Chen R-C, Li X-Y, Guan L-L, et al. Effectiveness of neuromuscular electrical stimulation for the rehabilitation of moderate-to-severe COPD: A meta-analysis. *Int J Chron Obstruct Pulmon Dis*. 2016;11:2965-2975. Doi: 10.2147/COPD.S120555.

Chiang C-F, Lin M-T, Hsiao M-Y, et al. Comparative efficacy of noninvasive neurostimulation therapies for acute and subacute poststroke dysphagia: A systematic review and network meta-analysis. *Arch Phys Med Rehabil.* 2019;100(4):739-750.e734. Doi: 10.1016/j.apmr.2018.09.117.

Conley CEW, Mattacola CG, Jochimsen KN, et al. A comparison of neuromuscular electrical stimulation parameters for postoperative quadriceps strength in patients after knee surgery: A systematic review. *Sports Health.* 2021:13(2):116-127. Doi: 10.1177/1941738120964817.

de Freitas GR, Szpoganicz C, Ilha J. Does neuromuscular electrical stimulation therapy increase voluntary muscle strength after spinal cord injury? A systematic review. *Top Spinal Cord Inj Rehabil.* 2018;24(1):6-17. Doi: 10.1310/sci16-00048.

Dewar R, Love S, Johnston LM. Exercise interventions improve postural control in children with cerebral palsy: A systematic review. *Dev Med Child Neurol.* 2015;57(6):504-520. Doi: 10.1111/dmcn.12660.

Di Sante L, Paoloni M, Dimaggio M, et al. Ultrasound-guided aspiration, and corticosteroid injection compared to horizontal therapy for treatment of knee osteoarthritis complicated with Baker's cyst: A randomized, controlled trial. *Eur J Phys Rehabil Med*. 2012;48(4):561-567. https://www.minervamedica.it/en/journals/europa-medicophysica/article.php?cod=R33Y2012N04A0561.

Diéguez-Pérez I, Leirós-Rodríguez R. Effectiveness of different application parameters of neuromuscular electrical stimulation for the treatment of dysphagia after a stroke: A systematic review. *J Clin Med.* 2020;9(8). Doi: 10.3390/jcm9082618.

Doucet BM, Lam A, Griffin L. Neuromuscular electrical stimulation for skeletal muscle function. *Yale J Biol Med.* 2012;85(2):201-215. National Center for Biotechnology Information. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3375668/pdf/yjbm_85_2_201.pdf.

Fehlings MG, Tetreault LA, Aarabi B, et al. A clinical practice guideline for the management of patients with acute spinal cord injury: Recommendations on the type and timing of rehabilitation. *Global Spine J.* 2017;7(3 Suppl):231S-238S. Doi: 10.1177/2192568217701910.

Gatewood CT, Tran AA, Dragoo JL. The efficacy of post-operative devices following knee arthroscopic surgery: A systematic review. *Knee Surg Sports Traumatol Arthrosc.* 2017;25(2):501-516. Doi: 10.1007/s00167-016-4326-4.

Hajibandeh S, Hajibandeh S, Antoniou GA, Scurr JR, Torella F. Neuromuscular electrical stimulation for thromboprophylaxis: A systematic review. *Phlebology.* 2015;30(9):589-602. Doi: 10.1177/0268355514567731.

Hako-Med Holdings, Inc. Products Page. PRO ElecDT® 2000 WITH VasoPulse®2000. http://www.electromedicine.com/. Published 2021.

Hauger AV, Reiman MP, Bjordal JM, et al. Neuromuscular electrical stimulation is effective in strengthening the quadriceps muscle after anterior cruciate ligament surgery. *Knee Surg Sports Traumatol Arthrosc.* 2018;26(2):399-410. Doi: 10.1007/s00167-017-4669-5.

Ho CH, Triolo RJ, Elias AL, et al. Functional electrical stimulation, and spinal cord injury. *Phys Med Rehabil Clin N Am.* 2014;25(3):631-654, ix. Doi: 10.1016/j.pmr.2014.05.001.p

Jones S, Man WD, Gao W, et al. Neuromuscular electrical stimulation for muscle weakness in adults with advanced disease. *Cochrane Database Syst Rev.* 2016;10:Cd009419. Doi: 10.1002/14651858.CD009419.pub3.

Lee JH, Baker LL, Johnson RE, Tilson JK. Effectiveness of neuromuscular electrical stimulation for management of shoulder subluxation post-stroke: A systematic review with meta-analysis. *Clin Rehabil.* 2017;31(11):1431-1444. Doi: 10.1177/0269215517700696.

López-Liria R, Parra-Egeda J, Vega-Ramírez FA, et al. Treatment of dysphagia in Parkinson's disease: A systematic review. *Int J Environ Res Public Health.* 2020;17(11). Doi: 10.3390/ijerph17114104.

Maltais F, Decramer M, Casaburi R, et al. An official American Thoracic Society/European Respiratory Society statement: Update on limb muscle dysfunction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2014;189(9):e15-62. Doi: 10.1164/rccm.201402-0373ST.

Martimbianco ALC, Torline MR, Andriolo BN, Porfirio GJ, Riera R. Neuromuscular electrical stimulation (NMES) for patellofemoral pain syndrome. *Cochrane Database Syst Rev.* 2017;12:Cd011289. Doi: 10.1002/14651858.CD011289.pub2.

McAlindon TE, Bannuru RR, Sullivan MC, et al. OARSI guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage.* 2014;22(3):363-388. Doi: 10.1016/j.joca.2014.01.003.

McCaughey EJ, Borotkanics RJ, Gollee H, Folz RJ, McLachlan AJ. Abdominal functional electrical stimulation to improve respiratory function after spinal cord injury: A systematic review and meta-analysis. *Spinal Cord.* 2016;54(9):628-639. Doi: 10.1038/sc.2016.31.

Moll I, Vles JSH, Soudant D, et al. Functional electrical stimulation of the ankle dorsiflexors during walking in spastic cerebral palsy: A systematic review. *Dev Med Child Neurol.* 2017;59(12):1230-1236. Doi: 10.1111/dmcn.13501.

Monte-Silva K, Piscitelli D. Electromyogram-related neuromuscular electrical stimulation for restoring wrist and hand movement in poststroke hemiplegia: A systematic review and meta-analysis. *Neurorehabil Neural Repair.* 2019;33(2):96-111. Doi: 10.1177/1545968319826053.

National Institute for Health and Care Excellence. Functional electrical stimulation for drop foot of central neurological origin. Interventional procedures guidance [IPG278]. https://www.nice.org.uk/guidance/ipg278/chapter/1-Guidance. Published January 2009.

National Institute for Health and Care Excellence. Stroke rehabilitation in adults. Clinical guideline [CG162]. https://www.nice.org.uk/guidance/CG162. Published June 12, 2013.

Newberry SJ, FitzGerald J, SooHoo NF, et al. Treatment of osteoarthritis of the knee: An update review. Comparative Effectiveness Review No. 190. (Prepared by the RAND Southern California Evidence-based Practice Center under Contract No. 290-2015-00010-I.) AHRQ Publication No.17-EHC011-EF. Rockville, MD. Agency for Healthcare Research and Quality website. https://effectivehealthcare.ahrq.gov/products/osteoarthritis-knee-update/research-2017. Published May 4, 2017.

Novak S, Guerron G, Zhou Z, Cheung G, Berteau J-P. New guidelines for electrical stimulation parameters in adult patients with knee osteoarthritis based on a systematic review of the current literature. *Am J Phys Med Rehabil*. 2020;99(8):682-688.

Prenton S, Hollands KL, Kenney LP. Functional electrical stimulation versus ankle foot orthoses for foot-drop: A meta-analysis of orthotic effects. *J Rehabil Med.* 2016;48(8):646-656. Doi: 10.2340/16501977-2136.

Qaseem A, Wilt TJ, McLean RM, Forciea MA. Noninvasive treatments for acute, subacute, and chronic low back pain: A clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2017;166(7):514-530. Doi: 10.7326/m16-2367.

Schardong J, Stein C, Della Méa Plentz R. Neuromuscular electrical stimulation in chronic kidney failure: A systematic review and meta-analysis. *Arch Phys Med Rehabil.* 2020;101(4):700-711. Doi: 10.1016/j.apmr.2019.11.008.

Scutt P, Lee HS, Hamdy S, Bath PM. Pharyngeal electrical stimulation for treatment of poststroke dysphagia: Individual patient data meta-analysis of randomized controlled trials. Stroke Res Treat. 2015;2015:429053. Doi: 10.1155/2015/429053.

Thomaz SR, Cipriano G, Jr., Formiga MF, et al. Effect of electrical stimulation on muscle atrophy and spasticity in patients with spinal cord injury - a systematic review with meta-analysis. *Spinal Cord.* 2019;57(4):258-266. Doi: 10.1038/s41393-019-0250-z.

U.S. Food and Drug Administration. 510(k) Premarket Notification database searched using product codes IPF, GZI, and LIH. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. Last updated March 7, 2022 (a)

U.S. Food and Drug Administration. Premarket approval (PMA) database searched using product code MKD. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm. Last updated March 7, 2022 (b)

Valenzuela PL, Morales JS, Ruilope LM, et al. Intradialytic neuromuscular electrical stimulation improves functional capacity and muscle strength in people receiving haemodialysis: A systematic review. *J Physiother.* 2020;66(2):89-96. Doi: 10.1016/j.jphys.2020.03.006.

Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke and recovery: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2016;47(6):e98-e169. Doi: 10.1161/str.0000000000000098.

Wylde V, Dennis J, Gooberman-Hill R, Beswick AD. Effectiveness of postdischarge interventions for reducing the severity of chronic pain after total knee replacement: Systematic review of randomised controlled trials. *BMJ Open.* 2018;8(2):e020368. Doi: 10.1136/bmjopen-2017-020368.

Yang J-D, Liao C-D, Huang S-W, et al. Effectiveness of electrical stimulation therapy in improving arm function after

stroke: A systematic review and a meta-analysis of randomised controlled trials. *Clin Rehabil.* 2019;33(8):1286-1297. Doi: 10.1177/0269215519839165.

Zambito A, Bianchini D, Gatti D, et al. Interferential and horizontal therapies in chronic low back pain due to multiple vertebral fractures: A randomized, double blind, clinical study. *Osteoporos Int*. 2007;18(11):1541-1545. Doi: 10.1007/s00198-007-0391-3.

Zambito A, Bianchini D, Gatti D, et al. Interferential and horizontal therapies in chronic low back pain: A randomized, double blind, clinical study. *Clin Exp Rheumatol*. 2006;24(5):534-539. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwjp3c3r1-vgAhVRh-AKHSTqAvAQFjAAegQIBxAC&url=https%3A%2F%2Fwww.clinexprheumatol.org%2Farticle.asp%3Fa%3D2957&usg=AOvVaw0cmEjpnWcvgDDM337Er5Rw.

Zayed Y, Kheiri B, Barbarawi M, et al. Effects of neuromuscular electrical stimulation in critically ill patients: A systematic review and meta-analysis of randomised controlled trials. *Aust Crit Care.* 2020;33(2):203-210. Doi: 10.1016/j.aucc.2019.04.003.

Policy updates

4/2018: initial review date and clinical policy effective date: 5/2018
5/2019: Policy references updated. Consolidated CCP.1027 into this policy. Policy ID changed.
5/2020: Policy references updated.
5/2021: Policy references updated.
5/2022: Policy references updated.
5/2023: Policy references updated.
5/2024: Policy references updated.

Gastroparesis evaluations

Clinical Policy ID: CCP.1357

Recent review date: 2/2024

Next review date: 5/2025

Policy contains: Gastric emptying breath test; gastric emptying scintigraphy; gastroparesis; wireless motility capsule.

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Gastroparesis evaluation is clinically proven and, therefore, may be medically necessary when all of the following criteria are met (Camilleri, 2022; Schol, 2021):

- Presence of symptoms of suspected gastroparesis, including, but not limited to, nausea, vomiting, early satiety, postprandial fullness, bloating, and upper abdominal pain.
- Absence of demonstrable mechanical obstruction of the gastric outlet.
- Non-diagnostic basic clinical investigations, including upper endoscopy.
- Documentation of delayed gastric emptying by either:
    - Gastric emptying scintigraphy of a radiolabeled solid meal.
        - If gastric emptying scintigraphy is contraindicated or not feasible, a wireless motility capsule (e.g., SmartPill™ Motility Testing System, Medtronic Inc., Minneapolis, Minnesota) or stable isotope breath test may be used.
- Evaluation by a gastroenterologist trained to use and interpret the results.

Limitations

All other modalities of verification of delayed gastric emptying in the absence of demonstrable mechanical obstruction of the gastric outlet are not medically necessary.
Contraindications to the wireless motility capsule include a history of gastric bezoar, swallowing disorders, dysphagia, suspected strictures/fistulae in the gastrointestinal tract, physiologic gastrointestinal obstruction, gastrointestinal surgery within the previous three months, Crohn's disease, diverticulitis, or those who have an implanted electromechanical medical device (such as pacemaker or infusion pump) (Rao, 2011).
The wireless motility capsule is investigational/not clinically proven and, therefore, not medically necessary in pediatric members, as it has not been approved for use in this population (U.S. Food and Drug Administration, 2017).

Alternative covered services

Routine patient evaluation and management by a network health care provider.

Background

Gastroparesis is a gastric motility disorder characterized by delayed gastric emptying of fluids and/or solids without evidence of a mechanical gastric outlet obstruction (Saliakellis, 2013). Approximately three of four cases of gastroparesis are idiopathic or related to diabetes mellitus (Ye, 2021). Among individuals with diabetes, the pathogenic changes in gastrointestinal function can damage the enteric nervous system leading to gastrointestinal motility disorders and increased disease morbidity (Rodrigues, 2012). Gastroparesis is associated with significant psychological distress and poor quality of life (Woodhouse, 2017).

Individuals typically present with nonspecific symptoms that may indicate several possible gastric disorders. These symptoms include nausea, vomiting, early satiety, postprandial fullness, bloating, weight loss, and upper abdominal pain. The differential diagnosis can be particularly challenging in children, in whom the most common symptoms are typically age-dependent. For example, nausea and abdominal pain are more frequent in older children and adolescents, while vomiting is more frequent in younger children (Usai-Satta, 2020).

Evaluation and management of suspected gastroparesis requires documentation of delayed gastric emptying and exclusion of other potential causes. Gastric emptying scintigraphy using Technecium-99, gastric emptying C13-spirulina (C13) breath testing, and wireless capsule endoscopy are available diagnostic alternatives. An upper gastrointestinal barium contrast study and esophagogastroduodenoscopy can rule out mechanical obstruction. Tests of gastric, small intestinal, and colonic motor function may provide adjunctive physiologic information for diagnosing and guiding the management of gastrointestinal dysmotilities (Usai-Satta, 2020).

Findings

For evaluation of gastroparesis in patients with upper gastrointestinal symptoms, an updated guideline by the American College of Gastroenterology issued the following recommendations (Camilleri, 2022):

- Gastric emptying scintigraphy of a solid phase meal is the standard test for its ability to provide a noninvasive, direct, and quantifiable measure of gastric emptying. While scintigraphic protocols vary among providers, the most reliable measure is the emptying of a solid meal over a duration of at least three hours (strong recommendation, moderate level of evidence).
- Radiopaque markers testing is not suggested (conditional recommendation, very low level of evidence).

- Wireless motility capsule testing and stable isotope C-13 breath testing may be alternatives to gastric emptying scintigraphy (conditional recommendation, low quality of evidence).

Butler (2017) in a narrative review noted that breath tests (e.g., the 13C urea breath test for the diagnosis and monitoring of Helicobacter pylori) are an excellent gastric diagnostic tool, particularly for studying children, as testing is painless and noninvasive. Several stable isotope breath tests for assessing gastric emptying have been designed and validated against scintigraphic methods. These tests have also been combined with nonabsorbable carbohydrates, such as lactulose, using hydrogen molecule measurements in exhaled breath to determine orocecal transit time. However, as the tracer target moves more distally away from the stomach, there may be variations in transit time that reduce the sensitivity and specificity of the test.

Stein (2013) in a systematic review identified the wireless motility capsule as an effective modality for diagnosing gastric and colonic motility disorders when compared with other tests of gastric and colonic motility; however, the quality of evidence regarding its ability to detect gastroparesis or slow-transit constipation was graded as low. Seven studies evaluated diagnosis of gastric emptying delay and found the wireless motility capsule comparable to scintigraphy for diagnostic accuracy, accuracy of motility assessment, effect on treatment decisions, and effect on resource utilization. Sensitivity of the wireless motility capsule compared with gastric scintigraphy ranged from 59% to 86% and specificity ranged from 64% to 81%.

The main limitations of the review were inconsistencies in reporting the performance of motility testing modalities. There is also a built-in bias in favor of the wireless motility capsule as subjects had undergone other testing suggestive of gastric emptying delay, in effect preselecting those individuals most likely to be affirmed with positive findings for wireless mobility capsule study. Data were insufficient to determine the optimal timing of motility capsule testing in diagnostic algorithms, but the wireless motility capsule constitutes another viable and useful diagnostic modality. Capsule retention and obstruction are potential complications, but serious complications are rare. They are contraindicated in children and patients with a known history of esophageal stricture (Stein, 2013).

For gastric emptying the choice test for gastroparesis is scintigraphy which involves the consumption of a meal that has a radioactive substance in it, that can be visualized and track the digestion time for and rate of stomach emptying. It takes approximately two to four hours (International Foundation for Gastrointestinal disorders, 2023). In 2019, we added a consensus guideline from the American and European Neurogastroenterology and Motility Societies (Rao, 2011) and one narrative review (Bruno, 2013) to the policy, and deleted two studies from the policy. Limited evidence supports breath testing using 13C-octanoate or -spirulina as a safe, valid test that correlates well with gastric emptying scintigraphy for measuring the gastric emptying rate of solids (Bruno, 2013). There are no contraindications to the test, and it can be used in individuals with diabetes with suspected gastroparesis. However, technical factors such as concurrent diseases, the test meal used, the duration of breath collection, and the cut-off limits of the normative data can influence the results.

In 2022, we added a guideline from a European consensus group, which stated that upper gastrointestinal endoscopy is mandatory for diagnosing gastroparesis. The guideline also states that scintigraphy, breath testing, wireless motility capsule assessment, and gastric ultrasound are all valid tests for diagnosing the condition (Schol, 2021).

According to the American and European Neurogastroenterology and Motility Societies, wireless motility capsules and breath tests are safe, validated, and radiation-free alternatives that offer advantages to individuals in whom gastric emptying scintigraphy is contraindicated or not feasible, such as pregnant women, breast-feeding women, and children (, Rao, 2011). Scintigraphy and wireless motility capsules are capable of assessing regional and whole-gut transit and offer value for individuals with suspected alterations of gastrointestinal motility in multiple regions. Breath testing as a measure of orocecal transit time with lactulose provides semiquantitative assessment of small bowel transit, but its clinical use for whole-gut transit is unclear. Other tests such as transabdominal ultrasonography, magnetic resonance imaging, capsule endoscopy, radiopaque markers, and antroduodenal

manometry may be used to evaluate small bowel and colonic transit, depending on availability and provider preferences.

We modified the policy to include the wireless motility capsule to the list of clinically proven methods for evaluating delayed gastric emptying, as it offers an acceptable alternative to scintigraphy, particularly in those whom gastric emptying scintigraphy is contraindicated or not feasible. The policy ID was changed from CP# 08.01.11 to CCP.1357.

In 2020, we identified no newly published, relevant literature to add to the policy. We modified the coverage to emphasize gastric emptying scintigraphy as the primary modality for evaluating gastric emptying and make wireless motility capsule and isotope breath tests medically necessary alternatives for those in whom gastric emptying scintigraphy is contraindicated or not feasible.
In 2021, we identified no newly published, relevant literature to add to the policy and deleted one older reference.

