Clinical Policy: OnabotulinumtoxinA (Botox)

Reference Number: CP.PHAR.232
Effective Date: 07/16
Last Review Date: 07/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for onabotulinumtoxinA (Botox®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Botox is **medically necessary** when one of the following criteria is met:

ContentsDescription 1

I. Initial Approval Criteria

A. Cervical Dystonia (must meet all):

1. Prescribed by or in consultation with a neurologist, orthopedist or physiatrist;
2. Age ≥ 18 years;
3. Diagnosis of cervical dystonia (CD) (see definition in Appendix B):
4. Experiencing involuntary contractions of the neck and shoulder muscles (e.g., splenius, sternocleidomastoid, levator scapulae, scalene, trapezius, posterior cervical) resulting in abnormal postures or movements of the neck, shoulder or head;
5. Contractions are causing pain and functional impairment;
6. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
7. Prescribed dose of Botox does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

B. Blepharospasm *(a focal dystonia)* or Strabismus (must meet all)**:**

1. Prescribed by or in consultation with a neurologist or ophthalmologist;
2. Age ≥ 12 years;
3. Diagnosis (a or b):
   a. Blepharospasm (i.e., abnormal contraction of eyelid muscles);
   b. Strabismus (i.e., misalignment of the eyes);
4. Member has significant disability in daily functional activities due to interference with vision;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed (a or b):
   a. Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period);
   b. Strabismus: 25 units per muscle per treatment session.

Approval duration: 12 weeks (single treatment session)

C. Other Dystonias – Off Label Use (must meet all)**:**

1. Prescribed by or in consultation with a neurologist, orthopedist or physiatrist;
2. Diagnosis of dystonia (see definitions and types in Appendices B and C);
3. If not contraindicated, member has tried and failed or is intolerant to carbidopa/levodopa and trihexyphenidyl;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
5. Prescribed dose of Botox does not exceed 400 units per single treatment with the following exceptions:
   a. Oromandibular dystonia: 25 units per muscle per treatment session;
   b. Laryngeal dystonia (spasmodic dysphonia): 3 units per treatment session.

Approval duration: 12 weeks (single treatment session)

D. Upper and Lower Limb Spasticity (must meet all)**:**
1. Prescribed by or in consultation with a neurologist, orthopedist or physiatrist;
2. Age ≥ 18 years;
3. Diagnosis of upper or lower limb spasticity (a or b):
   a. Upper limb: intent of treatment is to decrease severity of increased muscle tone in elbow flexors (i.e., biceps brachii, brachialis, pronator teres, brachioradialis), wrist flexors (i.e., flexor carpi radialis, flexor carpi ulnaris), finger flexors (i.e., flexor digitorum profundus, flexor digitorum sublimis [superficialis]), or thumb flexors (i.e., adductor pollicis, flexor pollicis longus);
   b. Lower limb: intent of treatment is to decrease severity of increased muscle tone in ankle or toe flexors (i.e., gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, flexor digitorum longus);
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
5. Prescribed dose of Botox does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

E. Spasticity Associated with Cerebral Palsy – Off Label Use (must meet all)**:**
1. Prescribed by or in consultation with a neurologist;
2. Age ≥ 2 years;
3. Diagnosis of spasticity associated with cerebral palsy (CP);
4. Focal increased muscle tone interferes with function or is likely to lead to joint contracture with growth;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed 400 units per treatment session.

Approval duration: 12 weeks (single treatment session)

F. Chronic Migraine (must meet all)**:**
1. Prescribed by or in consultation with a neurologist;
2. Age ≥ 18 years;
3. Diagnosis of chronic migraine (≥ 15 days per month with headache lasting 4 hours a day or longer);
4. Member has tried and failed, or is intolerant or contraindicated to, at least 2 oral migraine preventative therapies, each for at least 8 weeks (e.g., antiepileptic drugs: divalproex sodium, sodium valproate, topiramate; beta-blockers: metoprolol, propranolol, timolol; antidepressants: amitriptyline, venlafaxine);
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed 155 units per treatment session.

Approval duration: 24 weeks (two 12-week treatment sessions)

G. Primary Axillary Hyperhidrosis (must meet all)**:**
1. Prescribed by or in consultation with a neurologist or dermatologist;
2. Age ≥ 18 years;
3. Diagnosis of severe primary axillary hyperhidrosis (e.g., resulting in medical complications such as skin maceration and infection or significant disruption of professional/social life);
4. Member has tried and failed 6 months of topical aluminum chloride;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed 50 units per axilla per treatment session.