In 2022, we added a systematic review of 23 studies of persons with gastric emptying problems or upper gastrointestinal symptoms given promotility agents. Those who had optimal tests (scintigraphy, breath test, or solid meal > 2 hours duration) had significantly better improvements (P = .02) than those who had suboptimal tests (Vijayvargiya, 2019a). We also added a meta-analysis of 25 studies (n = 4,287) that documented an association between optimally measured (scintigraphy and breath tests) delayed gastric emptying and early satiety/fullness in patients with gastroparesis (Vijayvargiya, 2019b).

We added a prospective comparison of patients (n = 150) with gastroparesis symptoms tested with both scintigraphy and wireless motility capsule. The latter resulted in more treatment changes (P < .0001), elimination of additional tests (P < .0001), and orders of prokinetics (P = .0007) and laxatives (P < .0001) (Hasler, 2019).

In 2023, no newly published relevant literature to add to the policy. No new testing for gastroparesis has been developed. All information is current and standard of care. No coverage changes are warranted.

In 2024, we updated the references and added an updated American College of Gastroenterology guideline (Camilleri, 2022) to the policy with no policy changes warranted.

References

On December 5, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Gastroparesis/diagnosis” (MeSH), “Gastric Emptying” (MeSH), “Breath Tests” (MeSH), “gastroparesis evaluation,” “impedance,” “intestinal motility,” and “wireless endoscopy.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Bruno G, Lopetuso LR, Ianiro G, et al. 13C-octanoic acid breath test to study gastric emptying time. *Eur Rev Med Pharmacol Sci.* 2013;17 Suppl 2:59-64. https://www.europeanreview.org/wp/wp-content/uploads/059-064.pdf.

Butler RN, Kosek M, Krebs NF, et al. Stable isotope techniques for the assessment of host and microbiota response during gastrointestinal dysfunction. *J Pediatr Gastroenterol Nutr.* 2017;64(1):8-14. Doi: 10.1097/mpg.0000000000001373.

Camilleri M, Kuo B, Nguyen L, et al. ACG clinical guideline: Gastroparesis. *Am J Gastroenterol*. 2022;117(8):1197-1220. Doi: 10.14309/ajg.0000000000001874.

Hasler WL, Rao SSC, McCallum RW, et al. Influence of gastric emptying and gut transit testing on clinical management decisions in suspected gastroparesis. *Clin Transl Gastroenterol*. 2019;10(10):e00084. Doi: 10.14309/ctg.0000000000000084.

International Foundation for Gastrointestinal Disorders. Diagnosis & tests. https://aboutgastroparesis.org/signs-and-symptoms/diagnosis-tests/. Updated October 2023.

Rao SS, Camilleri M, Hasler WL, et al. Evaluation of gastrointestinal transit in clinical practice: Position paper of the American and European Neurogastroenterology and Motility Societies. *Neurogastroenterol Motil.* 2011;23(1):8-23. Doi: 10.1111/j.1365-2982.2010.01612.x.

Rodrigues ML, Motta ME. Mechanisms and factors associated with gastrointestinal symptoms in patients with diabetes mellitus. *J Pediatr (Rio J).* 2012;88(1):17-24. Doi: 10.2223/JPED.2153.

Saliakellis E, Fotoulaki M. Gastroparesis in children. *Ann Gastroenterol.* 2013;26(3):204-211. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3959432/.

Schol J, Wauters L, Dickman R, et al. ESNM Gastroparesis Consensus Group. United European Gastroenterology (UEG) and European Society for Neurogastroenterology and motility (ESNM) consensus on gastroparesis. *United European Gastroenterol J*. 2021;9(3):287-306. Doi: 10.1002/ueg2.12060.

Stein E, Berger Z, Hutfless S, et al. Wireless motility capsule versus other diagnostic technologies for evaluating gastroparesis and constipation: A comparative effectiveness review [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US). http://www.ncbi.nlm.nih.gov/books/NBK143974/. Published May 2013.

U.S. Food and Drug Administration. SmartPill GI monitoring system, version 2.0. 510(k) premarket approval letter. K092342. http://www.accessdata.fda.gov/cdrh_docs/pdf9/K092342.pdf. Published January 10, 2017.

Usai-Satta P, Bellini M, Morelli O, Geri F, Lai M, Bassotti G. Gastroparesis: New insights into an old disease. *World J Gastroenterol*. 2020;26(19):2333-2348. Doi: 10.3748/wjg.v26.i19.2333.

Vijayvargiya P, Camilleri M, Chedid V, Mandawat A, Erwin A, Murad MH. Effects of promotility agents on gastric emptying and symptoms: A systematic review and meta-analysis. *Gastroenterology*. 2019;156(6):1650-1660. Doi: 10.1053/j.gastro.2019.01.249. (a)

Vijayvargiya P, Sameie-Oskooei S, Camilleri M, Chedid V, Erwin PJ, Murad MH. Association between delayed gastric emptying and upper gastrointestinal symptoms: A systematic review and meta-analysis. *Gut*. 2019;68(5):804-813. Doi: 10.1136/gutjnl-2018-316405. (b)

Woodhouse S, Hebbard G, Knowles SR. Psychological controversies in gastroparesis: A systematic review. *World J Gastroenterol.* 2017;23(7):1298-1309. Doi: 10.3748/wjg.v23.i7.1298.

Ye Y, Jiang B, Manne S, et al. Epidemiology and outcomes of gastroparesis, as documented in general practice records, in the United Kingdom. *Gut*. 2021;70(4):644-653. Doi: 10.1136/gutnj-2020-321-277.

Policy updates

1/2018: initial review date and clinical policy effective date: 2/2018
3/2019: Policy references updated. Wireless motility capsule added and policy ID changed.
2/2020: Policy references updated. Policy coverage modified.
2/2021: Policy references updated.
2/2022: Policy references updated.
2/2023: Policy references updated.
2/2024: Policy references updated.

AmeriHealth Caritas Louisiana

Lung Transplants

Clinical Policy ID: CCP.1202

Recent review date: 11/2023

Next review date: 2/2025

Policy contains: Heart-lung transplant; lung transplant, pulmonary transplant.

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Lung transplantation is clinically proven and, therefore, may be medically necessary in cases of end-stage lung disease, when all of the following general selection criteria are met:

- A > 50% risk of death due to lung disease within two years if lung transplantation is not performed.
- A > 80% likelihood of five-year post-transplant survival from a general medical perspective provided there is adequate graft function.
- No absolute contraindications (See limitations) (Leard, 2021).

Heart-lung transplantation is clinically proven and, therefore, may be medically necessary for members with intrinsic lung disease or severe pulmonary artery hypertension and severe structural or cardiac dysfunction unlikely to improve with normalization of pulmonary pressures (Bermudez, 2021; Leard, 2021).

Limitations

The transplanting institution may require additional general selection criteria or disease-specific criteria for medical necessity determination.
Absolute contradictions to lung transplantation include (Leard, 2021):

- Lack of patient willingness or acceptance of transplant.

- Malignancy with high risk of recurrence or death related to cancer.
- Glomerular filtration rate < 40 mL/min/1.73m^2 unless being considered for multi-organ transplant.
- Acute coronary syndrome or myocardial infarction within 30 days (excluding demand ischemia).
- Stroke within 30 days.
- Liver cirrhosis with portal hypertension or synthetic dysfunction unless being considered for multi-organ transplant.
- Acute liver failure.
- Acute renal failure with rising creatinine or on dialysis and low likelihood of recovery.
- Septic shock.
- Active extrapulmonary or disseminated infection.
- Active tuberculosis infection.
- Human immunodeficiency virus infection with detectable viral load.
- Limited functional status (e.g., non-ambulatory) with poor potential for post-transplant rehabilitation.
- Progressive cognitive impairment.
- Repeated episodes of non-adherence without evidence of improvement (Note: This is not an absolute contraindication for pediatric members. Ongoing assessment of non-adherence should occur as they progress through different developmental stages.)
- Active substance use or dependence including current tobacco use, vaping, marijuana smoking, or intravenous drug use.
- Other severe uncontrolled medical conditions expected to limit survival after transplant.

Relative contraindications are listed in the Appendix.

Alternative covered services

Guideline-directed maximum medical management of underlying disease.

Background

Lung transplantation, or pulmonary transplantation, is a surgical procedure in which a patient's diseased lung(s) are partially or totally replaced by healthy lungs from a donor. Donor lungs can be retrieved from a living donor or a deceased donor. A living donor can only donate one lung lobe. With some lung diseases, a recipient may only need to receive a single lung. With other lung diseases, such as cystic fibrosis, it is imperative that a recipient receive two lungs. While lung transplants carry certain associated risks, such as life-threatening complications and infections, especially in the first year after surgery, they can also extend life expectancy and enhance the quality of life for patients with end-stage pulmonary disease (U.S. National Heart, Lung, and Blood Institute, 2022).

The number of Americans undergoing a lung transplant was 2,562 in 2018, an increase of 31% from five years earlier (Valapour, 2020). As of August 23, 2022, 1,011 registered Americans were awaiting a lung transplant, plus an additional 36 for heart/lung transplants (U.S. Health Resources and Services Administration, 2023b).

The United Network for Organ Sharing maintains a national U.S. registry for organ matching. Its purposes are to operate and monitor a system for allocation of organs donated for transplantation, maintain a waiting list of potential recipients, and match potential recipients with organ donors according to established medical criteria (U.S. Health Resources and Services Administration, 2023a). Over time, the system for lung allocation has evolved to increase the availability of organs for transplant and their success through better donor matching.

The expanding waiting list for lung transplants prompted a 2005 change in the United States to assign priority to candidates based on a greater predicted survival benefit from transplantation and waitlist urgency, calculated as the Lung Allocation Score, instead of waiting time. These changes impacted patients aged 12 years and older. Subsequent changes included exceptions for younger patients and geographic distribution. On December 6, 2021, the Continuous Distribution system was approved to replace the Lung Allocation Scoring system and is anticipated to take effect early in 2023 (Benvenuto, 2021).

A deceased donor, also known as cadaveric donor, is the most common donor source used for lung transplantation. Use of a live donor as a source for lung transplantation was initiated in 1993 due to the higher demand than supply for patients waiting for lung transplantation. Deceased donor transplantation is preferred, and the proportion of transplants from live donors is falling due to the change in allocating lungs from deceased donors (Date, 2017). In 2022, there were 1,918 deceased donor lungs and no living donor lungs transplanted in U.S. recipients (U.S. Health Resources and Services Administration, 2023c).

Findings

A number of guidelines affecting lung transplants have been published. The definitive work addressing criteria on selecting lung transplant patients, and contraindications against performing surgery, were written by the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation, which published versions in 1998, 2006, and 2015 (Weill, 2015, 2018). The same group of international experts that wrote the 2006 guidelines recently developed a consensus opinion on timing of referral and listing for lung transplantation. The panel included lung allocation scores and expanded indications for and contraindications to lung transplant (Weill, 2015).

In 2021, the International Society for Heart and Lung Transplantation updated its consensus guidance on selection of lung transplant candidates (Leard, 2021). This guidance differs from prior versions by creating categories for risk factors, considering the candidate as a whole and the risk tolerance and expertise of transplant centers. They stressed optimizing all potentially modifiable risk factors prior to lung transplant to improve long-term outcomes.

Two consensus papers from the International Society for Heart and Lung Transplantation provide additional guidance on cardiothoracic transplantation in patients with connective tissue disease (Bermudez, 2021; Crespo, 2021). Patients with connective tissue disease and advanced lung disease are

medically complex and often regarded as poor surgical risks, but research demonstrates comparable survival and allograft dysfunction outcomes for carefully selected patients undergoing lung transplantation for other indications.

The Society defined the disease states considered connective tissue diseases and described their unique extrapulmonary manifestations that require special management before, during, and after lung or heart-lung transplantation. They recommend considering lung transplantation. Finally, they listed absolute and relative contraindications for several connective tissue diseases to improve risk stratification and selection of candidates for lung transplantation based on consensus, recognizing the paucity of evidence on specific predictors of prognosis after cardiothoracic transplantation in this population (Crespo, 2021).

Bilateral lung transplantation is generally preferred over single lung transplantation for its theoretical survival and functional advantages over time, but single lung transplantation can be offered in the absence of secondary pulmonary hypertension when the clinical condition requires a shorter time on the waiting list. Heart-lung transplantation is reserved for patients with intrinsic lung disease or severe pulmonary artery hypertension and severe structural or cardiac dysfunction unlikely to improve with normalization of pulmonary pressures. Patients with moderate/severe left ventricular dysfunction or profound right ventricular dilation and dysfunction on high doses of inotropic support should be considered at high risk for lung transplantation alone (Bermudez, 2021).

Lung re-transplants are now being performed in increasing numbers. The median survival rate for those with re-transplants is lower than that of transplants (2.6 years versus 5.6 years), and the five-year survival rate is lower as well, at 34.5% versus 53.3%. Lower survival was associated with single lung transplants (P = .021), transplantations done between 2009 and 2013 (P = .041), multiple retransplantations (P = .023), and recipients requiring pre-transplantation ventilator support. Careful selection of candidates for re-transplant is advised (Thomas, 2015).

A systematic review/meta-analysis of 54 studies of over 5,000 subjects determined that *B. cepacia complex* significantly increased the risk of mortality after lung transplantation. Other factors that did not affect mortality included *P. aeruginosa* colonization, forced expiratory volume in one second, pulmonary hypertension, body mass index, pancreatic insufficiency, and cystic fibrosis-related diabetes (Koutsokera, 2019).

One study of 8,778 lung transplant patients showed a significantly lower survival (P < .001) for single lung transplants. Nearly 92% of the patients had a lung allocation score over 75, representing patients more likely to benefit from a lung transplant (Black, 2014). A study of 580 Canadian lung transplant patients with cystic fibrosis found the five- and 10-year survival rates to be 67% and 50%, with significantly higher death rates for young and old patients, plus those with pancreatic sufficiency or *B. cepacia* infection (Stephenson, 2015).

A systematic review/meta-analysis of 30 studies (n = 4,092) concluded that bilateral (versus unilateral) lung transplants had better long-term survival, better postoperative lung function and less bronchiolitis obliterans syndrome. No differences existed for in-hospital mortality and postoperative complications (Yu, 2019).
Another systematic review of 5,601 lung transplant recipients showed a clear pattern of greater survival among double transplant patients, namely 57% versus 50% after five years, 35.3% versus 27.8% after 10 years, and 24% versus 13.9% after 15 years (Wilson-Smith, 2020).

An exception to the pattern of lower mortality for double lung transplants was found in a recent systematic review/meta-analysis of 16 studies (n = 17,872) that addressed outcomes of lung transplant patients with idiopathic pulmonary fibrosis. Those with single transplants had a lower post-treatment percentage of Forced Exhaled Volume in one second than those with double transplants ($P < .001$). Survival outcomes were not significantly different at $P < .39$, but after single transplants, significantly fewer deaths were due to primary graft dysfunction and more due to malignancy, both $P < .001$ (Li, 2020).

A systematic review of six studies (n = 1,305) showed enhancement in quality of life for lung transplant candidates in five of the studies, using the SF-36 questionnaire and the six-minute walk test (Hoffman, 2017). A large systematic review of 73 studies showed that quality of life after lung transplants is enhanced, especially during the first year after the procedure in physical health and functioning domains, and may improve more after bilateral transplants and heart and liver transplants than after single lung transplants (Singer, 2013).

Some studies have identified factors that increase the risk of mortality in lung transplant patients. A review of 13 cohort studies (n = 40,742) reviewed weight at surgery and found significantly elevated relative risks compared to normal weight for underweight (1.36), obese (1.90), and overweight plus underweight (1.36) (Upala, 2016). Clinical risk factors were identified in 13 studies (n = 10,042) of primary graft dysfunction; the main causes of elevated morbidity and mortality include female gender, African American race, idiopathic pulmonary fibrosis, sarcoidosis, primary pulmonary hypertension, elevated body mass index, and use of cardiopulmonary bypass (Liu, 2014).

Non-adherence to medical regimens after transplants was the focus of a systematic review. While non-adherence rates varied across risk factors, they were not a significant factor in mortality (Hu, 2017).

Lung transplantations from deceased donors remain a minority of all such procedures; one meta-analysis of nine studies (n = 301) compared the mortality of patients who received a graft from deceased and live (conventional) donors. One year survival ranged from 50% to 100% among transplants from deceased donors, compared to 72% to 88% from live donors. One of the studies included nearly half of the transplants (138 of 301); one-year survival was significantly lower among deceased donor transplants (65.1% versus 84.1% for live donor transplants, $P < .001$) (Eberlein, 2017).

A comparison of lungs transplanted after > 12 hours ex-vivo preservation by splitting one cold ischemic time into two shorter ones (n = 97, average 875.7 minutes) with lungs transplanted with single waits < 12 hours (n = 809, average 400.8 minutes) was made. Median length of stay for both hospital and intensive-care unit lengths of stay did not differ significantly between groups (23.0 days versus 25.5 days, $P = .60$, and 4.0 days versus 4.0 days, $P = .53$). Primary graft dysfunction grade was not significantly different between the groups 72 hours after transplantation ($P = .85$), and there was no significant difference in survival ($P = .61$) (Yeung, 2017).

A systematic review of 13 studies found the ability of cardiopulmonary exercise testing to assist in making decisions in optimal timing for lung transplantation was limited due to problems of retrospective studies, patient selection, insufficient adjustment for confounders, and inadequate statistical analyses (Barratt, 2020).

An analysis of 65,265 lung transplant patients (median age 50.3 years) followed an average of 5.2 years found 17.3% died of cancer after surgery, a rate 4.28-fold higher than the general population. The most common types of malignancies causing death were lymphatic/hematological, integumentary, respiratory, digestive, and reproductive/urinary. Use of immunosuppressive therapy contributed in part to high rates. Authors state findings can improve individualized guidance for transplant patients (Ge, 2020).

In 2022, we added three updated consensus statements (Bermudez, 2021; Crespo, 2021; Leard, 2021), described earlier, and three new systematic reviews and meta-analyses. A meta-analysis of 72 eligible studies found no donor variables and only post-transplantation need for extra-corporeal membrane oxygenation that predicted one-year mortality with high certainty (hazard ratio 1.91, 95% confidence interval 1.79 to 2.04) in adult recipients. The authors stated lack of prognostic significance for some widely accepted factors (e.g., donor smoking, age) may relate to limits in the range of these variables found in selected donors and recipients (Foroutan, 2022).

A systematic review of 27 low-quality studies found 95% early survival rates in recipients with end-stage lung disease from COVID-19 infection. The data suggest bilateral lung transplantation is an effective option with reasonable short-term outcomes for these patients (Hawkins, 2021).

A systematic review of 51 prospective studies examined primary or secondary patient-important outcomes. The outcomes considered were mortality, pain, physical function, pulmonary, gastrointestinal, neuropsychological, cardiac, sleep or sexual symptoms, and quality of life. Mortality was the most frequently reported patient-important outcome (29.4% of studies), and quality of life was studied in 12%. The authors concluded outcomes other than mortality were insufficiently considered in lung transplantation studies.

We updated the references and modified the coverage based on new guidance and added an appendix of risk factor considerations from an updated consensus statement by the International Society for Heart and Lung Transplantation (Leard, 2021).

In 2023, we added four systematic reviews and meta-analyses to the policy with no policy changes warranted.

Two analyses provided mixed results regarding the outcomes of coronary revascularization performed before or during lung transplantation. In one analysis of 12 studies, the pooled mortality rates at one, three, and five years suggested significantly inferior survival in recipients with a prior history of coronary artery bypass grafting ($P < .00001$, $P = .0003$, $P = .008$, respectively) (Fialka, 2022). Another analysis of seven studies found no difference in mortality at one, three, and five years (overall hazard ratio = 1.02, 95% confidence interval = 0.80 to 1.31, $P = .99$) or hospital length of stay (standardized mean difference = 0.32, 95% confidence interval = -0.91 to 1.55) among participants who underwent lung transplantation with or without concomitant cardiac surgery. The group undergoing concomitant surgery experienced higher postoperative complication rates (Meng, 2022). For lung transplantation candidates who present with coronary artery disease, the optimum revascularization strategy has not been determined. Coronary artery disease should be regarded as a relative, not absolute, contraindication.

Two systematic reviews provide evidence of improved health-related quality of life outcomes following lung transplantation. In participants with advanced-stage cystic fibrosis, one systematic review of ten generally low-quality studies (n = 1,494) found lung transplantation improved health-related quality of

life for up to five years, and to levels comparable to the general population and non-waitlisted candidates, even as medical management continues to evolve (Raguragavan, 2023a). The second analysis of ten studies (n = 1,916) found bilateral lung transplantation recipients reported significantly greater scores in both the physical and mental health domains of health-related quality of life beyond one-year post-lung transplantation, and recipients maintained these gains over the long-term compared to single lung transplantation recipients (Raguragavan, 2023b).

References

On August 24, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "lung transplantation (MeSH)," "heart lung transplantation (MeSH)," "lung transplantation," and "pulmonary arterial hypertension." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Barratt SL, Davis R, Sharp C, Pauling JD. The prognostic value of cardiopulmonary exercise testing in interstitial lung disease: A systematic review. *ERJ Open Res*. 2020;6(3):00027-2020. Doi: 10.1183/23120541.00027-2020.

Benvenuto LJ, Arcasoy SM. The new allocation era and policy. *J Thorac Dis*. 2021;13(11):6504-6513. Doi: 10.21037/jtd-2021-17.

Bermudez CA, Crespo MM, Shlobin OA, et al. ISHLT consensus document on lung transplantation in patients with connective tissue disease: Part II: Cardiac, surgical, perioperative, operative, and post-operative challenges and management statements. *J Heart Lung Transplant*. 2021;40(11):1267-1278. Doi: 10.1016/j.healun.2021.07.016.

Black MC, Trivedi J, Schumer EM, et al. Double lung transplants have significantly improved survival compared with single lung transplants in high lung allocation score patients. *Ann Thorac Surg*. 2014;98(5):1737-1741. Doi: 10.1016/j.athoracsur.2014.05.072.

Crespo MM, Lease ED, Sole A, et al. ISHLT consensus document on lung transplantation in patients with connective tissue disease: Part i: Epidemiology, assessment of extrapulmonary conditions, candidate evaluation, selection criteria, and pathology statements. *J Heart Lung Transplant*. 2021;40(11):1251-1266. Doi: 10.1016/j.healun.2021.07.014.

Date H. Living-related lung transplantation. *J Thorac Dis*. 2017;9(9):3362-3371. Doi: 10.21037/jtd.2017.08.152.

Eberlein M, Reed RM, Chahla M, et al. Lobar lung transplantation from deceased donors: A systematic review. *World J Transplant*. 2017;7(1):70-80. Doi: 10.5500/wjt.v7.i1.70.

Fialka NM, Bozso SJ, El-Andari R, et al. A systematic review and meta-analysis of coronary artery disease and revascularization in lung transplant patients. *Coron Artery Dis*. 2022;33(8):661-669. Doi: 10.1097/mca.0000000000001153.

Foroutan F, Malik A, Clark KE, et al. Predictors of 1-year mortality after adult lung transplantation: Systematic review and meta-analyses. *J Heart Lung Transplant*. 2022;41(7):937-951. Doi: 10.1016/j.healun.2022.03.017.

Ge F, Li C, Xu X, et al. Cancer risk in heart or lung transplant recipients: A comprehensive analysis of 21 prospective cohorts. *Cancer Med*. 2020;9(24):9595-9610. Doi: 10.1002/cam4.3525.

Hawkins RB, Mehaffey JH, Charles EJ, Mannem HC, Roeser M. Lung transplantation for severe post-coronavirus disease 2019 respiratory failure. *Transplantation*. 2021;105(6):1381-1387. Doi: 10.1097/tp.0000000000003706.

Hoffman M, Chaves G, Ribeiro-Samora GA, Britto RR, Parreira VF. Effects of pulmonary rehabilitation in lung transplant candidates: A systematic review. *BMJ Open*. 2017;7(2):e013445. Doi: 10.1136/bmjopen-2016-013445.

Hu L, Lingler JH, Sereika SM, et al. Nonadherence to the medical regimen after lung transplantation: A systematic review. *Heart Lung*. 2017;46(3):178-186. Doi: 10.1016/j.hrtlng.2017.01.006.

Koutsokera A, Varughese RA, Sykes J, et al. Pre-transplant factors associated with mortality after lung transplantation in cystic fibrosis: A systematic review and meta-analysis. *J Cyst Fibros*. 2019;18(3):407-415. Doi: 10.1016/j.jcf.2018.10.013.

Leard LE, Holm AM, Valapour M, et al. Consensus document for the selection of lung transplant candidates: An update from the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant*. 2021;40(11):1349-1379. Doi: 10.1016/j.healun.2021.07.005.

Li D, Liu Y, Wang B, et al. Single versus bilateral lung transplantation in idiopathic pulmonary fibrosis: A systematic review and meta-analysis. *PLoS One*. 2020;15(5):e0233732. Doi: 10.1371/journal.pone.0233732.

Liu Y, Liu Y, Su L, Jiang SJ. Recipient-related clinical risk factors for primary graft dysfunction after lung transplantation: A systematic review and meta-analysis. *PLoS One*. 2014;9(3):e92773. Doi: 10.1371/journal.pone.0092773.

Meng E, Jiang SM, Servito T, Payne D, El-Diasty M. Lung transplantation and concomitant cardiac surgical procedures: A systematic review and meta-analysis. *J Card Surg*. 2022;37(10):3342-3352. Doi: 10.1111/jocs.16740.

Raguragavan A, Jayabalan D, Saxena A. Health-related quality of life following lung transplantation for cystic fibrosis: A systematic review. *Clinics (Sao Paulo)*. 2023;78:100182. Doi: 10.1016/j.clinsp.2023.100182. (a)

Raguragavan A, Jayabalan D, Saxena A. Health-related quality of life outcomes following single or bilateral lung transplantation: A systematic review. *Transplantation*. 2023;107(4):838-848. Doi: 10.1097/tp.0000000000004385. (b)

Singer J, Chen J, Blanc PD, Leard LE, Kukreja J, Chen H. A thematic analysis of quality of life in lung transplant: The

existing evidence and implications for future directions. *Am J Transplant*. 2013;13(4):839-850. Doi: 10.1111/ajt.12174.

Stephenson AL, Sykes J, Berthiaume Y, et al. Clinical and demographic factors associated with post–lung transplantation survival in individuals with cystic fibrosis. *J Heart Lung Transplant*. 2015;34(9):1139-1145. Doi: 10.1016/j.healun.2015.05.003.

Thomas M, Belli EV, Rawal B, Agnew RC, Landolfo KP. Survival after lung retransplantation in the United States in the current era (2004 to 2013): Better or worse? *Ann Thorac Surg*. 2015;100(2):452-457. Doi: 10.1016/j.athoracsur.2015.04.036.

U.S. Health Resources and Services Administration. Organ Procurement and Registration Network. About. https://optn.transplant.hrsa.gov/about/. Published August 25, 2023.(a)

U.S. Health Resources and Services Administration. Organ Procurement and Registration Network, United Network for Organ Sharing. National database searched on August 25, 2023 for current waiting list candidates by organ https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/#. Database updated August 24, 2023.(b)

U.S. Health Resources and Services Administration. Organ Procurement and Registration Network, United Network for Organ Sharing. National database searched on August 25, 2023 for donors recovered in the United States by donor type for lung. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data/. Database updated August 24, 2023.(c)

U.S. National Heart, Lung, and Blood Institute. Lung transplant. https://www.nhlbi.nih.gov/health/health-topics/topics/lungtxp. Published March 24, 2022.

Upala S, Panichsillapakit T, Wijarnpreecha K, Jaruvongvanich V, Sanquankeo A. Underweight and obesity increase the risk of mortality after lung transplantation: A systematic review and meta-analysis. *Transpl Int*. 2016;29(3):285-296. Doi: 10.1111/tri.12721.

Valapour M, Lehr CJ, Skeans MA, et al. OPTN/SRTR 2018 annual data report: Lung. *Am J Transplant*. 2020;20 Suppl s1:427-508. Doi: 10.1111/ajt.15677.

Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014--an update from the Pulmonary Transplantation Council of the International Society for Heart and Lung Transplantation *J Heart Lung Transplant.* 2015;34(1):1-15. Doi: 10.1016/j.healun.2014.06.014.

Weill D. Lung transplantation: Indications and contraindications. *J Thorac Dis*. 2018;10(7):4574-4587. Doi: 10.21037/jtd.2018.06.141.

Wilson-Smith AR, Kim YS, Evans GE, Yan TD. Single versus double lung transplantation for fibrotic disease – systematic review. *Ann Cardiothorac Surg*. 2020;9(1):10-19. Doi: 10.21037/acs.2019.12.04.

Yeung JC, Krueger T, Yasufuku K, et al. Outcomes after transplantation of lungs preserved for more than 12 h: A retrospective study. *Lancet Respir Med*. 2017;5(2):119-124. Doi: 10.1016/S2213-2600(16)30323-X.

Yu H, Bian T, Yu Z, et al. Bilateral lung transplantation provides better long-term survival and pulmonary function than single lung transplantation: A systematic review and meta-analysis. *Transplantation*. 2019;103(12):2634-2644. Doi: 10.1097/TP.0000000000002841.

Policy updates

10/2015: initial review date and clinical policy effective date: 1/2016
10/2016: Policy references updated.
10/2017: Policy references updated.
10/2018: Policy references updated.
10/2019: Policy references updated. Policy ID changed to CCP.1202.
10/2020: Policy references updated.
11/2021: Policy references updated.
11/2022: Policy references updated. Coverage modified.
11/2023: Policy references updated.

Appendix

Table 1. International Society for Heart and Lung Transplantation factors associated with high or substantially increased risk.
Members with these conditions may be considered in centers with expertise specific to the condition. There may be insufficient data supporting transplantation in members with these risk factors, or currently available data suggest substantially increased risk, and further research is needed to better inform future recommendations. Presence of more than one of these risk factors may be multiplicative in terms of increasing risk of adverse outcomes. Modifiable conditions should be optimized when possible.

1. Age > 70 years.
2. Severe coronary artery disease that requires coronary artery bypass grafting at transplant.
3. Reduced left ventricular ejection fraction < 40%.
4. Significant cerebrovascular disease.
5. Severe esophageal dysmotility.
6. Untreatable hematologic disorders including bleeding diathesis, thrombophilia, or severe bone marrow dysfunction.
7. Body mass index > 35 kg/m^2.
8. Body mass index < 16 kg/m^2.
9. Limited functional status with potential for post-transplant rehabilitation.
10. Psychiatric, psychological, or cognitive conditions with potential to interfere with medical adherence without sufficient support systems.
11. Unreliable support system or caregiving plan.
12. Lack of understanding of disease and / or transplant despite teaching.
13. *Mycobacterium abscessus* infection.
14. *Lomentospora prolificans* infection.

15. *Burkholderia cenocepacia or gladioli* infection.
16. Hepatitis B or C infection with detectable viral load and liver fibrosis.
17. Chest wall or spinal deformity expected to cause restriction after transplant.
18. Extracorporeal life support.
19. Retransplant < one year following initial lung transplant.
20. Retransplant for restrictive chronic lung allograft dysfunction.
21. Retransplant for antibody mediated rejection as etiology for chronic lung allograft dysfunction.

Source: Leard (2021).

Table 2. Additional International Society for Heart and Lung Transplantation risk factors.
These risk factors have unfavorable implications for short- or long-term outcomes after lung transplantation. While members with these risk factors may be acceptable for lung transplantation programs to consider, multiple risk factors together may increase risk for adverse lung transplant outcomes.

1. Age 65-70 years.
2. Glomerular filtration rate 40-60 mL/min/1.73m^2.
3. Mild to moderate coronary artery disease.
4. Severe coronary artery disease that can be revascularized via percutaneous coronary intervention prior to transplant.
5. Member with prior coronary artery bypass grafting.
6. Reduced left ventricular ejection fraction 40-50%.
7. Peripheral vascular disease.
8. Connective tissue diseases (scleroderma, lupus, inflammatory myopathies).
9. Severe gastroesophageal reflux disease.
10. Esophageal dysmotility.
11. Thrombocytopenia, leukopenia, or anemia with high likelihood of persistence after transplant.
12. Osteoporosis.
13. Body mass index 30-34.9 kg/m^2.
14. Body mass index 16-17 kg/m^2.
15. Frailty.
16. Hypoalbuminemia.
17. Poorly controlled diabetes.
18. Edible marijuana use.

19. *Scedosporium apiospermum* infection.

20. Human immunodeficiency virus infection with undetectable viral load.

21. Previous thoracic surgery.

22. Prior pleurodesis.

23. Mechanical ventilation.

24. Retransplant > one year for obstructive chronic lung allograft dysfunction.

Source: Leard (2021).

Pancreas transplantation

Clinical Policy ID: CCP.1201

Recent review date: 3/2024

Next review date: 6/2025

Policy contains: Diabetes; islet cell; pancreas-kidney.

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Pancreas transplantation is clinically proven and, therefore, may be medically necessary in members with type 1 diabetes mellitus when the following criteria are met (Kidney Disease: Improving Global Outcomes Transplant Work Group, 2009; Paty, 2013; Sung, 2015):

- For simultaneous pancreas–kidney transplantation using deceased donor pancreas and kidney or deceased donor pancreas and live donor kidney, members must meet all the criteria for kidney transplantation.
- For pancreas transplantation after a previous kidney transplantation (pancreas-after-kidney) in members with stable kidney graft function (creatinine clearance > 40 mL/min).
- For pancreas transplantation alone using deceased donor whole organ in members who meet all of the following criteria:
    - Diagnosis of type 1 diabetes mellitus and one of the following:
        - Be beta cell autoantibody-positive.
        - Demonstrate insulinopenia, defined as a fasting C-peptide level of ≤ 110% of the lower limit of normal of the laboratory's measurement method. Fasting C-peptide levels will only be considered valid with a concurrently obtained fasting glucose of ≤ 225 mg/dL.

- A history of severely disabling and potentially life-threatening complications due to hypoglycemia unawareness and persistent labile diabetes despite optimal medical management.
- Optimally and intensively managed by an endocrinologist for at least 12 months with the most medically recognized advanced insulin formulations and delivery systems.
- Satisfactory kidney function (creatinine clearance > 40 mL/min).
- Adequate cardiac status (e.g., no angiographic evidence of significant coronary artery disease, ejection fraction ≥ 40, no myocardial infarction in the last six months or negative stress test).
- Documentation of compliance with medical management.
- An acceptable psychosocial risk for transplantation surgery and the lifelong need for immunosuppression.
- Otherwise a suitable candidate for transplantation.

Pancreas transplantation in members with type 2 diabetes mellitus is clinically proven and, therefore, may be medically necessary when all of the following criteria are met (Weems, 2014):

- Simultaneous pancreas–kidney transplantation using deceased donor pancreas and kidney or deceased donor pancreas and live donor kidney is performed.
- Body mass index less than 30 kg/m^2.
- Insulin dependence.
- Low total insulin requirements (< 1 U/kg of ideal body weight per day).
- Imminent or established renal failure (dialysis dependent or pre-dialysis advanced diabetic nephropathy with glomerular filtration rate ≤ 20 mL/min/1.73 m^2).
- Fasting C-peptide less than 10 ng/mL.
- Low cardiac and vascular disease risk.
- History of medical and dietary compliance.

Pancreas re-transplantation is clinically proven and, therefore, may be medically necessary upon individual case review.

Autologous islet cell transplantation is clinically proven and, therefore, may be medically necessary to prevent postsurgical diabetes in patients with medically refractory chronic pancreatitis who require total pancreatectomy (American Diabetes Association, 2020a).

The following procedures are investigational/not clinically proven and, therefore, not medically necessary:

- Allogeneic islet cell transplantation (Speight, 2010).
- Autologous islet cell transplantation in persons with type 1 diabetes mellitus.

Limitations

Requests for pancreas transplantation in members with the following conditions require secondary review:

- Chronic liver disease.
- Clinical evidence of severe cerebrovascular or peripheral vascular disease (e.g., ischemic ulcers, previous amputation secondary to vascular disease). Adequate peripheral arterial supply should be determined by standard evaluation in the vascular laboratory, including Doppler examination and plethysmographic readings of systolic blood pressure.
- Past psychosocial abnormality.
- Body mass index ≥ 30 kg/m^2 but < 35 kg/m^2.

- Structural genitourinary abnormality or recurrent urinary tract infection.
- Substance use history (other than persistent substance use).
- Treated malignancy (simultaneous pancreas–kidney transplantation is considered medically necessary in persons with malignant neoplasm if the neoplasm has been adequately treated and the risk of recurrence is small).
- Uncontrolled hypertension.

Absolute contraindications to pancreas transplantation include, but are not limited to acquired immune deficiency syndrome diagnosis with CD4 count < 200 cells/mm^3 (Centers for Disease Control and Prevention, 2022) **unless** all of the following criteria are met:

- CD4 count greater than 200 cells/mm^3 for more than six months.
- Human immunodeficiency virus type 1 RNA undetectable.
- Consistent anti-retroviral therapy for more than three months.
- Absence of acquired immune deficiency syndrome complications (e.g., opportunistic infection, Kaposi's sarcoma, or other neoplasm).
- Criteria met for pancreas or pancreas–kidney transplantation.
- Active drug use and alcohol dependence.
- Active hepatitis or cirrhosis.
- Active or recent malignancy.
- Active peptic ulcer.
- Body mass index ≥ 35 kg/m^2 (bariatric surgery should be considered).
- Demonstrated patient non-adherence to medical recommendations (e.g., failure to comply with prescribed drug regimens).
- Ongoing or recurring infections that are not effectively treated.
- Potential complications from immunosuppressive medications unacceptable to the patient.
- Psychiatric disease that may compromise patient compliance.
- Serious cardiac or other ongoing insufficiencies that create an inability to tolerate surgery.
- Serious conditions unlikely to be improved by transplantation as life expectancy can be finitely measured.

All other uses of pancreas transplantation are not medically necessary.

Alternative covered services

- Exogenous insulin therapy.
- Hemodialysis.
- Peritoneal dialysis.

Background

The pancreas is an organ behind the stomach with digestive (exocrine) and hormonal (endocrine) functions. The digestive enzymes secreted by the exocrine (via ducts) portion help ~~to~~ break down protein, fats, carbohydrates, and acids ingested in the duodenum, and secretes bicarbonate to neutralize stomach acid. The endocrine gland portion (via bloodstream) secretes glucagon, insulin, and somatostatin to regulate release of insulin and glucagon needed for metabolism and other cellular functions. Diabetes develops as a result of a poorly functioning pancreas, or cells ~~to~~ not effectively using insulin, or both (Longnecker, 2021).

Every year about 80,000 people are diagnosed with chronic pancreatitis that can occur over several years and become life threatening. The debilitation from the disease results in frequent hospitalizations, increasing narcotic use for pain control, and a resultant decrease in quality of life. Islet cell transplant is critical for patients with immense pain who have failed other treatments. The autologous islet cell transplant procedure consists of extracting islet cells from the pancreas and reintroducing them into the patients liver via the portal vein where the cells continue to produce insulin to regulate glucose. This process removes the diseased organ's debilitating symptoms and creates a new pathway for the production of insulin, thus eliminating the risk of becoming a diabetic (PRWeb 2021).