Approval duration: 12 weeks (single treatment session)

H. Overactive Bladder and Urinary Incontinence (must meet all)**:**
1. Prescribed by or in consultation with a neurologist or urologist;
2. Age ≥ 18 years;
3. Diagnosis (a or b):
   a. Overactive bladder with symptoms of urge urinary incontinence, urgency and frequency;
   b. Urinary incontinence due to detrusor over activity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis);
4. Member has tried and failed behavioral therapy (e.g., bladder training, pelvic floor muscle training, fluid management) for at least 8 weeks;
5. Member has tried and failed, or is intolerant or contraindicated to, at least 2 anticholinergic or oral beta-3 agonist medications (e.g., oxybutynin chloride, tolterodine tartrate; mirabegron) at the maximum tolerated dose for at least 30 days;
6. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
7. Prescribed dose of Botox does not exceed (a or b):
   a. Overactive bladder: 100 units per treatment session;
   b. Urinary incontinence: 200 units per treatment session.

Approval duration: 12 weeks (single treatment session)

I. Esophageal Achalasia – Off Label Use (must meet all)**:**
1. Prescribed by or in consultation with a gastroenterologist;
2. Age ≥ 18 years;
3. Diagnosis of esophageal achalasia (i.e., failure of relaxation of the lower esophageal sphincter accompanied by loss of peristalsis in the distal esophagus);
4. Member is not a good candidate for pneumatic dilation or myotomy;
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed 100 units.

Approval duration: 24 weeks (single treatment session)

J. Hirschsprung's Disease and Internal Anal Sphincter Achalasia – Off Label Use (must meet all):
1. Prescribed by or in consultation with a gastroenterologist;
2. Diagnosis (a or b):
   a. Hirschsprung's disease (HD) (i.e., heritable motor disorder of the gut with failure of the colon to relax causing functional obstruction; usually diagnosed infancy or childhood) (i or ii):
      i. Botox will be used for constipation due to increased internal anal sphincter tone after surgery;
      ii. Member is diagnosed with ultra-short segment HD;
   b. Internal anal sphincter (IAS) achalasia (i.e., lack of rectoanal inhibitory reflex on anal manometry; presents in infancy – may mimic HD);
3. Member has tried and failed, or is intolerant or contraindicated to, high fiber diet, adequate fluids, stool softeners, and laxatives for at least 2 months;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
5. Prescribed dose of Botox does not exceed 100 units.

Approval duration: 12 weeks (single treatment session)

K. Chronic Anal Fissure – Off Label Use (must meet all)**:**
1. Prescribed by or in consultation with a gastroenterologist or colorectal surgeon;
2. Age ≥ 18 years;
3. Diagnosis of chronic anal fissures;
4. Member has tried and failed, or is intolerant or contraindicated to, at least 2 months of conventional therapy (e.g., high fiber diet and adequate fluids, bulk fiber supplements, stool softeners, warm sitz baths, nitroglycerin 0.2% ointment);
5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed 100 units.

Approval duration: 12 weeks (single treatment session)

L. Other diagnoses/indications:
1. Refer to CP.PHAR.57 - Global Biopharm Policy if requested indication is non-cosmetic.

II. Continued Approval

A. Chronic Migraine (must meet all):
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. If member has received 2 or more Botox treatment sessions, has experienced and maintained a 30% reduction in monthly migraine headache frequency from baseline;
4. It has been at least 12 weeks since the last injection of Botox;

5. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
6. Prescribed dose of Botox does not exceed 155 units per treatment session.

Approval duration: 12 weeks (single treatment session)

B. Esophageal Achalasia (must meet all):
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. It has been at least 24 weeks since the last injection of Botox;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
5. Prescribed dose of Botox does not exceed 100 units per treatment session.

Approval duration: 24 weeks (single treatment session)

C. All Other Indications in Section I (must meet all):
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. It has been at least 12 weeks since the last injection of Botox;
4. Provider submits treatment plan detailing the quantity (in units) of Botox to be injected in each muscle site;
5. Botox administration has not exceeded 400 units over the last 3 months;
6. Prescribed dose of Botox does not exceed the following indication-specific maximums:
    a. Dystonias:
        i. CD, upper/lower limb spasticity, CP: 400 units per treatment session;
        ii. Blepharospasm: 5 units per site per treatment session (maximum of 200 units total in a 30-day period);
        iii. Strabismus: 25 units per muscle per treatment session;
        iv. Oromandibular dystonia: 25 units per muscle per treatment session;
        v. Laryngeal dystonia (spasmodic dysphonia): 3 units per treatment session;
    b. Primary axillary hyperhidrosis: 50 units per axilla per treatment session;
    c. Overactive bladder, HD, IAS achalasia, chronic anal fissures: 100 units per treatment session;
    d. Urinary incontinence: 200 units per treatment session.