The primary cause of pancreatic disease is type 1 diabetes mellitus, followed by type 2 diabetes mellitus, chronic pancreatitis, cancer, and cystic fibrosis (Kandaswamy, 2015). A pancreas transplantation provides an endogenous, self-regulated source to achieve physiologic insulin regulation without inducing adverse effects associated with administration of exogenous insulin. The goal of pancreas transplantation is to produce a lasting normoglycemic state that enhances quality of life. The procedure may involve the whole pancreas, a pancreas segment, a large group of pancreatic islet cells, or be in combination with a kidney transplant.

The U.S. Food and Drug Administration (2019) does not regulate the transplantation of human organs containing blood vessels, such as kidney, liver, heart, lung, or pancreas. However, it does regulate allogeneic islet cell transplantation as somatic cell therapy. Clinical studies to determine safety and effectiveness outcomes of allogeneic islet cell transplantation must be conducted under an investigational new drug regulation.

Findings

We identified two systematic reviews (Bramis, 2012; Speight, 2010), one survival analysis (Sung, 2015), one economic analysis (Wilson, 2015), and two evidence-based guidelines (Kidney Disease: Improving Global Outcomes Transplant Work Group, 2009; Paty, 2013) for this policy. The majority of the evidence assessed pancreas transplantation in persons with difficult-to-control type 1 diabetes mellitus in whom a kidney transplantation had been performed or was imminent. Transplantation techniques examined were pancreas transplantation alone, simultaneous pancreas–kidney transplantation, pancreas-after-kidney transplantation, and allogeneic islet cell. Pancreas transplantation using deceased or living donor organ, is associated with significant perioperative risks; as with other solid organ transplantations, contraindications are a large consideration that contribute to candidate selection and best outcomes. Increasing age has been a part of the exclusion criteria used when determining eligibility. While an upper age limit has not been established in the literature, a United Network for Organ Sharing database review of all adult pancreas alone and simultaneous pancreas–kidney transplantations between 1996 and 2012 found decreased patient and graft survival in patients of increasing age compared with patients younger than age 50 (Siskind, 2014).

Pancreas alone and pancreas/kidney transplants have one year and five year survival rates of 96% and 89% (NHS, 2020. There is sufficient evidence to support pancreas transplantation alone (deceased or living-donor segmental) in patients with type 1 diabetes mellitus and preserved renal function to correct severe metabolic complications. It has been performed mostly in patients with hypoglycemic unawareness or labile diabetes (including patients with frequent episodes of ketoacidosis) who have failed insulin-based management and may have incapacitating clinical or emotional problems with exogenous insulin therapy. Procedural success can eliminate the acute complications commonly experienced by individuals with type 1 diabetes mellitus, stabilize neuropathy, and improve quality of life primarily by eliminating the need for exogenous insulin, frequent daily blood glucose measurements, and many of the dietary restrictions imposed by the disorder.

Two Organ Procurement and Transplantation Network/United Network for Organ Sharing database analyses

underscore the importance of monitoring kidney function before and after pancreas transplantation alone. Kidney failure developed in approximately 10% of patients at five years' follow-up, and kidney transplantations were required (Nata, 2013). Kidney function before pancreas transplantation alone is a strong, independent predictor of end-stage renal disease (Kim, 2014).

A glycemic control comparison post pancreas transplant was performed by Andacoglu and colleagues (2019) in which both the type 1 and type 2 diabetic recipients at a high volume center were reviewed. Increased complication rates such as increased Basal metabolic index, higher short term insulin requirements, and transplant rejection occurred more frequently in the type 2 diabetic recipients than in the type 1. Graft survival was 95% and 82% for the type 1 and type 2 diabetics at the two year time frame although both remained statistically insignificant.

There is sufficient evidence to support the use of pancreas–kidney transplantation either simultaneously or sequentially in patients with uremia and type 1 diabetes mellitus who have been carefully selected. Successful transplantation does not jeopardize patient survival, may improve kidney survival, will restore normoglycemia and improves quality of life. As a single procedure, simultaneous pancreas–kidney transplantation offers the potential benefits of shorter waiting time, an expanded organ donor pool and improved short-term and long-term renal graft function. Regarding metabolic function, a selected group of type 2 diabetic recipients benefit from the simultaneous pancreatic-kidney transplant. For those who have a living kidney donor, pancreas-after-kidney is preferable to waiting years for a cadaver donor for a simultaneous procedure (Hau, 2020).

There is insufficient evidence to support the use of islet cell transplantation for treating type 1 diabetes mellitus. It holds significant potential advantages over whole-gland transplantation and for patients with benign prostatic disease (e.g., chronic pancreatitis), but its long-term survival has yet to be achieved. At this time, it is a rapidly evolving technology that also requires systemic immunosuppression and should be performed only within the setting of controlled research studies.

The rate of pancreas transplantation among individuals with type 2 diabetes mellitus has increased significantly. Currently 18.6% of persons with simultaneous transplants, 4.8% with kidney transplant after pancreas transplant, and 15.3% with pancreas transplant after kidney transplant have type 2 diabetes (Amara, 2022).

Yet, there remains an absence of unified and defined criteria for candidacy. Results from a small number of case series suggest five-year patient and graft survival after simultaneous pancreas–kidney transplantation is comparable between patients with type 1 diabetes mellitus and those with type 2 diabetes mellitus, but long-term outcomes are lacking. Simultaneous pancreas-kidney transplantation candidates with type 2 diabetes mellitus tend to be younger with a relatively lean body habitus and limited advanced diabetic cardiovascular disease. For potential candidates with type 2 diabetes mellitus, Weems (2014) proposed the following selection criteria for simultaneous pancreas–kidney transplantation:

- Younger than age 55 years.
- Body mass index less than 30 kg/m^2.
- Insulin dependence.
- Low total insulin requirements (< 1 U/kg of ideal body weight per day).
- Presence of renal failure (dialysis-dependent or pre-dialysis advanced diabetic nephropathy with glomerular filtration rate ≤ 20 $mL/min/1.73\ m^2$).
- Fasting C-peptide less than 10 ng/mL.
- Low cardiac and vascular disease risk.
- History of medical and dietary compliance.

Growing evidence suggests chronologic age alone should not exclude a patient for candidacy. One large case series

found that while complications may occur, older recipients (age 55 and older) of pancreas transplantation had comparable long-term patient and graft survival rates to those of younger recipients; additionally, type of organ transplantation did not correlate with patient survival in older patients (Scalea, 2016). Patient selection should be based on clinical criteria other than absolute age.

In 2018, we added an evidence-based guideline from the American Diabetes Association (2018) supporting autologous islet cell transplantation for patients requiring total pancreatectomy for medically refractory chronic pancreatitis to prevent postsurgical complete insulin and glucagon deficiency. This indication was added to the policy.

In 2019, we added no new information to the policy, removed three older systematic reviews, and made no policy changes. The policy ID was changed from CP# 08.02.06 to CCP.1201.

In 2020, we updated the American Diabetes Association Standards of Diabetes Care (2019). There continues to be interest in both allogenic and autologous islet cell transplantation as potential alternatives to whole-organ pancreas transplantation for restoring normoglycemia and reducing or eliminating long-term complications in people with type 1 diabetes. As both techniques continue to evolve, the impact on net health outcomes remains uncertain, although longer term data are beginning to emerge (Vantyghem, 2019a, 2019b). No policy changes are warranted at this time.

In 2021, we updated the references to the American Diabetes Association Standards of Diabetes Care (2020a, 2020b, updates of 2019a, 2019b) and deleted two older references. We added three large cohort studies that confirm earlier findings of a long-term graft and individual survival benefit and improved metabolic outcomes after simultaneous pancreas-kidney transplantation among diabetic recipients (Esmeijer, 2020; Parajuli, 2020; Sucher, 2019). No policy changes are warranted.

In 2022, we included additional definition to the background, post-transplant data and updated the references. No policy changes are warranted.

In 2023, we included additional data, updated the references, confirmed the information contained is current and unchanged. No policy changes are warranted.

In 2024, we added a systematic review of 39 studies of pancreas transplantation in patients with type 2 diabetes. Studies found favorable outcomes in patient survival, graft survival, and glycemic control. Authors suggest better characterization of these patients would help predict who would benefit most from the procedure (Amara, 2022).

No policy changes are warranted.

References

On December 5, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “pancreas transplantation” “pancreas-kidney transplant” (MeSH) and “islets of Langerhans transplantation” ”end stage renal disease” (MeSH). We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Amara D, Hansen KS, Kupiec-Weglinski SA, et al. Pancreas transplantation for type 2 diabetes: A systematic review,

critical gaps in the literature, and a path forward. *Transplantation*. 2022;106(10):1916-1934. Doi: 10.1097/TP.0000000000004113.

American Diabetes Association. 4. Comprehensive medical evaluation and assessment of comorbidities: Standards of medical care in diabetes-2020. *Diabetes Care.* 2020;43(Suppl 1):S37-s47. Doi: 10.2337/dc20-S004.(a)

American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: Standards of medical care in diabetes-2020. *Diabetes Care.* 2020;43(Suppl 1):S98-s110. Doi: 10.2337/dc20-S009.(b)

Andacoglu OM, Himmler A, Geng X, Ahn J, Ghasemian S, Cooper M, Abrams P. Comparison of glycemic control after pancreas transplantation for type 1 and type 2 diabetic recipients at a high volume center. *Clin Transplant.* 2019;33(8):e13656. Doi: 10.1111/ctr.13656.

Bramis K, Gordon-Weeks AN, Friend PJ, et al. Systematic review of total pancreatectomy and islet autotransplantation for chronic pancreatitis. *Br J Surg.* 2012;99(6):761-766. Doi: 10.1002/bjs.8713.
Centers for Disease Control and Prevention. About HIV/AIDS. https://www.cdc.gov/hiv/basics/whatishiv.html. Reviewed June 30, 2022.

Esmeijer K, Hoogeveen EK, van den Boog PJM, et al. Superior long-term survival for simultaneous pancreas-kidney transplantation as renal replacement therapy: 30-year follow-up of a nationwide cohort. *Diabetes Care.* 2020;43(2):321-328. Doi: 10.2337/dc19-1580.

Hau HM, Jahn N, Brunotte M,et al. Short and long- term metabolic outcomes in patients with type 1 and type 2 diabetes receiving a simultaneous pancreas kidney allograft. *BMC Endocr Disord*. 2020;20(1):30. Doi: 10.1186/s12902-020-0506-9.

Kandaswamy R, Skeans MA, Gustafson SK, et al. OPTN/SRTR 2013 Annual Data Report: Pancreas. *Am J Transplant.* 2015;15 Suppl 2:1-20. Doi: 10.1111/ajt.13196.

Kidney Disease: Improving Global Outcomes Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant.* 2009;9 Suppl 3:S1-155. Doi: 10.1111/j.1600-6143.2009.02834.x.

Kim SJ, Smail N, Paraskevas S, et al. Kidney function before pancreas transplant alone predicts subsequent risk of end-stage renal disease. *Transplantation.* 2014;97(6):675-680. Doi: 10.1097/01.TP.0000437556.87109.45.

Longnecker DS. American Pancreatic Association. Anatomy and histology of the pancreas. *Pancreapedia: Exocrine pancreas knowledge base.* 2021. https://www.pancreapedia.org/reviews/anatomy-and-histology-of-pancreas. Doi: 10.3998/panc.2021.01.

Nata N, Huang E, Kamgar M, et al. Kidney failure requiring kidney transplantation after pancreas transplant alone. *Clin Transpl.* 2013:45-52. http://www.ncbi.nlm.nih.gov/pubmed/25095491. Published 2013.

NHS Blood and Transplant. Annual report on pancreas and islet transplantation: Report for 2019/2020 (1 April 2010-31 March 2020). https://nhsbtdbe.blob.core.windows.net/umbraco-assets-corp/19868/nhsbt-pancreas-and-islet-transplantation-annual-report-2019-2020.pdf. Published September 2020.

Parajuli S, Bath NM, Aziz F, et al. More than 25 years of pancreas graft survival after simultaneous pancreas and kidney transplantation: Experience from the world's largest series of long-term survivors. *Transplantation.* 2020;104(6):1287-1293. Doi: 10.1097/tp.0000000000002960.

Paty BW, Koh A, Senior P. Pancreas, and islet transplantation. *Can J Diabetes.* 2013;37 Suppl 1:S94-96. Doi:

10.1016/j.jcjd.2013.01.028.

PRWeb. AHN performs its first islet cell transplants to treat chronic pancreatitis: Advanced capability compliments network's unique islet cell isolation lab at AGH, making organization one of a select group across the country offering comprehensive care for debilitating condition. https://www.prweb.com/releases/ahn-performs-its-first-islet-cell-transplants-to-treat-chronic-pancreatitis-844118706.html. Published October 5, 2021.

Scalea JR, Redfield RR, 3rd, Arpali E, et al. Pancreas transplantation in older patients is safe, but patient selection is paramount. *Transpl Int.* 2016;29(7):810-818. Doi: 10.1111/tri.12754.

Siskind E, Maloney C, Akerman M, et al. An analysis of pancreas transplantation outcomes based on age groupings--an update of the UNOS database. *Clin transplant.* 2014;28(9):990-994. Doi: 10.1111/ctr.12407.

Speight J, Reaney MD, Woodcock AJ, Smith RM, Shaw JA. Patient-reported outcomes following islet cell or pancreas transplantation (alone or after kidney) in Type 1 diabetes: A systematic review. *Diabet Med.* 2010;27(7):812-822. Doi: 10.1111/j.1464-5491.2010.03029.x.

Sucher R, Rademacher S, Jahn N, et al. Effects of simultaneous pancreas-kidney transplantation and kidney transplantation alone on the outcome of peripheral vascular diseases. *BMC Nephrol.* 2019;20(1):453. Doi: 10.1186/s12882-019-1649-7.

Sung RS, Zhang M, Schaubel DE, et al. A Reassessment of the survival advantage of simultaneous kidney-pancreas versus kidney-alone transplantation. *Transplantation.* 2015;99(9):1900-1906. Doi: 10.1097/tp.0000000000000663.

U.S. Food and Drug Administration. Guidance for industry. Considerations for allogeneic pancreatic islet cell products.

Vantyghem MC, Chetboun M, Gmyr V, et al. Ten-year outcome of islet alone or islet after kidney transplantation in type 1 diabetes: A prospective parallel-arm cohort study. *Diabetes Care.* 2019;42(11):2042-2049. Doi: 10.2337/dc19-0401.

Vantyghem MC, de Koning EJP, Pattou F, Rickels MR. Advances in beta-cell replacement therapy for the treatment of type 1 diabetes. *Lancet.* 2019;394(10205):1274-1285. Doi: 10.1016/s0140-6736(19)31334-0.

Weems P, Cooper M. Pancreas transplantation in type II diabetes mellitus. *World Journal of Transplantation.* 2014;4(4):216-221. Doi: 10.5500/wjt.v4.i4.216.

Wilson GC, Ahmad SA, Schauer DP, Eckman MH, Abbott DE. Cost-effectiveness of total pancreatectomy and cell autotransplantation for the treatment of minimal change chronic pancreatitis. *J Gastrointestl Surg.* 2015;19(1):4654; discussion 54-45. Doi: 10.1007/s11605-014-2612-3.

Policy updates

10/2015: initial review date and clinical policy effective date: 3/2016
2/2017: Policy references updated.
2/2018: Policy references updated. Coverage expanded per American Diabetes Association (2018) guideline.
2/2019: Policy references updated. Policy ID changed.
2/2020: Policy references updated.

2/2021: Policy references updated.
2/2022: Policy references updated.
3/2023: Policy references updated.
3/2024: Policy references updated.

Phototherapy and photochemotherapy skin conditions

Clinical Policy ID: CCP.1169

Recent review date: 2/2024

Next review date: 5/2025

Policy contains: Photochemotherapy; phototherapy; psoralen ultraviolet A; psoriasis.

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Ultraviolet A phototherapy, ultraviolet B therapy, and photochemotherapy using psoralen ultraviolet A are clinically proven and, therefore, may be medically necessary for the following skin conditions after conventional therapies have failed Davis, 2023; Elmets, 2019; Ling, 2016; Menter, 2020; Olsen, 2016:

- Atopic dermatitis (eczema).
- Cutaneous T-cell lymphoma, including mycosis fungoides and Sézary syndrome.
- Dermatoses (other).
- Lichen planus.
- Psoriasis.

- Vitiligo.

Psoralen ultraviolet A home therapy is investigational/not clinically proven and, therefore, not medically necessary.

Ultraviolet B home phototherapy is clinically proven and, therefore, may be medically necessary when all of the following conditions are met (Davis, 2023; Elmets, 2019):

- The member is diagnosed with any of the conditions listed above.
- The member is unable to travel for office-based therapy.
- The condition is considered severe and extensive.
- Disease is refractory to conventional treatments for at least four months.
- The member requires treatment at least three times per week.

Ultraviolet B home phototherapy is investigational/not clinically proven and, therefore, not medically necessary for any of the following (Hum, 2019):

- When treatment is conducted at home for member convenience.
- When ultraviolet B therapy is used as first-line therapy.
- When ultraviolet B therapy is used for cosmetic purposes.
- For any treatment beyond a single course.
- For any condition other than those listed above.

Limitations

All other uses of psoralen ultraviolet A and narrowband ultraviolet B are investigational/not clinically proven, and therefore, not medically necessary.

Alternative covered services

Standard-of-care first-line treatments for skin conditions.

Background

Ultraviolet light — a cause of sunburns, wrinkles, and skin cancer — can be used in a medical setting as therapy for certain hard-to-treat skin problems and other medical conditions. Phototherapy is the controlled administration of non-ionizing radiation to the skin involving ultraviolet light. The main forms of phototherapy apply ultraviolet A (with or without a photosensitizing agent) and ultraviolet B (Rathod, 2023).

Psoralen ultraviolet A uses psoralens to sensitize target cells to the effects of ultraviolet A light at 320 to 400 nanometers in wavelength. Psoralen ultraviolet A treatment typically involves administration of an oral drug (e.g., methoxypsoralen) followed by exposure to ultraviolet A 45 to 60 minutes. Topical administration of psoralen ultraviolet A treatment include (Rathod, 2023):

- Bath psoralen ultraviolet A, in which the affected area is immersed in a basin of water containing 8-methoxypsoralen; it is rarely used in the United States.
- Application of 8-methoxypsoralen ointment or lotion directly to lesions on palms and plantar surfaces of the feet, followed by ultraviolet A exposure.

The original intent of psoralen ultraviolet A was treatment of psoriasis, a relatively common skin disorder. Other uses include conditions such as vitiligo and mycosis fungoides (the most common type of T-cell lymphoma). While topical medications often control mild psoriasis, severe cases often require treatments involving ultraviolet A light exposure (Cole, 2023).

There is the potential for psoralen ultraviolet A to increase the risk of skin cancer, especially when treating psoriasis. Persons at elevated risk for skin cancer from psoralen ultraviolet A include children and persons with a genetic predisposition, a history of skin cancer, or a history of at least 150 prior psoralen ultraviolet A treatments. Types of toxicity to psoralen ultraviolet A include erythema, pruritus, xerosis, irregular pigmentation, and gastrointestinal symptoms. Altering or dividing the dose can avoid most toxicity (Cole, 2023).

Oral psoralen ultraviolet A is contraindicated in patients younger than 10 years, pregnant patients, nursing mothers, and patients with a personal history of melanoma, lupus erythematosus, or xeroderma pigmentosa (Elmets, 2019). Caution should be exercised for: patients age 10 to 18 years; patients with skin types 1 and 2 who tend to burn easily; those with a history of dysplastic nevi, photosensitivity, melanoma or nonmelanoma skin cancer; or those with exposure to carcinogenic agents (e.g., arsenic intake or ionizing radiation) or immunosuppressive agents.

Available forms of ultraviolet B treatment are broadband, narrowband, and targeted applications. Broadband emits wavelengths ranging from 270 to 390 nanometers. Narrowband emits wavelengths ranging from 311 to 313 nanometers. Targeted ultraviolet B treatments may employ narrowband, excimer laser (308 nanometers), or excimer light (308 nanometers) (Elmets, 2019).

Narrowband ultraviolet B administered two to three times weekly has largely replaced broadband ultraviolet B as the technique of choice, although a small portion of persons with skin conditions who do not respond well to narrowband do respond to broadband. Narrowband ultraviolet B may be administered as monotherapy or in combination with oral or topical medications to increase efficacy. Targeted ultraviolet treatment options may be appropriate for localized lesions. Home narrowband ultraviolet B may offer a treatment alternative for patients with limited access to outpatient treatment (Elmets, 2019).

Narrowband ultraviolet B is contraindicated in patients with photosensitive disorders (e.g., xeroderma pigmentosa). It should be used cautiously in patients with a history of melanoma, multiple nonmelanoma skin cancers, arsenic intake, or exposure to ionizing radiation. Narrowband ultraviolet B is considered safe to use in pregnant patients and may be used cautiously in patients with lupus erythematosus who have no history of photosensitivity and are Ro(SSA)-negative (Elmets, 2019).

Findings

In general, phototherapy serves as a reasonable and effective treatment option for patients requiring more than topical medications, wishing to avoid systemic medications, or needing an adjunct to a failing regimen. Psoralen ultraviolet A or ultraviolet B therapy-related guidelines are often specific to a patient's condition:

- A practice guideline by the American Academy of Dermatology conditionally recommends phototherapy (primarily narrowband ultraviolet B), for adults with atopic dermatitis based on low certainty evidence of safety and efficacy; psoralen ultraviolet A is not recommended (Davis, 2023)
- A 2014 practice guideline by the American Academy of Dermatology on atopic dermatitis treatment recommended phototherapy as a second-line treatment if emollients, topical steroids, and calcineurin

inhibitors have failed, and that phototherapy may be considered for home use if patients are unable to receive the treatment in an office setting (Sidbury, 2014). Phototherapy can be used as maintenance therapy in patients with chronic disease.

- A National Institute for Health and Care Excellence (2012) guideline on psoriasis suggests offering narrowband ultraviolet B phototherapy to psoriasis patients whose condition cannot be controlled with topical treatments alone, but recommends not using any type of phototherapy as maintenance therapy.
- A review of guidelines for psoriasis concludes that narrowband ultraviolet B is an effective treatment option for psoriasis (Mehta, 2016).
- A guideline for topical eczema states corticosteroids are the first-line treatment, but adjuvant therapies can include ultraviolet B (311 nanometers) or ultraviolet A (Wollenberg, 2018a, 2018b).
- An American Academy of Dermatology (Menter, 2011) guideline on psoriasis observes that psoralen ultraviolet A is more effective than narrowband ultraviolet B for thick lesions, while narrowband ultraviolet B generally results in shorter time to remission.
- An American Academy of Dermatology guideline includes treatments for atopic dermatitis with phototherapy using ultrasound A and B (Eichenfeld, 2017).
- A 2012 guideline on alopecia areata from the British Association of Dermatologists recommends against psoralen ultraviolet A use due to potentially serious side effects and inadequate evidence of efficacy (Messenger, 2012).
- A 2016 guideline on mycosis fungoides and Sézary syndrome, for which ultraviolet light is often used, suggests a more refined guideline based on patient stage and centers, and in combination with other agents in practice and clinical trials (Olsen, 2016).
- A 2013 guideline recommends psoralen ultraviolet A as a second-line therapy (behind narrowband ultraviolet B) for vitiligo, along with psoralen ultraviolet A in various combination therapies for the disease (Taieb, 2013).

A 2016 guideline from the British Association of Dermatologists and British Photodermatology Group (Ling, 2016) states as follows, based on evidence in the professional literature:

- For psoriasis, narrowband ultraviolet B is the preferred treatment. Ultraviolet A is indicated for chronic plaque psoriasis and atopic eczema if ultraviolet B treatment is ineffective.
- For some indications, ultraviolet A is the first-line phototherapy — mycosis fungoides beyond patch stage, pustular psoriasis, pompholyx, hand and foot eczema, and adult generalized pityriasis rubra pilaris.
- For eczema, narrowband ultraviolet B is the first-line phototherapy.
- For cutaneous T-cell lymphoma, ultraviolet A is the first-line treatment. Ultraviolet B can be used in early stages of the disease.
- For vitiligo, narrowband ultraviolet B is at least as effective as psoralen ultraviolet A.
- For photodermatoses, ultraviolet A and B are equally effective, with safety concerns.
- For hand and foot dermatoses, ultraviolet A and B are equally effective.

<u>Reviews – phototherapy efficacy and safety</u>

Psoriasis

Psoriasis is the condition most studied for phototherapy outcomes. A systematic review of 10 trials of pediatric psoriasis cases showed narrowband ultraviolet B to be 80% effective (Kim, 2020). A systematic review of 35 studies found systemic treatment for psoriasis, including ultraviolet B phototherapy, reduced pruritus but did not reduce prevalence of lesions (Therene, 2018).

A systematic review of 29 articles (n = 675) of persons with palmoplantar pustular psoriasis found that phototherapy, cyclosporine, and topical corticosteroids each controlled palmoplantar pustular psoriasis, with psoralen ultraviolet A having greater efficacy than ultraviolet B therapy (Sevrain, 2014). Another meta-analysis of psoriasis (23 studies, n = 765) also found psoralen ultraviolet A to be more efficacious than non-larger targeted ultraviolet B phototherapy, although both treatments had positive outcomes (Almutawa, 2015). Psoralen ultraviolet A's superiority to narrowband ultraviolet B was also observed in a 2012 meta-analysis of 29 trials (n = 773) of chronic plaque psoriasis and accomplished these results in fewer sessions (Archier, 2012b).

A Cochrane review of 13 trials (n = 662) on psoriasis found the psoralen ultraviolet A/ultraviolet B comparison to be hampered by heterogeneous evidence, and could not make a definitive conclusion on which was more effective (Chen, 2013). Another systematic review of 41 trials (n = 2,416) found that psoralen ultraviolet A was more effective than narrowband ultraviolet B as a monotherapy, and narrowband ultraviolet B was more effective than broadband ultraviolet B and bath psoralen ultraviolet A in treating adults with moderate to severe psoriasis (Almutawa, 2013).

Risk of cancer from psoralen ultraviolet A was the focus of a systematic review of 41 studies of chronic plaque psoriasis. Risk was elevated for nonmelanoma skin cancer for squamous cell carcinomas, even at low exposures, with risk persisting after treatment cessation for basal cell carcinoma in participants receiving more than 100 psoralen ultraviolet A treatments and for melanoma in persons receiving more than 200 psoralen ultraviolet A treatments. Narrowband ultraviolet B use had no skin cancer risk (Archier, 2012a).

Atopic dermatitis

An analysis of 28 systematic reviews found reasonable evidence that ultraviolet B treatment is effective for atopic eczema (Solman, 2019). A systematic review of 22 studies with low risk of bias concluded that various treatments, including ultraviolet radiation, were effective treatments for eczema (Nankervis, 2017).

A systematic review of 21 randomized controlled trials including 961 participants determined that narrowband ultraviolet B and ultraviolet A1 phototherapy in moderate to severe atopic dermatitis were helpful, but data on psoralen ultraviolet A use and phototherapy in children are scarce (Perez-Ferriols, 2015). Another systematic review of 19 studies (n = 905) found that ultraviolet A1 and narrowband ultraviolet B were the most effective treatments for reducing signs and symptoms of atopic dermatitis (Garritsen, 2014).

Vitiligo

A meta-analysis of 38 studies of persons with vitiligo compared narrowband ultraviolet B phototherapy (n = 1,201) to psoralen ultraviolet A phototherapy (n = 227). The ultraviolet B group had more "at least mild" responses at six and 12 months after therapy (74.2% and 75.0%) than did the psoralen ultraviolet A group (51.4% and 61.6%). Marked responses were more common in the face and neck (44.2%) than in the trunk (26.1%) and the extremities (17.3%) after six months of ultraviolet B phototherapy (Bae, 2017).
A systematic review determined narrowband ultraviolet B had fewer side effects and was marginally better than psoralen ultraviolet A for vitiligo, and that (along with topical corticosteroids) it offered the greatest benefits of any vitiligo treatment (Whitton, 2016). A systematic review of seven studies (n = 232) comparing vitiligo treatment by psoralen ultraviolet A and narrowband ultraviolet B revealed no statistically significant difference between the two on the rate of participants who achieved more than 50% or more than 75% repigmentation (Xiao, 2015).

Mycosis fungoides/cutaneous T-cell lymphoma

Mycosis fungoides is the most common cutaneous T-cell lymphoma, and conventional therapy is not always effective in treating it. A review of 20 papers documented photodynamic therapy as a promising and well-

tolerated option for treating localized lesions, with excellent cosmetic outcomes (Xue, 2017). Psoralen ultraviolet A and narrowband ultraviolet B monotherapy were effective first-line interventions for mycosis fungoides; the effectiveness of psoralen ultraviolet A either as maintenance therapy or combined with drugs as first-line therapy is uncertain, but may be beneficial for relapse and late-stage disease (Dogra, 2015).

A systematic review/meta-analysis of seven studies (n = 778 participants with mycosis fungoides) compared 527 treated with psoralen ultraviolet A and 251 with narrowband ultraviolet B. The ultraviolet A group had superior outcomes in percent with any response (*P* = .20) and complete response (*P* = .04). The ultraviolet A group was superior in the percent with partial response (*P* = .07). Rates of adverse effects were similar (Phan, 2019).
A Cochrane review of 20 randomized controlled trials (n = 1,369) included five studies addressing psoralen ultraviolet , and found no evidence challenging the general consensus that it be used as first-line treatment for mycosis fungoides (Valipour, 2020).

Lichen planus

In a Cochrane review of 16 studies, 11 of which were randomized controlled trials, psoralen ultraviolet A treatment for cutaneous lichen planus had comparable outcomes to a psoralen ultraviolet A bath and narrowband ultraviolet B (Atzmony, 2016).

A review of 14 studies (n = 64) of pediatric participants with pityriasis lichenoides determined that broadband ultraviolet B, narrowband ultraviolet B, and psoralen ultraviolet A had initial clearance rates of 90%, 73%, and 83%, respectively, with recurrence rates of 23.1%, 0%, and 60%, respectively (Maranda, 2016).
An analysis of two systematic reviews and nine randomized controlled trials upheld the efficacy of narrowband ultraviolet B treatment for lichen planus (Fazel, 2015).

Reviews - home phototherapy efficacy and safety

Phototherapy is usually administered in an outpatient setting, but this treatment is also available for home use.
A multicenter randomized controlled trial (n = 196) concluded that home narrowband ultraviolet B delivered at practitioner-determined dosing schedules was as safe, effective, and cost-effective as outpatient treatment for mild to severe psoriasis, was more convenient, and generated higher satisfaction compared to outpatient treatment; data on patient adherence and adverse events were not reported (Koek, 2009; PLUTO study; ClinicalTrials.gov identifier NCT00150930).

A recent systematic review found no other randomized trials of narrowband ultraviolet B phototherapy home treatment and reached similar conclusions (Ontario Health [Quality], 2020). Other observational studies were heterogeneous with respect to types of ultraviolet light used, making comparisons across studies difficult, and double-blind or placebo-controlled trials were not available. The authors were uncertain about any potential differences in risk of adverse events between the two settings.

A Cochrane review failed to support or refute home-based phototherapy for non-hemolytic jaundice in infants over 37 weeks gestation (Malwade, 2014). A systematic review of 23 articles observed high levels of participant satisfaction, high levels of safety, and mostly positive reports of high quality of life after home phototherapy (Franken, 2016).

Several reviews identified criteria for selecting patients for home treatment who are candidates for office-based narrowband ultraviolet B phototherapy. Home phototherapy is feasible for many patients for whom office-based phototherapy is not accessible (e.g., patients who live far from a phototherapy center, are unable to travel because of extensive disease, or incur prohibitive travel). Treatment schedules generally vary based on skin condition, but Hum (2019) recommended narrowband ultraviolet B (311 nanometers), administered on alternating days, as a safe and effective treatment mode for home phototherapy.

In 2022, we removed four older reviews and added two updated guidelines from the American Academy of Dermatology and six new systematic reviews. The results are consistent with previous findings, and no policy changes are warranted.

For treating psoriasis in adults, the American Academy of Dermatology (Elmets, 2019) recommends:

- Narrowband ultraviolet B phototherapy or oral psoralens ultraviolet A over broadband ultraviolet B as monotherapy, but broadband ultraviolet B therapy may be used when narrowband ultraviolet B therapy is unavailable.
- Narrowband ultraviolet B monotherapy for patients with guttate psoriasis, regardless of age, consider broadband ultraviolet B monotherapy for adults with guttate psoriasis.
- Narrowband ultraviolet B phototherapy for pregnant women with generalized plaque psoriasis and guttate psoriasis.
- Topical psoralen ultraviolet A phototherapy over narrowband ultraviolet B phototherapy for localized plaque psoriasis, particularly for palmoplantar psoriasis and palmoplantar pustular psoriasis.
- Bath psoralen ultraviolet A for treatment of moderate to severe plaque psoriasis.
- Combination therapy for patients with generalized plaque psoriasis who do not respond adequately to monotherapy.
- Home narrowband ultraviolet B phototherapy for whom travel to an outpatient facility is a limiting factor.
- Guideline-directed maintenance phototherapy to maintain clinical response.

For treating psoriasis in pediatric populations, the American Academy of Dermatology recommends narrowband ultraviolet B phototherapy for moderate to severe pediatric plaque and guttate psoriasis (Menter, 2020). Excimer laser or psoralen ultraviolet A therapy may be efficacious and well-tolerated, but the supportive evidence for these options is limited.

Four new systematic reviews and meta-analyses examined the efficacy of phototherapy as monotherapy or combination therapy for repigmentation of vitiligo. The results suggest combination therapy using either narrowband-ultraviolet B phototherapy or excimer laser with tacrolimus (Chang, 2021), or narrowband ultraviolet B, psoralen ultraviolet A, or excimer laser with calciprotriol (Hu, 2021) may provide greater clinical improvement than phototherapy alone. The results supporting the superiority of narrowband ultraviolet B with or without fractional CO_2 laser are mixed, likely the result of heterogeneous selection criteria and treatment protocols (Chang, 2020; Kim, 2021).

A Cochrane review of phototherapy for atopic dermatitis (eczema) included 32 trials of 1,219 participants from secondary care dermatology clinics with a range severities who underwent any form of phototherapy (Musters, 2021). Low-certainty evidence supported all reported outcomes. The strongest evidence suggests that, compared to placebo or no treatment, narrowband ultraviolet B (13 trials) may improve physician-rated signs, patient-reported symptoms, and Investigator Global Assessment after 12 weeks, without a difference in withdrawal due to adverse events. Comparisons to other forms of phototherapy were inconclusive.

Another Cochrane review of 37 randomized controlled trials (n = 1,663) found insufficient evidence supporting the effectiveness of various interventions for chronic palmoplantar pustulosis, including ultraviolet A phototherapy (Obeid, 2020).

In 2023, we added several systematic reviews to the policy. The new information warrants no changes to the policy. Systematic reviews of randomized controlled trials confirmed previous policy findings that home-based phototherapy (Ashraf, 2022; Cohen, 2022) and phototherapy for psoriasis (Damiani, 2022; Li, 2022), vitiligo (Wu, 2022), and atopic dermatitis (Xiao, 2022) are safe and effective treatment options, although the optimal treatment

administration has not been determined.

New indications for phototherapy and photochemotherapy are emerging. Currently, the evidence from research is insufficient, and no guidelines support routine clinical use for the following indications:

- In patients with systemic sclerosis, limited low-quality evidence from small observational studies and individual case reports suggests ultraviolet A (340-400 nm) and psoralen ultraviolet A reduced skin thickening and increase skin elasticity with no serious side effects (Miziołek, 2022).
- A systematic review of 31 case series examined the safety and effectiveness of light- and laser-based treatments for granuloma annulare. The clearance rates for the phototherapies were psoralen ultraviolet A (59%; n = 131), ultraviolet A (31%, n = 86), and ultraviolet light B or narrowband ultraviolet light B (40%; n = 47). Although psoralen ultraviolet A had higher complete response rate, concerns for carcinogenesis may limit its use and, instead, favor ultraviolet B modalities for their moderate effectiveness and safety profile (Mukovozov, 2022).

In 2024, we added the following literature to the policy with no policy changes warranted:

- For atopic dermatitis. a systematic review and updated guideline by the American Academy of Dermatology stated most current literature reported on the efficacy and safety of narrow band ultraviolet B. The investigators found insufficient evidence on which to recommend psoralen ultraviolet A for this indication. While home ultraviolet B phototherapy units can increase access to phototherapy, evidence of safety and efficacy is not available (Davis, 2023).
- A systematic review of eight studies was unable to draw conclusions about the oncogenic risk in patients with psoriasis based on skin phototypes (Thatiparthi, 2022).
- For patients with vitiligo, a systematic review and network meta-analysis of 22 randomized controlled trials (n = 1,194) concluded that hospital-based narrowband ultraviolet B combined with carboxytherapy, Er: YAG laser plus topical 5% 5-fluorouracil, needling/micro-needling, betamethasone intramuscular injection, or topical tacrolimus was more efficacious than monotherapy in inducing a successful repigmentation response rate ≥ 75% and avoiding failed treatment. Narrowband ultraviolet B combined with either Er: YAG laser plus topical 5% 5- fluorouracil or needling/microneedling would be the preferred therapeutic approaches, as they were less likely to result in an ineffective repigmentation response (≤ 25%). Data limitations prevented a quantitative analysis of adverse effects. Commonly reported phototoxic effects were erythema, edema, pruritus, pain, and burning sensation; two studies reported serious adverse effects of Koebner's phenomenon and scarring (Zhu, 2023).
- For port wine stains, a systematic review and meta-analysis found low-quality evidence from three randomized clinical trials and 23 cohort studies supporting the safety and effectiveness of photodynamic therapy. Collectively, 51.5% of participants achieved at least a 60% improvement in port wine stain appearance across different administrations of treatment, age groups, lesion locations, and subtypes. Adverse effects were documented infrequently, but most experienced moderate pain and edema. Other adverse effects such as photosensitive dermatitis, hyperpigmentation, blister, and scar were infrequently reported (Wang, 2023).

References

On December 4, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers

for Medicare & Medicaid Services. Search terms were “phototherapy," "photochemotherapy," “PUVA therapy,” “UVA,” “UVB,” “psoriasis,” “vitiligo,” “eczema,” “mycosis,” and “fungoides.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Almutawa F, Alnomair N, Wang Y, Hamzavi I, Lim HW. Systematic review of UV-based therapy for psoriasis. *Am J Clin Dermatol*. 2013;14(2):87-109. Doi: 10.1007/s40257-013-0015-y.

Almutawa F, Thalib L, Hekman D, et al. Efficacy of localized phototherapy and photodynamic therapy for psoriasis: A systematic review and meta-analysis. *Photodermatol Photoimmunol Photomed.* 2015;31(1):5-14. Doi: 10.1111/phpp.12092.