Approval duration: 12 weeks (single treatment session)

D. Other diagnoses/indications (1 or 2):
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy; coverage is not approved for cosmetic use, including for treatment of glabellar lines.

Background

Description/Mechanism of Action:

OnabotulinumtoxinA is a purified botulinum toxin type A produced from fermentation of Clostridium botulinum. It blocks neuromuscular transmission by binding to acceptor sites on motor or sympathetic nerve terminals, entering the nerve terminals, and inhibiting the release of acetylcholine. This inhibition occurs as the neurotoxin cleaves SNAP-25, a protein integral to the successful docking and release of acetylcholine from vesicles situated within nerve endings.

Formulations:

Botox: Vacuum-dried powder for reconstitution in single-use vials containing 100 units or 200 units of onabotulinumtoxinA.

FDA Approved Indications (non-cosmetic):

Botox is an acetylcholine release inhibitor/neuromuscular blocking agent formulated for intramuscular, intradetrusor or intradermal use and indicated for:

Dystonias and strabismus

- Treatment of
  - Adults with cervical dystonia, to reduce the severity of abnormal head position and neck pain associated with cervical dystonia
  - Strabismus and blepharospasm associated with dystonia, including benign essential blepharospasm or VII nerve disorders in patients 12 years of age and above

Spasticity

- Treatment of
  - Uper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), finger flexors (flexor digitorum profundus and flexor digitorum sublimis), and thumb flexors (adductor pollicis and flexor pollicis longus)
  - Lower limb spasticity in adult patients to decrease the severity of increased muscle tone in ankle and toe flexors (gastrocnemius, soleus, tibialis posterior, flexor hallucis longus, and flexor digitorum longus)

  Limitations of use: Safety and effectiveness of Botox have not been established for the treatment of other upper or lower limb muscle groups. Safety and effectiveness of Botox have not been established for the treatment of spasticity in patients < 18 years. Botox has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with Botox is not intended to substitute for usual standard of care rehabilitation regimens.

Migraine

- Prophylaxis of
  - Headaches in adult patients with chronic migraine (≥15 days per month with headache lasting 4 hours a day or longer)

  Limitations of use: Safety and effectiveness have not been established for the prophylaxis of episodic migraine (14 headache days or fewer per month) in seven placebo-controlled studies.

Hyperhidrosis

- Treatment of
  - Severe primary axillary hyperhidrosis that is inadequately managed with topical agents

  Limitations of use: The safety and effectiveness of Botox for hyperhidrosis in other body areas have not been established. Weakness of hand muscles and blepharoptosis may occur in those who receive Botox for palmar hyperhidrosis and facial hyperhidrosis, respectively. Patients should be evaluated for potential causes of secondary hyperhidrosis (e.g., hyperthyroidism) to avoid symptomatic treatment of hyperhidrosis without the diagnosis and/or treatment of the underlying disease. Safety and effectiveness of Botox have not been established for the treatment of axillary hyperhidrosis in those < 18 years.

Genitourinary

- Treatment of
  - Overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency, in adults who have an inadequate response to or are intolerant of an anticholinergic medication
  - Urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., SCI [spinal cord injury], MS [multiple sclerosis]) in adults who have an inadequate response to or are intolerant of an anticholinergic medication

Appendices

Appendix A: Abbreivation Key

CD: cervical dystonia
CNS: central nervous system
CP: cerebral palsy
HD: Hirschsprung's disease
IAS: internal anal sphincter
MS: multiple sclerosis
SCI: spinal cord injury

Appendix B: Definition and Classification of Dystonia[11]

Dystonia is defined as a movement disorder characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both.

- Dystonic movements are typically patterned and twisting, and may be tremulous.
- Dystonia is often initiated or worsened by voluntary action and associated with overflow muscle activation.

Dystonia is classified along two axes:

- Clinical characteristics: Age at onset, body distribution, temporal pattern, associated features (additional movement disorders or neurological features) - *the clinical characteristics fall into several specific dystonia syndromes that help to guide diagnosis and treatment*;
- Etiology: Nervous system pathology, inheritance.