Archier E, Devaux S, Castela E, et al. Carcinogenic risks of psoralen UV-A therapy and narrowband UV-B therapy in chronic plaque psoriasis: A systematic literature review. *J Eur Acad Dermatol Venereol.* 2012;26 Suppl 3:22-31. Doi: 10.1111/j.1468-3083.2012.04520.x.(a)

Archier E, Devaux S, Castela E, et al. Efficacy of psoralen UV-A therapy vs. narrowband UV-B therapy in chronic plaque psoriasis: A systematic literature review. *J Eur Acad Dermatol Venereol*. 2012;26 Suppl 3:11-21. Doi: 10.1111/j.1468-3083.2012.04519.x.(b)

Ashraf AZ, Azurdia RM, Cohen SN. The effectiveness of home-based phototherapy for vitiligo: A systematic review of randomised controlled trials. *Photodermatol Photoimmunol Photomed*. 2022;38(5):409-417. Doi: 10.1111/phpp.12766.

Atzmony L, Reiter O, Hodak E, Gdalevich M, Mimouni D. Treatments for cutaneous lichen planus: A systematic review and meta-analysis. *Am J Clin Dermatol.* 2016;17(1):11-22. Doi: 10.1007/s40257-015-0160-6.

Bae JM, Jung HM, Hong BY, et al. Phototherapy for vitiligo: A systematic review and meta-analysis. *JAMA Dermatol*. 2017;153(7):666-674. Doi: 10.1001/jamadermatol.2017.0002.

Chang HC, Lin MH, Tsai HH. Efficacy of combination therapy with fractional carbon dioxide laser and ultraviolet B phototherapy for vitiligo: A systematic review and meta-analysis. *Aesthet Surg J.* 2020;40(1):Np46-np50. Doi: 10.1093/asj/sjz250.

Chang HC, Sung CW. Efficacy of combination therapy of narrowband-ultraviolet B phototherapy or excimer laser with topical tacrolimus for vitiligo: An updated systematic review and meta-analysis. *Photodermatol Photoimmunol Photomed.* 2021;37(1):74-77. Doi: 10.1111/phpp.12593.

Chen X, Yang M, Cheng Y, Liu GJ, Zhang M. Narrow-band ultraviolet B phototherapy versus broad-band ultraviolet B or psoralen-ultraviolet A photochemotherapy for psoriasis. *Cochrane Database Syst Rev.* 2013;10:CD009481. Doi: 10.1002/14651858.CD009481.pub2.

Cohen M, Austin E, Masub N, Kurtti A, George C, Jagdeo J. Home-based devices in dermatology: A systematic review of safety and efficacy. *Arch Dermatol Res*. 2022;314(3):239-246. Doi: 10.1007/s00403-021-02231-0.

Cole GW. PUVA therapy (Photochemotherapy). MedicineNet. https://www.medicinenet.com/puva_therapy_photochemotherapy/article.htm#what_is_puva. Last reviewed January 10, 2023.

Damiani G, Pacifico A, Chu S, Chi CC. Frequency of phototherapy for treating psoriasis: A systematic review. *Ital J Dermatol Venerol*. 2022;157(3):215-219. Doi: 10.23736/s2784-8671.21.06975-3.

Davis DMR, Drucker AM, Alikhan A, et al. Guidelines of care for the management of atopic dermatitis in adults with phototherapy and systemic therapies. *J Am Acad Dermatol*. 2023;Doi: 10.1016/j.jaad.2023.08.102.

Dogra S, Mahajan R. Phototherapy for mycosis fungoides. *Indian J Dermatol Venereol Leprol.* 2015;81(2):124-135. Doi: 10.4103/0378-6323.152169.

Elmets CA, Lim HW, Stoff B, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. *J Am Acad Dermatol.* 2019;81(3):775-804. Doi: 10.1016/j.jaad.2019.04.042.

Fazel N. Cutaneous lichen planus: A systematic review of treatments. *J Dermatolog Treat*. 2015;26(3):280-283. Doi: 10.3109/09546634.2014.933167.

Franken SM, Vierstra CL, Rustmeyer T. Improving access to home phototherapy for patients with psoriasis: Current challenges and future prospects. *Psoriasis (Auckl)*. 2016;6:55-64. Doi: 10.2147/PTT.S81958.

Garritsen FM, Brouwer MW, Limpens J, Spuls PI. Photo(chemo) therapy in the management of atopic dermatitis: An updated systematic review with implications for practice and research. *Br J Dermatol*. 2014;170(3):501-513. Doi: 10.1111/bjd.12645.

Hu M, Liao K, Lei W, Zhang R, Tu C. The addition of topical calcipotriol to phototherapy enhance the efficacy of treatment in patients with vitiligo: A systematic review and meta-analysis. *Int Immunopharmacol.* 2021;98:107910. Doi: 10.1016/j.intimp.2021.107910.

Hum M, Kalia S, Griadecki R. Prescribing home narrowband and UVB phototherapy: A review of current approaches. *J Cutan Med Surg*. 2019;23(1):91-96. Doi: 10.1177/1203475418800947.

Kim E, Lee G, Fischer G. Use of narrowband ultraviolet B (NBUVB) in paediatric psoriasis: A systematic literature review and meta-analysis. *Australas J Dermatol*. 2020;62(2):124-129. . Doi: 10.1111/ajd.13471.

Kim WI, Kim S, Lee SH, Cho MK. The efficacy of fractional carbon dioxide laser combined with narrow-band ultraviolet B phototherapy for non-segmental vitiligo: A systematic review and meta-analysis. *Lasers Med Sci.* 2021;36(1):165-173. Doi: 10.1007/s10103-020-03069-0.

Koek MB, Buskens E, van Weelden H, et al. Home versus outpatient ultraviolet B phototherapy for mild to severe psoriasis: Pragmatic multicentre randomised controlled non-inferiority trial (PLUTO study). *Bmj.* 2009;338:b1542. Doi: 10.1136/bmj.b1542.

Li Y, Cao Z, Guo J, et al. Assessment of efficacy and safety of UV-based therapy for psoriasis: A network meta-analysis of randomized controlled trials. *Ann Med*. 2022;54(1):159-169. Doi: 10.1080/07853890.2021.2022187.
Ling TC, Clayton TH, Crawley J, et al. British Association of Dermatologists and British Photodermatology Group guidelines for the safe and effective use of psoralen-ultraviolet A therapy 2015. *Br J Dermatol.* 2016;174(1):24-55. Doi: 10.1111/bjd.14317.

Malwade US, Jardine LA. Home- versus hospital-based phototherapy for the treatment of non-haemolytic jaundice I infants at more than 37 weeks' gestation. *Cochrane Database Syst Rev*. 2014;(6):CD010212. Doi: 10.1002/14651858.CD010212.pub2.

Maranda EL, Smith M, Nguyen AH, Patel VN, Schachner LA, Joaquin JJ. Phototherapy for pityriasis lichenoides in the pediatric population: A review of the published literature. *Am J Clin Dermatol*. 2016;17(6):583-591. Doi:

10.1007/s40257-016-0216-2.

Mehta D, Lim HW. Ultraviolet B phototherapy for psoriasis: Review of practical guidelines. *Am J Clin Dermatol*. 2016;17(2):125-133. Doi: 10.1007/s40257-016-0176-6.

Menter A, Cordoro KM, Davis DMR, et al. Joint American Academy of Dermatology-National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis in pediatric patients. *J Am Acad Dermatol.* 2020;82(1):161-201. Doi: 10.1016/j.jaad.2019.08.049.

Messenger AG, McKillop J, Farrant P, McDonagh AJ, Sladden M. British Association of Dermatologists' guidelines for the management of alopecia areata 2012. *Br J Dermatol*. 2012;166(5):916-926. Doi: 10.1111/j.1365-2133.2012.10955.x.

Miziołek B, Tworek M, Łapczyńska E, et al. Utility of phototherapy in patients with systemic sclerosis: Systematic review. *Dermatol Ther*. 2022;35(6):e15478. Doi: 10.1111/dth.15478.

Mukovozov IM, Kashetsky N, Richer V. Light- and laser-based treatments for granuloma annulare: A systematic review. *Photodermatol Photoimmunol Photomed*. 2022;38(4):301-310. Doi: 10.1111/phpp.12756.

Musters AH, Mashayekhi S, Harvey J, et al. Phototherapy for atopic eczema. *Cochrane Database Syst Rev.* 2021;10:Cd013870. Doi: 10.1002/14651858.CD013870.pub2.

Nankervis H, Thomas KS, Delamere FM, et al. What is the evidence base for atopic eczema treatments? A summary of published randomized controlled trials. *Br J Dermatol*. 2017;176(4):910-927. Doi: 10.1111/bjd.14999.

National Institute for Health and Care Excellence. Psoriasis: The assessment and management of psoriasis. Clinical guideline CG153. https://www.nice.org.uk/guidance/cg153/chapter/1-Guidance#phototherapy-broad--or-narrow-band-uvb-light-and-puva. Published October 2012. Last updated September 1, 2017.

Obeid G, Do G, Kirby L, et al. Interventions for chronic palmoplantar pustulosis. *Cochrane Database Syst Rev.* 2020;1(1):Cd011628. Doi: 10.1002/14651858.CD011628.pub2.

Olsen EA, Hodak E, Anderson T, et al. Guidelines for phototherapy of mycosis fungoides and Sezary syndrome: A consensus statement of the United States Cutaneous Lymphoma Consortium. *J Am Acad Dermatol*. 2016;74(1):27-58. Doi: 10.1016/j.jaad.2015.09.033.

Ontario Health (Quality). Home narrowband ultraviolet B phototherapy for photoresponsive skin conditions: A health technology assessment. *Ont Health Technol Assess Ser*. 2020;20(12):1-134. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7668536/.

Perez-Ferriols A, Aranegui B, Pujol-Montcusi JA, et al. Phototherapy in atopic dermatitis: A systematic review of the literature. *Actas Dermosifiliogr*. 2015;106(5):387-401. Doi: 10.1016/j.ad.2014.12.017.

Phan K, Ramachandran V, Fassihi H, Sebaratnam DF. Comparison of narrowband UV-B with psoralen-UV-A phototherapy for patients with early-stage mycosis fungoides: A systematic review and meta-analysis. *JAMA Dermatol*. 2019;155(3):335-341. Doi: 10.1001/jamadermatol.2018.5204.

Rathod DG, Muneer H, Masood S. Phototherapy. In *Statpearls* [Internet]. Treasure Island (FL): StatPearls Publishing. 2023 Jan-. https://www.ncbi.nlm.nih.gov/books/NBK563140/. Updated February 16, 2023.

Sevrain M, Richard MA, Bametche T, et al. Treatment for palmoplantar pustular psoriasis: Systematic literature

review, evidence-based recommendations, and expert opinion. *J Eur Acad Dermatol Venereol*. 2014;28 Suppl 5:13-16. Doi: 10.1111/jdv.12561.

~~Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis. Section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-349. Doi: 10.1016/j.jaad.2014.03.030.~~

Solman L, Lloyd-Lavery A, Grindlay DJC, Rogers NK, Thomas KS, Harman KE. What's new in atopic eczema? An analysis of systematic reviews published in 2016. Part 1: Treatment and prevention. *Clin Exp Dermatol*. 2019;44(4):363-369. Doi: 10.1111/ced.13885.

Thatiparthi A, Martin A, Liu J, Wu JJ. Risk of skin cancer with phototherapy in moderate-to-severe psoriasis: An updated systematic review. *J Clin Aesthet Dermatol*. 2022;15(6):68-75.

Therene C, Brenaut E, Barnetche T, Misery L. Efficacy of systemic treatments of psoriasis on pruritus: A systemic literature review and meta-analysis. *J Invest Dermatol*. 2018;138(1):38-45. Doi: 10.1016/j.jid.2017.05.039.

Valipour A, Jager M, Wu P, Schmitt J, Bunch C, Weberschock T. Interventions for mycosis fungoides. *Cochrane Database Syst Rev*. 2020;7(7):CD008946. Doi: 10.1002/14651858.CD008946.pub3.

Wang L, Li L, Huang C. Efficacy of photodynamic therapy in the treatment of port wine stains: A systematic review and meta-analysis. *Front Med (Lausanne)*. 2023;10:1111234. Doi: 10.3389/fmed.2023.1111234**.**

Whitton ME, Pinart M, Batchelor J, et al. Interventions for vitiligo. *Cochrane Database Syst Rev.* 2016;174(5):962-969. Doi: 10.1111/bjd.14356.

Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol.* 2018;32(5):657-682. Doi: 10.1111/jdv.14891.(a)

Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. *J Eur Acad Dermatol Venereol*. 2018;32(6):850-878. Doi: 10.1111/jdv.14888.(b)

Wu YH, Chou CL, Chang HC. Risk of skin cancer after ultraviolet phototherapy in patients with vitiligo: A systematic review and meta-analysis. *Clin Exp Dermatol*. 2022;47(4):692-699. Doi: 10.1111/ced.15010.

Xiao BH, Wu Y, Sun Y, Chen HD, Gao XH. Treatment of vitiligo with NB-UVB: A systematic review. *J Dermatolog Treat*. 2015;26(4):340-346. Doi: 10.3109/09546634.2014.952610.

Xue J, Liu C, Liu Y. Photodynamic therapy as an alternative treatment for relapsed or refractory mycosis fungoides: A systemic review. *Photodiagnosis Photodyn Ther*. 2017;17:87-91. Doi: 10.1016/j.pdpdt.2016.11.010.

Zhu B, Liu C, Zhang L, Wang J, Chen M, Wei Y. Comparison of NB-UVB combination therapy regimens for vitiligo: A systematic review and network meta-analysis. *J Cosmet Dermatol*. 2023;22(3):1083-1098. Doi: 10.1111/jocd.15534.

Policy updates

5/2015: initial review date and clinical policy effective date: 9/2015
5/2016: Policy references updated.
4/2017: Policy references updated.
3/2018: Policy references updated.
5/2019: Policy references updated. The policy ID changed to CCP.1169.
3/2020: Policy references updated.
2/2021: Policy references updated.
2/2022: Policy references updated.
2/2023: Policy references updated.
2/2024: Policy references updated.

AmeriHealth Caritas Louisiana

Sacral nerve modulation/stimulation

Clinical Policy ID: CCP.1522

Recent review date: 2/2024

Next review date: 6/2025

Policy contains: Overactive bladder syndrome; sacral nerve stimulation; urinary incontinence; fecal incontinence.

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Sacral nerve stimulation or sacral neuromodulation (e.g., InterStim System, Medtronic, Inc., Minneapolis, Minnesota) is clinically proven and, therefore, may be medically necessary as a third-line treatment option for severe, refractory overactive bladder syndrome and urinary incontinence when all of the following criteria are met (Abrams, 2017; Gormley, 2019):

- Symptoms of incontinence have been present for at least 12 months, resulting in significant disability, such as the limited ability to work or participate in activities outside of the home.
- The incontinence is non-neurologic in nature.
- A percutaneous stimulation test to determine candidacy for a permanent implantation demonstrates at least a 50% reduction in incontinence symptoms as documented in voiding diaries.
- More conservative first- and second-line approaches have been ineffective or are contraindicated, and member is willing to undergo a surgical procedure (see Appendix).

Sacral nerve stimulation or sacral neuromodulation is clinically proven and, therefore, medically necessary as a third-line treatment option for fecal incontinence when the above criteria are met, plus all of the following (Abrams, 2017):

- No rectal surgery has been performed in the past 12 months.

- The condition is not related to anorectal malformations.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Pharmacotherapy.
- Behavioral modification.
- Pelvic floor muscle training.
- Bladder training.
- Anterior colporrhaphy with bladder neck (Kelly-Kennedy) plication.
- Retropubic suspension (e.g., retropubic urethropexy or Burch procedure).
- Sling procedures (e.g., pubovaginal or suburethral sling, midurethral sling [transvaginal tapes, transobturator slings], bulbourethral sling).
- Artificial urinary sphincter implantation.
- Periurethral bulking injections, including Botox.
- Peripheral tibial nerve stimulation.
- Non-implantable pelvic floor electrical stimulator.

For any determinations of medical necessity for medications, refer to the applicable state-approved pharmacy policy.

Background

Previously referred to as “stress incontinence,” urge incontinence,” or “detrusor instability,” the term “overactive bladder syndrome,” adopted by the International Continence Society, provides a comprehensive and descriptive approach to the condition. The International Continence Society (Haylen, 2010) defines overactive bladder syndrome as:

- Urgency, which is the complaint of a sudden need to void.
- Involuntary loss of urine with urgency symptoms (with or without urge incontinence).
- Usually with increased daytime frequency, often defined as more than eight voids during waking hours, or increased nocturia, which is awakening from sleep to empty the bladder.
- Absence of urinary tract infection or other detectable disease.

Categories of urinary incontinence include total (associated with urinary tract fistula or ectopic ureter), functional (associated with psychiatric or mobility disorders), uncategorized, overflow, post-micturition dribble, radiation therapy incontinence, and climacturia. Urinary incontinence encompasses stress incontinence, urge incontinence, mixed incontinence, total incontinence, and reversible incontinence (Haylen, 2010). While etiology remains elusive, aberrations in neurologic signals from the bladder (sensation) and in central and peripheral nervous system regulation have been implicated.

Treatments for overactive bladder syndrome include conservative interventions such as behavior modification and pelvic floor training, and pharmacologic treatments. More invasive options, such as surgery or neuromodulation, may be indicated when the symptoms are more severe or when conservative measures are unsatisfactory. The

mechanism by which neuromodulation acts to improve symptoms is not well understood, but electrical stimulation of the afferent nerves may allow for appropriately transmitting bladder sensations.

Fecal incontinence can be categorized into urgent or passive cases. Causes are multiple: the most common symptom of fecal incontinence is diarrhea, but constipation can also occur. Multiple treatment options are available, with prescription medications being most frequently used as first-line therapy (National Institute for Diabetes and Digestive and Kidney Diseases, 2017).

Two devices are currently approved to provide sacral neuromodulation (U.S. Food and Drug Administration, 2022). These are the InterStim and Axonics r-SNM Systems. The U.S. Food and Drug Administration (1997) authorized the use of the InterStim sacral neuromodulation device in 1997. The Administration approved the Axonics r-SNM System in 2019 (U.S. Food and Drug Administration, 2019).

The InterStim device lasts for about 4.4 years, after which it must be replaced. The implantation procedure requires two stages. The first consists of a "test" stimulation using a percutaneous needle to stimulate the S3 nerve root. If this results in a favorable response, then a pulse generator can be surgically implanted to provide long-term stimulation. The implantable pulse generator is usually placed in the fatty tissues overlying the buttocks, a shift from abdominal placement used in some earlier research. A permanent lead may be used for the test stimulation, which may be removed if the test is unsuccessful. If the test is successful, the lead can be attached to the permanent implantable pulse generator, ensuring that stimulation is provided in the exact location as during the test period.

The Axonics r-SNM System is a miniaturized, rechargeable sacral neuromodulation system designed to deliver therapy for at least 15 years. The device does not require two steps for implantation. The longer period of 15 years before which explantation is expected to be necessary offers the potential to increase efficacy and to reduce procedures and costs.

Fecal incontinence, which can be caused by numerous factors, can be treated with medications, biofeedback therapy, vaginal balloons, bulking agents, and surgery. In cases that are refractory to conservative treatments, sacral nerve stimulation can also be considered (National Institute of Diabetes and Digestive and Kidney Diseases, 2017).

Findings

The American Urological Association guideline, first published in 2012 and most recently updated by Gormley (2019), states that sacral neuromodulation may be offered as third-line treatment in a "carefully selected patient population characterized by severe refractory overactive bladder symptoms or patients who are not candidates for second-line therapy and are willing to undergo a surgical procedure." These recommendations are based upon strength of evidence of Grade C (see Appendix).
The International Consultation on Incontinence guideline includes support for sacral neuromodulation in both urinary and fecal incontinence as third-line treatment for refractory cases (Abrams, 2017).