*Appendix C: Descriptions and Examples of Dystonia Syndromes**

Category	Subcategory	Description and Examples
Isolated dystonias	Early-onset generalized isolated dystonia	Dystonia with focal-onset in childhood often progresses to generalized involvement. Cases may be sporadic, familial, genetically defined or without known cause. • Early-onset generalized dystonia (DYT-TOR1A)

Category	Subcategory	Description and Examples
		• Adolescent-onset dystonia of mixed type (DYT-THAP1)
	Adult-onset focal or segmental isolated dystonia	Usually begins after age 30 years. Most are sporadic without identifiable cause. Rarely progress to generalized dystonia but can extend to contiguous body regions. • Adult-onset segmental dystonia (DYT-GNAL) • Cervical dystonia • Blepharospasm • Writer's cramp • Oromandibular dystonia • Laryngeal dystonia (spasmodic dysphonia) • Limb dystonia
Combined dystonias	Dystonia-parkinsonism	Disorders that combine dystonia and parkinsonian features. May be accompanied by pyramidal tract involvement or nonmotor features including cognitive decline. Many are inherited. • Dopa-responsive dystonia (DYT-GCH1, DYT-TH, and DYT-SPR) • Wilson disease • Early-onset parkinsonism (PARK-PARKIN) • Conditions associated with neurodegeneration with brain iron accumulation
	Myclonus-dystonia	Disorders in which there is a combination of dystonia and myoclonus. Dystonia may be mild and myoclonus generally predominates. • Myoclonus-dystonia (DYT-SGCE)
	Paroxysmal dyskinesia with dystonia	Disorders characterized by episodes of spontaneous or induced dyskinesia with dystonia. • Paroxysmal nonkinesigenic dyskinesia (DYT-MR1)

**Table adapted with permission from: Comella C. Classification and evaluation of dystonia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available at www.uptodate.com. Accessed on June 22, 2017.*

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0585	Injection, onabotulinumtoxinA, 1 unit

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.09.	05/16	07/16

Reviews, Revisions, and Approvals	Date	Approval Date
Added new FDA indication of lower limb spasticity per FDA labeling. Added compendial indication of laryngeal spasm/spasmodic dysphonia. -Overactive bladder: modified requirement for trial/failure of previous therapy to include oral beta-3 agonist medications per AUA guidelines. -Migraine: modified continuation criteria to require 30% reduction in headache frequency after 2 injections rather than just 1 per literature review and NICE guidelines. -Added general max dosing limit for cerebral palsy and spastic conditions and indication-specific max dosing limit for cervical dystonia, strabismus, primary axillary hyperhidrosis, upper limb spasticity, overactive bladder, urinary incontinence, and chronic migraine per PI. -Added indication-specific max dosing limit for chronic anal fissures, esophageal achalasia, laryngeal spasm/spasmodic dysphonia, Hirschsprung's disease, and dystonias per literature review. -Added prescriber requirement for overactive bladder, urinary incontinence, chronic migraines, upper limb spasticity, primary axillary hyperhidrosis, chronic anal fissures, cerebral palsy, esophageal achalasia, dystonias, Hirschsprung's disease, and spastic conditions. -Added age restriction for upper limb spasticity and primary axillary hyperhidrosis per PI, and for chronic anal fissures, esophageal achalasia, and Hirschsprung's disease per literature review. -Added route of administration for each labeled indication per PI. -Removed reauthorization criteria requiring attestation of significant improvement in symptoms and/or health-related quality of life. Added positive response to therapy to continuation criteria.		
-Chronic migraine initial approval duration lengthened from 12 to 24 weeks (from one to two treatment sessions) to allow assessment of response as outlined in continuation criteria.	11/16	
The off-label criteria set entitled "Spastic Conditions" is deleted due to its broad scope; off-label requests not covered elsewhere in the policy are referred to the CP.PHAR.57.Global Biopharm policy so that they may be reviewed individually. Requirement that provider submits detailed treatment plan added to curtail abuse	02/17	
Indications reorganized. Definition of CD is edited per AAN guidelines. Laryngeal dystonia is merged with off-label dystonias which in turn are entitled "Other Dystonias". Clarified "blepharospasm" as a focal dystonia. Deleted causes and classifications of blepharospasm; blepharospasm and strabismus definitions are added. Dystonia information is added at Appendices B and C. Added esophageal achalasia definition. IAS achalasia is given its own line item. HD and IAS achalasia definitions added. Background FDA indication section and references categorized. "Non-cosmetic" parenthetical added to the background FDA indication section;	06/17	07/17

Reviews, Revisions, and Approvals	Date	Approval Date
cosmetic coverage restriction reworded under the "Other Diagnoses/Indications" section to include notation of glabellar lines.		