Results of recent large reviews addressing efficacy and safety of sacral neuromodulation are summarized below:

<u>Overactive bladder</u>
A network meta-analysis of 21 studies (n = 1,433) documented that in adults with overactive bladder syndrome, sacral neuromodulation was more effective than other treatments for quality of life, urinary episodes, and urinary

frequency, but not for urgency incontinence episodes or number of pads (Huang, 2023).

A meta-analysis of 45 randomized controlled trials of women by the European Association of Urology showed similar success rates and a superior success rate for sacral nerve stimulation compared with antimuscarines (61% versus 42%, *P* = .02). Sacral nerve stimulation had a similar efficacy rate compared with Onabotulinumtoxin-A. The removal and revision rates for stimulation were 9% and 3%, respectively (Farag, 2023).

A meta-analysis of 55 studies (n = 32,507) comparing treatments found sacral neuromodulation was most likely to be ranked first for reducing micturition frequency, urgency episodes, and urgency urinary incontinence episodes (Liu, 2022).

A comprehensive literature search concluded sacral neuromodulation was safe and effective in the short and long term. In studies with at least two years follow-up, surgical re-intervention was high (median 33.2%). The review suggested ways to optimize success (Tilborghs, 2022).

A systematic review of 14 articles of sacral electric stimulation used to treat children found consistently positive results (improved outcomes with few adverse effects). Limits are a dearth of long-term outcomes and heterogeneity in reporting, as there is no standard protocol for the pediatric population (Casal Beloy, 2021).

A review of 24 studies of men assessed treatment options other than antimuscarinics but found little data on nerve stimulation (De Nunzio, 2021).

A study of symptomatic persons (n = 590) found women undergo neuromodulation and experience initial success more frequently than men. Urge incontinence episodes improved only in men and urge incontinence severity improved only in women (Nguyen, 2018).

A systematic review of 99 studies found improvement after sacral neuromodulation was superior to antimuscarinic treatment (Olivera, 2016).

Urinary incontinence

A review of four recent studies showed sacral neuromodulation and onabotulinumtoxinA had similar success in reducing urinary incontinence over two years (Abreu-Mendes, 2021).

A systematic review/network meta-analysis of 17 articles in which subjects were followed for three to six months found sacral neuromodulation had the greatest reduction in urinary incontinence episodes and voiding frequency, compared with onabotulinumtoxinA and percutaneous tibial nerve stimulation (Lo, 2020).

A systematic review indicated that sacral nerve stimulation has been associated with a 50% to 80% improvement in urinary and bowel dysfunction. Greater efficacy was observed when using especially high frequency sacral neuromodulation, a narrow/wide pulse, and use of short cycling intervals (Assmann, 2020).

A systematic review and meta-analysis of nine studies (n = 1,649) found onabotulinumtoxinA and sacral neuromodulation reduced refractory urinary urge incontinence for six months after treatment. Sacral neuromodulation was inferior in treatment but superior in safety (Niu, 2018).

A systematic review of 30 studies included findings included data that sacral nerve stimulation provided benefits in refractory cases of urinary incontinence in women (Schreiner, 2013).

A systematic review of 73 studies observed similar reductions in incontinence episodes and voiding frequency for implanted sacral nerve stimulation and percutaneous posterior tibial nerve stimulation (Monga, 2012).

Fecal incontinence

A review of 13 studies found that sacral neuromodulation after low anterior resection significantly improved symptoms and quality of life (Ram, 2020).

A systematic review/meta-analysis found that sacral nerve stimulation after low anterior resection reduced fecal incontinence by an average of 67% (Huang, 2019).

A systematic review showed sacral nerve stimulation in children showed varying degrees of effectiveness in improving bowel movements per day, transit times, and soiling (Dewberry, 2019).

A review of 14 papers revealed that sacral neuromodulation reduced constipation in children by 79% to 86% but had a complication rate of 17% to 50% (Iacona, 2019).

A systematic review/meta-analysis of four studies (n = 302) indicated sacral neuromodulation had similar effectiveness and greater improvements in functional outcomes and quality of life compared with percutaneous tibial nerve stimulation (Simillis, 2018).

A systematic review calculated a cure rate of 38.6% for fecal incontinence after treatment with sacral neuromodulation (Riemsma, 2017).

A Cochrane review of eight studies found sacral nerve stimulation improved incontinence, but did not improve constipation symptoms (Thaha, 2015).

Other

A systematic review of 11 studies (n = 291) of persons with neurogenic bladder revealed sacral neuromodulation was associated with a variety of improvements, including: incontinence episodes, frequency per 24 hours, voiding volume, cystometric capacity, post-void residual volume, and clean intermittent self-catheterization per 24 hours, each significant at $P < .001$ (Wei, 2023).

A systematic review of 21 publications showed that persons with urinary tract dysfunction found sacral neuromodulation improved leakage episodes ≥ 50% (range 29% to 76%). The overall dry rate ranged between 43% and 56%. Overall improvement after percutaneous tibial neural stimulation ranged from 54% to 59% (Tutolo, 2018).

An analysis (n = 2,680) showed patients with overactive bladder who received onabotulinumtoxinA therapy were at higher risk for urinary tract infection, hematuria, urinary retention, and an emergency room visit compared to those treated with sacral neuromodulation. The overall cost of onabotulinumtoxinA treatment was lower than that of sacral neuromodulation treatment ($2,896 versus $3,454 at one year, $15,343 versus $16,189 at three years, each $P < .01$) (Chug**h**tai, 2020).

References

On November 27, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “Interstim,” “sacral neuromodulation,” and “sacral nerve stimulation,” ”overactive bladder,” “urinary incontinence,” and “stress incontinence.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Abrams P, Cardozo L, Wagg A, Wein A (eds). Incontinence (6th Edition). 6th International Consultation on Incontinence, Tokyo, September 2016, pp. 1-2636. https://www.ics.org/publications/ici_6/Incontinence_6th_Edition_2017_eBook_v2.pdf. Published 2017.

Abreu-Mendes P, Martins-Silva C, Antunes-Lopes T, Cruz F. Treatment of non-neurogenic lower urinary tract symptoms – A review of key publications from 2018 onward. *Eur Urol Focus*. 2021;7(6):1438-1447. Doi: 10.1016/j.euf.2020.06.015.

Assmann R, Douven P, Kleijnen J, et al. Stimulation parameters for sacral neuromodulation on lower urinary tract and bowel dysfunction-related clinical outcome: A systematic review. *Neuromodulation*. 2020;23(8):1082-1093. Doi: 10.0000/ner.13255.

Casal Beloy I, Garcia-Novoa MA, Gonzalez MG, Somoza Argibay I. Update on sacral neuromodulation and overactive bladder in pediatrics: A systematic review. *Arch Esp Urol*. 2021;74(7):699-708. Doi: 10.1016/j.purol.2021.06.011.

Chughtai B, Clemens JQ, Thomas D, et al. Real world performance of sacral neuromodulation and onabotulinumtoxinA for overactive bladder: Focus on safety and cost. *J Urol.* 2020;203(1):179-184. Doi: 10.1097/ju.0000000000000462.

De Nunzio C, Brucker B, Bschleipfer T, et al. Beyond antimuscarinics: A review of pharmacological and interventional options for overactive bladder management in men. *Eur Urol*. 2021;79(4):492-504. Doi: 10.1016/j.eururo.2020.12.032.

Dewberry L, Trecartin A, Pena A, St. Pierre M, Bischoff A. Systematic review: Sacral nerve stimulation in the treatment of constipation and fecal incontinence in children with emphasis in anorectal malformation. *Pediatr Surg Int*. 2019;35(9):1009-1012. Doi: 10.1007/s00383-019-04515-z.

Farag F, Sakalis VI, Arteaga SM, et al. What are the short-term benefits and potential harms of therapeutic modalities for the management of overactive bladder syndrome in women? A review of evidence under the auspices of the European Association of Urology, Female Non-neurogenic Lower Urinary Tract Symptoms Guidelines Panel. *Eur Urol*. 2023;84(3):302-312. Doi: 10.1016/j.eururo.2023/05.014.

Gormley EA, Lightner DJ, Burgio KL et al: Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline. *J Urol* 2012;188:2455. Unabridged version of this guideline. American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) Guidelines. https://www.auanet.org/guidelines-and-quality/guidelines/overactive-bladder-(oab)-guideline. Published 2012. Amended 2014, 2019.

Haylen BT, de Ridder D, Freeman RM, et al. An international urogynecological association (IGUA)/international continence society (ICS) joint report on the terminology for female pelvic floor dysfunction. *Int Urogynecol J.* 2010;21(1):5-26. Doi: 10.1007/s00192-009-0976-9.

Huang Y, Koh H. Sacral nerve stimulation for bowel dysfunction following low anterior resection: A systematic review and meta-analysis. *Colorectal Dis*. 2019;21(11):1240-1248. Doi: 10.1111/codi.14690.

Huang J, Fan Y, Zhao K, et al. Comparative efficacy of neuromodulation technologies for overactive bladder in adults: A network meta-analysis of randomized controlled trials. *Neuromodulation*. 2023;26(8):1535-1548. Doi: 10.1016/j.neurom.2022.06.004.

Iacona R, Ramage L, Malakounides G. Current state of neuromodulation for constipation and fecal incontinence in children: A systematic review. *Eur J Pediatr Surg*. 2019;29(6):495-503. Doi: 10.1055/s-0038-1677485.

Liu P, Li Y, Shi B, Zhang Q, Guo H. Comparison of different types of therapy for overactive bladder: A systematic review and network meta-analysis. *Front Med (Lausanne)*. 2022;9:1014291. Doi: 10.3389//fmed/2022.1014291.

Lo CW, Wu M-Y, Yang S S-D, Jaw F-S, Chang S-J. Comparing the efficacy of OnabotulinumtoxinA, sacral neuromodulation, and peripheral tibial nerve stimulation as third line treatment for the management of overactive bladder symptoms in adults: Systematic review and network meta-analysis. *Toxins (Basel)*. 2020;12(2):128. Doi: 10.3390/toxins12020128.

Monga AK, Tracey MR, Subbaroyan J. A systematic review of clinical studies of electrical stimulation for treatment of lower urinary tract dysfunction. *Int Urogynecol J*. 2012;23(8):993-1005. Doi: 10.1007/s00192-012-1691-5.

National Institute of Diabetes and Digestive and Kidney Diseases. Treatment of fecal incontinence. https://www.niddk.nih.gov/health-information/digestive-diseases/bowel-control-problems-fecal-incontinence/treatment. Last reviewed July 2017.

Nguyen LN, Bartley J, Killinger KA, et al. Does sex matter? A matched pairs analysis of neuromodulation outcomes in women and men. *Int Urol Nephrol*. 2018;50(5):825-832. Doi: 10.1007/s11255/-018-1843-8.

Niu H-L, Ma Y-H, Zhang C-J. Comparison of OnabotulinumtoxinA versus sacral neuromodulation for refractory urinary urge incontinence: A systematic review and meta-analysis of randomized controlled trials. *Int J Surg*. 2018;60:141-148. Doi: 10.1016/j.ijsu.2018.10.041.

Olivera CK, Meriwether K, El-Nashar S, et al. Nonantinuscarinic treatment for overactive bladder: A systematic review. *Am J Obstet Gynecol*. 2016;215(1):34-57. Doi: 10.1016/j.ajog.2016.01.156.

Ram E, Meyer R, Carter D, Gutman M, Rosin D, Horesh N. The efficacy of sacral neuromodulation in the treatment of low anterior resection syndrome: A systematic review and meta-analysis. *Tech Coloproctol*. 2020;24(8):803-815. Doi: 10.1007/s10151-020-02231-8.

Riemsma R, Hagen S, Kirschner-Hermanns R, et al. Can incontinence be cured? A systematic review of cure rates. *BMC Med*. 2017;15(1):63. Doi: 10.1186/s12916-017-0828.

Schreiner L, dos Santos TG, de Souza ABA, Nygaard CC, da Silva Filbo IG. Electrical stimulation for urinary incontinence in women: A systematic review. *Int Braz J Urol*. 2013;39(4):454-464. Doi: 10.1590/S1677-5538.IBJU.2013.04.02.

Simillis C, Lal N, Qiu S, et al. Sacral nerve stimulation versus percutaneous tibial nerve stimulation for faecal incontinence: A systematic review and meta-analysis. *Int J Colorectal Dis*. 2018;33(5):645-648. Doi: 10.1007/s00384-018-2976-z.

Thaha MA, Abukar AA, Thin NN, Ramsanahie A, Knowles CH. Sacral nerve stimulation for faecal incontinence and constipation in adults. *Cochrane Database Syst Rev*, 2015;2015(8):CD004464. Doi: 10.1002/14651858.CD004464.pub3.

Tilborghs S, DeWachter S. Sacral neuromodulation for the treatment of overactive bladder: Systematic review and future prospects. *Expert Rev Med Devices*. 2022;19(2):161-187. Doi: 10.1080/17434440.2022.2032655.

Tutolo M, Ammirati E, Heesakkers J, et al. Efficacy and safety of sacral and percutaneous tibial neuromodulation in non-neurogenic lower urinary tract dysfunction and chronic pelvic pain: A systematic review of the literature. *European Urol.* 2018;73(3):406-418. Doi: 10.1016/j.eururo.2017.11.002.

U.S. Food and Drug Administration. Axonics sacral neuromodulation (SNM) system. Premarket approval — P190006. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P190006. Decision date November 13, 2019.

U.S. Food and Drug Administration. InterStim. Premarket approval — P970004. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?start_search=101&applicant=&tradename=&productcode=&pmanumber=P970004&advisorycommittee=&docketnumber=&supplementtype=&expeditedreview=&ivdproducts=off&decisiondatefrom=&decisiondateto=&noticedatefrom=&noticedateto=&sortcolumn=do_desc&PAGENUM=100. Decision date September 29, 1997.

U.S. Food and Drug Administration. Premarket approval database searched using product code "EZW." https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P970004. Published 2022.

Wei Z, Zhang Y, Hou J, et al. Effectiveness and safety of sacral neuromodulation for neurogenic bladder. *Neurol Res*. 2023;45(6):520-529. Doi: 10.1080/01616412.2022.2162223.

Policy updates

2/2023: initial review date and clinical policy effective date: 2/2023
2/2024: Policy references updated.

Appendix

The American Urological Association/Society of Urodynamics and Female Pelvic Medicine and Urogenital Reconstruction Guidelines: Diagnosis and treatment of non-neurogenic overactive bladder in adults (Gormley, 2019).

First-line treatment: behavioral therapies:

1. Clinicians should offer behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, and fluid management) as first-line therapy to all patients with overactive bladder. Standard (Evidence Strength Grade B).
2. Behavioral therapies may be combined with pharmacologic management. Recommendation (Evidence Strength Grade C).

Second-line treatments: pharmacologic management:

3. Clinicians should offer oral anti-muscarinics or oral β3-adrenoceptor agonists as second-line therapy. Standard (Evidence Strength Grade B).

4. If an immediate release and an extended release formulation are available, then extended release formulations should preferentially be prescribed over immediate release formulations because of lower rates of dry mouth. Standard (Evidence Strength Grade B).
5. Transdermal oxybutynin (patch or gel) may be offered. Recommendation (Evidence Strength Grade C).
6. If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one antimuscarinic medication, then a dose modification or a different anti-muscarinic medication or a β3-adrenoceptor agonist may be tried. Clinical Principle.
7. Clinicians may consider combination therapy with an anti-muscarinic and β3-adrenoceptor agonist for patients refractory to monotherapy with either anti-muscarinics or β3-adrenoceptor agonists. Option (Evidence Strength Grade B).
8. Clinicians should not use anti-muscarinics in patients with narrow-angle glaucoma unless approved by the treating ophthalmologist and should use anti-muscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention. Clinical Principle.
9. Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic therapy. Management may include bowel management, fluid management, dose modification or alternative antimuscarinics. Clinical Principle.
10. Clinicians must use caution in prescribing anti-muscarinics in patients who are using other medications with anticholinergic properties. Expert Opinion.
11. Clinicians should use caution in prescribing anti-muscarinics or β3-adrenoceptor agonists in the frail overactive bladder patient. Clinical Principle.
12. Patients who are refractory to behavioral and pharmacologic therapy should be evaluated by an appropriate specialist if they desire additional therapy. Expert Opinion.

Third-line treatments: peripheral tibial nerve stimulation and neuromodulation:

13. Clinicians may offer intradetrusor onabotulinumtoxinA (100U) as third-line treatment in the carefully-selected and thoroughly-counseled patient who has been refractory to first- and second-line overactive bladder treatments. The patient must be able and willing to return for frequent post-void residual evaluation and able and willing to perform self-catheterization if necessary. Standard (Evidence Strength Grade B).
14. Clinicians may offer peripheral tibial nerve stimulation as a third-line treatment in a carefully selected patient population. Recommendation (Evidence Strength Grade C).
15. Clinicians may offer sacral neuromodulation as a third-line treatment in a carefully selected patient population characterized by severe refractory overactive bladder symptoms or patients who are not candidates for second-line therapy and are willing to undergo a surgical procedure. Recommendation (Evidence Strength Grade C).
16. Practitioners and patients should persist with new treatments for an adequate trial in order to determine whether the therapy is efficacious and tolerable. Combination therapeutic approaches should be assembled methodically, with the addition of new therapies occurring only when the relative efficacy of the preceding therapy is known. Therapies that do not demonstrate efficacy after an adequate trial should be ceased. Expert Opinion.

Fourth-line treatments: augmentation cystoplasty and urinary diversion

17. In rare cases, augmentation cystoplasty or urinary diversion for severe, refractory, complicated overactive bladder patients may be considered. Expert Opinion.

Additional treatments:

18. Indwelling catheters (including transurethral, suprapubic, etc.) are not recommended as a management strategy for overactive bladder because of the adverse risk/benefit balance except as a last resort in selected patients. Expert Opinion.

Follow-up:

19. The clinician should offer follow up with the patient to assess compliance, efficacy, side effects and possible alternative treatments. Expert Opinion

AmeriHealth Caritas Louisiana

Speech therapy

Clinical Policy ID: CCP.1302

Recent review date: 12/2023

Next review date: 3/2025

Policy contains: Oral feeding therapy; oral aversion; speech disorder; speech fluency; speech therapy; swallowing disorder.

AmeriHealth Caritas Louisiana has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Louisiana's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case-by-case basis by AmeriHealth Caritas Louisiana when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Louisiana's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Louisiana's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Louisiana will update its clinical policies as necessary. AmeriHealth Caritas Louisiana's clinical policies are not guarantees of payment.

Coverage policy

Speech therapy is clinically proven and, therefore, may be medically necessary when all of the following criteria are met (American Speech-Language-Hearing Association, 2015):

- Either:
  - Objective standardized testing does not demonstrate age-appropriate, speech-language communication (Brady, 2016; Gubiani, 2015; Roulstone, 2015; Tosh, 2017).
  - Clinical assessment or objective standardized testing demonstrate a pediatric feeding disorder (impaired oral intake that is not safe or age-appropriate) and an associated medical, nutritional, feeding skill, or psychosocial dysfunction (World Health Organization International Classification of Functioning, Disability, and Health, 2001).
- Services are administered as part of a care plan with clearly defined type, amount, duration, and frequency of therapy services, and clearly defined therapeutic goals. Amount, frequency, and duration must be reasonable under accepted standards of practice.

- Services are administered by a trained, licensed healthcare professional experienced in the diagnosis and treatment of speech and feeding disorders.
- The member's condition is expected to improve from the services provided.

Limitations

Speech therapy services for which there is no evidence of improved outcomes or for which there is no defined benefit in state or federal policy are not medically necessary, including, but not limited to:

- Speech therapy administered for achievement of academic goals (e.g., grammar, vocabulary, and reading).
- Speech therapy administered in a language other than the member's language at home.
- Voice therapy for members undergoing gender reassignment in the absence of a functional limitation.
- Speech therapy for a member who is able to: 1) feed or swallow to maintain adequate nutrition, hydration, and pulmonary status, or 2) manage oral and pharyngeal saliva accumulations (American Speech-Language-Hearing Association, 2015).

A reevaluation of the member's performance and goals is medically necessary when a significant improvement, decline, or change in the member's condition occurs, or if it is requested by the Plan to determine the medical necessity of an ongoing intervention. A trained, licensed health care professional experienced in the diagnosis and treatment of speech disorders should perform the reevaluation.

Alternative covered services

Routine in-network evaluation and management by primary care physicians and specialists, including specialty therapists, working in the area of speech deficit, speech fluency, or swallowing disorders.

Background

A speech disorder is an impairment of the articulation of speech sounds, fluency, or voice (American Speech-Language-Hearing Association, 2023b). The prevalence of speech sound disorders in young children is 8% to 9%, mostly attributed to articulation disorders or phonologic disorders (National Institute on Deafness and Other Communication Disorders, 2016). By school age, an estimated 5% of children have noticeable speech disorders (e.g., stuttering, speech sound disorders, and dysarthria) with no clear etiology.

Aberrations in development and execution of speech are usually identified as a congenital or developmental deficit or as the result of an insult to the auditory organs or the brain during pediatric or adult life. Speech disorders can be organic resulting from an underlying motor/neurologic, structural, or sensory/perceptual cause, whereas functional speech disorders are idiopathic. Evaluation of speech consists of clinical examination and age-appropriate standardized tests with "standard scores" designed specifically to identify speech deficits and difficulties in speech fluency (American Speech-Language-Hearing Association, 2023b). Serial measurements can be administered at intervals over the course of therapy.

Speech therapy is a collection of interventions that focuses on improving speech/language production, voice production, swallowing function, cognitive-linguistic skills, or general communication abilities that have been impaired as a result of a disease, injury, developmental delay, or surgical procedure (American Speech-Language-Hearing Association, 2015). Management of speech deficit and aberrations of speech fluency generally is conducted in the language of the home at intervals appropriate to the global condition of the patient. Modern treatment focuses on individualized behavioral approaches combined with education and training. In children, the

emphasis of treatment is on manipulating environmental factors (indirect approaches) and working exclusively on the speech of the child with direct therapeutic approaches (Blomgren, 2013).

Screening for, and diagnosis and treatment of, speech disorders are mandated by federal statute: Section 1905r (Early and Periodic Screening, Diagnostic and Treatment) of the Social Security Act (the Act) provides for comprehensive prevention, diagnostic, and treatment services for low-income (Medicaid) infants, children, and adolescents younger than age 21 (American Speech-Language-Hearing Association, no date given).

Pediatric feeding disorders

Feeding involves any aspect of eating or drinking, including food and liquid gathering and preparation, sucking or chewing, and swallowing (American Speech-Language-Hearing Association, 2023a). Pediatric feeding disorders encompass a range of eating activities that may or may not include problems with swallowing (dysphagia). Feeding problems may involve food refusal, disruptive meal-time behavior, rigid food preferences, suboptimal growth, or failure to master self-feeding skills commensurate with the child's developmental abilities.

Pediatric feeding disorders are complex to diagnose and treat and often occur in children with other medical, developmental, or behavioral problems. Impairment in oral-motor control and function and swallowing and behavioral and/or sensory issues may interfere with normal feeding, resulting in choking, pulmonary complications, inadequate nutrition and hydration, weight loss, and failure to thrive (Borowitz, 2018; Riaz, 2021).

Pediatric feeding disorders comprise four related and complementary domains — medical, psychosocial, feeding skill-based systems, and associated nutritional complications — but have lacked a universally accepted definition (Goday, 2019). The World Health Organization International Classification of Functioning, Disability, and Health (2001) proposed defining a pediatric feeding disorder as "impaired oral intake that is not age-appropriate, and is associated with medical, nutritional, feeding skill, and/or psychosocial dysfunction." This framework complements the ICD-10 and presents a holistic linkage to the physiologic and functional impact that is critical to treatment planning and improving quality of life.

Pediatric feeding problems are typically treated in outpatient settings by individual practitioners or interdisciplinary care teams to address medically complex cases. The role of speech-language pathology is to identify the etiology and develop specific therapies and skills to make the process of eating easier, safer, and more nutritious and enjoyable (American Speech-Language-Hearing Association, 2023a). Clinical and age-appropriate instrumented assessments are needed to document the functional impairment and associated disability. Interventions may include: modifying the nature, consistence and volume of food and liquid intake; altering swallowing behavior; improving oral, pharyngeal, and laryngeal coordination, control, speed, and strength; and patient and caregiver counseling.

Findings

There is sufficient evidence for the effectiveness of speech therapy in terms of improved "functional communication" (e.g., reading, writing, and expressive language) compared with no therapy (standardized mean difference = 0.28, 95% confidence interval 0.06 to 0.49, *P* = .01), based on the results of a Cochrane review of 57 randomized controlled trials (n = 3,002 participants) (Brady, 2016). However, the definition of "functional communication" varies widely in practice. A lack of consistent application of formal tools like standardized tests to evaluate outcomes in speech therapy interventions hampers consistent interpretation of the available data. Indeed, there is awareness in the rehabilitative community that testing interventions are varied, often poorly described, and their quality is limited (Colquhoun, 2017; Costantino, 2014).

Moreover, a single standardized test may not measure all valid and accepted means of communication (e.g., gestures, facial expressions, tone of voice) encountered in a "functional" environment. Professional organizations within the speech and language therapy community, such as the International Collegium of Rehabilitative Audiology (Akeroyd, 2015) within the last 18 months have begun promulgating guidelines to promote a valid comparative basis for outcomes effectiveness.

There is limited evidence (Brady, 2016) that speech therapy at high intensity, high dose (four to 15 hours of speech therapy per week), or over a longer period (up to eight years) may be beneficial for persons with aphasia. However, the benefits of high-intensity/high-dose speech therapy are diminished by a significantly higher dropout rate in these intervention groups. Again, the data on different approaches to speech and language therapy lack consistent focus sufficient to draw conclusions based on sound medical evidentiary principles (American Speech-Language-Hearing Association, 2015; Gubiani, 2015; Roulstone, 2015). There is modest evidence that home speech therapy is an efficacious service delivery model, but it must be administered consistently and with direct parental involvement (Tosh, 2017).

During the last 12 months, there has been further information published regarding speech therapy.

In 2018, the American Academy of Otolaryngology-Head and Neck Surgery Foundation (Stachler, 2018) published a guideline on treating patients who present with dysphonia. They issued strong recommendations for voice therapy for patients with dysphonia from a cause amenable to voice therapy.

In 2019, we added two Cochrane reviews, the results of which require no changes to the policy (Brignell, 2018; Morgan, 2018). We added a bullet clarifying the requirements of a care plan as outlined by the American Speech-Language-Hearing Association (2015). The policy ID was changed from CP# 15.02.11 to CCP.1302.

In 2020, we added information from two reviews (Gray, 2019; Nolan, 2019) on the medical necessity of speech therapy for people undergoing gender reassignment. Voice is critical to the transition and identification of the transgender patient (American Speech-Language-Hearing Association, 2023c). Hormonal therapy and phonosurgery may not achieve the desired gender perception or pitch. As a result of attempting to elevate pitch, they may be susceptible to vocal injury and voice disorders. Voice or speech therapy may help patients masculinize or feminize their voice and communication style to align with their gender identity. Treatment approaches include working on pitch, resonance, vocal hygiene, and communication scenario role-plays that emphasize safe behaviors to avoid damaging the voice.

Most patients represented in the laryngology practice and the medical literature undergo male-to-female transition (Gray, 2019). A systematic review and meta-analysis (Nolan, 2019) of 20 studies found that voice therapy is effective for achieving a satisfactory vocal pitch noninvasively, whether used as a stand-alone intervention or after phonosurgery. Variations in vocal therapy procedures, patient satisfaction, and patient-reported outcomes are limitations in the literature, as is the underrepresentation of patients undergoing female-to-male transition. However, voice therapy is generally considered cosmetic in the absence of a functional limitation. We added this indication to the policy limitations.

In 2021, we updated the references and addressed a field request to determine the medical necessity of oral feeding therapy for pediatric feeding disorders, and for oral aversion, in particular. We included six systematic reviews that examined the effectiveness of feeding therapy with a focus on speech-language pathology interventions for oral aversion and other feeding difficulties. The results confirm the complex and multifactorial nature of pediatric feeding disorders. The contribution of speech-language pathology interventions is best recognized as an integral component of a treatment protocol with clearly define objectives that link the feeding problem with oral-motor interventions and a measurable reduction in impairment. We modified the coverage based on American Speech-Language-Hearing Association (2015) guidelines.

Two early comprehensive reviews provided a general assessment of the state of the literature that remains durable (Sharp, 2010; Williams, 2010). The research consisted of individual case reports, small case series, or small randomized controlled trials of diverse interventions and equally diverse populations that made optimal service delivery impossible to determine. The preponderance of the evidence examined intensive behavioral approaches offered individually or within a multidisciplinary team structure provided at day treatment centers or inpatient hospital settings. Core disciplines involved in this care may include psychology, nutrition, medicine, and speech-language pathology/occupational therapy, but their unique contributions have not been adequately explored. The authors call for higher quality research to address the methodological shortcomings.

In a more recent systematic review (Sharp, 2017) of 11 studies, multi-component interventions that applied operant conditioning, systematic desensitization, and changes to environment and familial practices were effective for children with complex medical or developmental histories who displayed persistent feeding concerns requiring formula supplementation. Three of the studies included oral-motor therapy, which consisted of decreasing tactile hypersensitivity or increasing the range, strength, and control of the lips, cheeks, jaw, and tongue. Reported outcomes of multi-component treatment were rates in successful weaning from tube feeding at discharge (71%, 95% confidence interval 54% to 83%), which persisted at varying lengths of follow up, and subjective improvements in oral intake and mealtime behaviors and reductions in parenting stress. The authors recommended multidisciplinary intervention, including speech-language pathology or occupational therapy, to ensure the necessary oversight and clinical guidance needed to address the behavioral, organic, dietary, and oral-motor concerns pervasive in severe feeding disorders.

A systematic review (Gosa, 2017) of 61 mixed-quality studies found sufficient evidence from four high-quality studies to establish the efficacy and benefit of joint nutrition and behavior intervention programs to improve functional feeding and swallowing outcomes in children with swallowing and feeding disorders. For other interventions, such as oral-motor or sensory therapies, there continues to be weak or conflicting evidence supporting their impact on functional feeding outcomes in pediatric populations.

A systematic review (Rhooms, 2019) of 35 low-quality studies examined the effects of unimodal (26 studies) and multimodal (nine studies) sensorimotor interventions on oral feeding outcomes (transition to full oral feeding, volume intake, weight gain, and length of hospital stay) in preterm infants. Unimodal interventions primarily targeted oral sensorimotor input and, to a lesser extent, tactile, auditory, and olfactory input. Multimodal interventions combined tactile and kinesthetic stimulation. The heterogeneity in the studies limited the ability to determine the effects of sensorimotor interventions on feeding outcomes provided by either mode.

A systematic review (Shortland, 2021) of 28 low-quality studies examined orofacial myofunctional therapy and myofunctional devices used for communication and swallow difficulties. Heterogeneity in study designs, treatment protocols, and outcome measures prevented conclusions about the effectiveness of these interventions.

A systematic review/meta-analysis of 67 studies determined that 25% of preterm infants experienced oromotor feeding difficulties in late infancy and/or childhood, with 20% classified as challenging eating behaviors. These figures exceed those for term infants. Authors note that mothers of preterm infants had increased anxiety while feeding and utilized coercive food parenting practices, while their children received less human milk, started solid foods earlier, and had poorer diet quality (Walton, 2022).

In 2023, we added no new references to the policy.

References

On September 28, 2023, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “speech deficit,” ”speech fluency,” “Feeding and Eating Disorders of Childhood/therapy" (MAJR), “Feeding behavior/therapy” (MeSH), “deglutition disorders” (MeSH), “dysphagia,” and “speech therapy” (MeSH). We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Akeroyd MA, Arlinger S, Bentler RA, et al.; International Collegium of Rehabilitative Audiology Working Group on Multilingual Speech Tests. International Collegium of Rehabilitative Audiology (ICRA) recommendations for the construction of multilingual speech tests. ICRA Working Group on Multilingual Speech Tests. *Int J Audiol*. 2015;54 Suppl 2:17-22. Doi: 10.3109/14992027.2015.1030513.

American Speech-Language-Hearing Association. Pediatric dysphagia (practice portal). https://www.asha.org/practice-portal/clinical-topics/pediatric-feeding-and-swallowing/#collapse. Published 202**3**. (a)

American Speech-Language-Hearing Association. Speech-language pathology medical review guidelines. https://www.asha.org/siteassets/uploadedFiles/SLP-Medical-Review-Guidelines.pdf. Published 2015.

American Speech-Language-Hearing Association. Speech sound disorders: Articulation and phonology. https://www.asha.org/practice-portal/clinical-topics/articulation-and-phonology/#collapse_9. Published 2023. (b)

American Speech-Language-Hearing Association. Voice and communication change for transgender people. https://www.asha.org/public/speech/disorders/Voice-and-Communication-Change-for-Transgender-People/. Published 2023. (c)

American Speech-Language-Hearing Association. Medicaid EPSDT Mandate Supports Children’s Communication. https://www.asha.org/siteassets/uploadedfiles/reimbursement/medicaid-epsdt-flyer.pdf. No date given.

Blomgren M. Behavioral treatments for children and adults who stutter: a review. *Psychol Res Behav Manag*. 2013;6:9-19. Doi: 10.2147/prbm.s31450.

Borowitz KC, Borowitz SM. Feeding problems in infants and children: Assessment and etiology. *Pediatr Clin North Am.* 2018;65(1):59-72. Doi: 10.1016/j.pcl.2017.08.021.

Brady MC, Kelly H, Godwin J, et al. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst Rev*. 2016;6:CD000425. Doi: 10.1002/14651858.CD000425.pub4.

Brignell A, Chenausky KV, Song H, et al. Communication interventions for autism spectrum disorder in minimally verbal children. *Cochrane Database Syst Rev.* 2018;11:Cd012324. Doi: 10.1002/14651858.CD012324.pub2.

Colquhoun HL, Lamontagne ME, Duncan EA, et al. A systematic review of interventions to increase the use of standardized outcome measures by rehabilitation professionals. *Clin Rehabil.* 2017;31(3):299-309. Doi: 10.1177/0269215516644309.

Costantino MA, Bonati M. A scoping review of interventions to supplement spoken communication for children with limited speech or language skills. *PLoS One*. 2014;9(3):e90744. Doi: 10.1371/journal.pone.0090744.

Goday PS, Huh SY, Silverman A, et al. Pediatric feeding disorder: Consensus definition and conceptual framework. *J*

Pediatr Gastroenterol Nutr. 2019;68(1):124-129. Doi: 10.1097/MPG.0000000000002188.

Gosa MM, Carden HT, Jacks CC, Threadgill AY, Sidlovsky TC. Evidence to support treatment options for children with swallowing and feeding disorders: A systematic review. *J Pediatr Rehabil Med.* 2017;10(2):107-136. Doi: 10.3233/prm-170436.

Gray ML, Courey MS. Transgender voice and communication. *Otolaryngol Clin North Am.* 2019;52(4):713-722. Doi: 10.1016/j.otc.2019.03.007.

Gubiani MB, Pagliarin KC, Keske-Soares M. Tools for the assessment of childhood apraxia of speech. *Codas*. 2015;27(6):610-615. Doi: 10.1590/2317-1782/20152014152.

Morgan AT, Murray E, Liegeois FJ. Interventions for childhood apraxia of speech. *Cochrane Database Syst Rev.* 2018;5:Cd006278. Doi: 10.1002/14651858.CD006278.pub3.

National Institute on Deafness and Other Communication Disorders. Quick statistics about voice, speech, language. https://www.nidcd.nih.gov/health/statistics/quick-statistics-voice-speech-language. Last updated May 19, 2016.

Nolan IT, Morrison SD, Arowojolu O, et al. The role of voice therapy and phonosurgery in transgender vocal feminization. *J Craniofac Surg.* 2019;30(5):1368-1375. Doi: 10.1097/scs.0000000000005132.

Rhooms L, Dow K, Brandon C, Zhao G, Fucile S. Effect of unimodal and multimodal sensorimotor interventions on oral feeding outcomes in preterm infants: An evidence-based systematic review. *Adv Neonatal Care.* 2019;19(1):E3-e20. Doi: 10.1097/anc.0000000000000546.

Riaz Y, Sergi C. Feeding disability in children. *Statpearls*. Treasure Island (FL): StatPearls Publishing Copyright © 2021, StatPearls Publishing LLC; 2021. https://www.ncbi.nlm.nih.gov/books/NBK564306/.

Roulstone SE, Marshall JE, Powell GG, et al. Evidence-based intervention for preschool children with primary speech and language impairments: Child Talk – an exploratory mixed-methods study. Southampton (UK): NIHR Journals Library (Programme Grants for Applied Research, No. 3.5.). Published August 2015. Doi: 10.3310/pgfar03050. https://pubmed.ncbi.nlm.nih.gov/26312364/.

Sharp WG, Jaquess DL, Morton JF, Herzinger CV. Pediatric feeding disorders: A quantitative synthesis of treatment outcomes. *Clin Child Fam Psychol Rev.* 2010;13(4):348-365. Doi: 10.1007/s10567-010-0079-7.

Sharp WG, Volkert VM, Scahill L, McCracken CE, McElhanon B. A systematic review and meta-analysis of intensive multidisciplinary intervention for pediatric feeding disorders: How standard is the standard of care? *J Pediatr.* 2017;181:116-124.e114. Doi: 10.1016/j.jpeds.2016.10.002.

Shortland HL, Hewat S, Vertigan A, Webb G. Orofacial myofunctional therapy and myofunctional devices used in speech pathology treatment: A systematic quantitative review of the literature. *Am J Speech Lang Pathol.* 2021;30(1):301-317. Doi: 10.1044/2020_ajslp-20-00245.

Stachler RJ, Francis DO, Schwartz SR, et al. Clinical practice guideline: Hoarseness (dysphonia) (update).*Otolaryngol Head Neck Surg*. 2018;158(1_suppl):S1-S42. Doi: 10.1177/0194599817751030.

Tosh R, Arnott W, Scarinci N. Parent-implemented home therapy programmes for speech and language: A systematic review. *Int J Lang Commun Disord.* 2017;52(3):253-269. Doi:10.1111/1460-6984.12280.

Walton K, Daniel AI, Mahood Q, et al. Eating behaviors, caregiver feeding interactions, and dietary patterns of

children born preterm: A systematic review and meta-analysis. *Adv Nutr*. 2022;13(3):875-912. Doi: 10.1093/advances/nmac017.

Williams KE, Field DG, Seiverling L. Food refusal in children: A review of the literature. *Res Dev Disabil.* 2010;31(3):625-633. Doi: 10.1016/j.ridd.2010.01.001.

World Health Organization. International Classification of Functioning, Disability and Health: ICF. Geneva, Switzerland: World Health Organization; https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health. Published 2001.

Policy updates

4/2017: initial review date and clinical policy effective date: 5/2017
6/2018: Policy references updated.
6/2019: Policy references updated. Policy modified and ID changed.
6/2020: Policy references updated. Limitations modified.
6/2021: Policy references updated. Coverage modified.
12/2022: Policy references updated.
12/2023: Policy references updated.