References

1. Botox Prescribing Information. Irvine, CA: Allergan, Inc.; April 2017. Available at http://www.allergan.com/assets/pdf/botox_pi.pdf. Accessed June 14, 2017.
2. OnabotulinumtoxinA. In: Micromedex. Ann Arbor, MI: Truven Health Analytics; 2013. Available from: www.micromedexsolutions.com. Accessed June 14, 2017.

Dystonias, Spasticity, Chronic Migraine

3. Simpson DM, Hallett M, Ashman EJ et al. Practice guideline update summary: botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2016; 86(19): 1818-1826.
4. Simpson DM, Gracies JM, Graham HK et al. Assessment: botulinum neurotoxin for the treatment of spasticity (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* 2008; 70(19): 1691-1698.
5. Simpson DM, Blitzer A, Brashear A, et al. Assessment: botulinum neurotoxin for the treatment of movement disorders (an evidence-based review): Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* 2008; 70: 1699-1706.
6. Delgado MR, Hirtz D, Aisen M et al. Practice parameter: pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review). *Neurology*. 2012; 74(4): 336-343.
7. Silberstein SD, Holland S, Freitag F et al. Evidence-based guideline update: Pharmacologic treatment for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology*. 2012; 78(17): 1337-1345.
8. Delnooze CC, van de Warrenburg BP. Current and future medical treatment in primary dystonia. *Ther Adv Neurol Disord*. 2012; 5(4): 221-240.
9. Hallet M, Benecke R, Blitzer A, Comella CL. Treatment of focal dystonias with botulinum neurotoxin. *Toxicon.* 2009; 54(5): 628-633.
10. Jankovic J. Treatment of dystonia. *Lancet Neuro*l. 2006; 5(10): 864-872.
11. Albanese A, Bhatia K, Bressman SB, et al. Phenomenology and classification of dystonia: a consensus update. *Mov Disord.* June 15, 2013; 28(7): 863-873. doi:10.1002/mds.25475.
12. Comella C. Classification and evaluation of dystonia. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available at www.uptodate.com. Accessed June 22, 2017.

Primary Axillary Hyperhidrosis, Overactive Bladder, Urinary Incontinence

13. Naumann M, So Y, Argoff, CE, et al. Assessment: Botulinum neurotoxin in the treatment of autonomic disorders and pain (an evidence-based review) Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* 2008; 70: 1707-1714.

14. Pariser DM, Ballard A. Topical therapies in hyperhidrosis care. *Dermatol Clin*. October 2014; 32(4): 485-90. doi: 10.1016/j.det.2014.06.008. Epub 2014 Jul 29.
15. Gormley EA, Lightner DJ, Burgio KL et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA (American Urological Association)/SUFU guideline. American Urological Association Education and Research, Inc. Available at http://www.auanet.org/education/guidelines/overactive-bladder.cfm. Published May 2014. Accessed June 14, 2017.
16. Gormley EA, Lightner DJ, Faraday M, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *Journal of Urology*. 2015; 193(5): 1572-1580.
17. Nambiar A, Lucas M. Chapter 4: Guidelines for the diagnosis and treatment of overactive bladder (OAB) and neurogenic detrusor overactivity (NDO). *Neurourol Urodynam.* 2014; 33(S3): S21-S25.

Esophageal Achalasia

18. Vaezi MF, Pandolfino JE, Vela MF. ACG (American College of Gastroenterology) clinical guideline: Diagnosis and management of achalasia. Am J *Gastroenterol.* 2013; 108(8): 1238-1259.

Hirschsprung's Disease, Internal Anal Sphincter Achalasia

19. Koivusalo AI, Pakarinen MP, Rintala RJ. Botox injection treatment for anal outlet obstruction in patients with internal anal sphincter achalasia and Hirschsprung's disease. *Pediatr Surg Int.* 2009; 25: 873-876.
20. Wesson DE. Congenital aganglionic megacolon (Hirschsprung disease). In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at www.uptodate.com. Accessed June 14, 2017.

Chronic Anal Fissures

21. Nelson RL, Thomas K, Morgan J, Jones A. Non-surgical therapy for anal fissure. *Cochrane Database of Sys Rev*. February 15 2012; (2): CD003431. doi: 10.1002/14651858.CD003431.pub3.
22. Utzig MJ, Kroesen AJ, Buhr HJ. Concepts in pathogenesis and treatment of chronic anal fissure: A review of the literature. *Am J Gastroenterol*. 2003; 98(5): 968-974.

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits

are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.