Pharmacy Benefit Determination Policy

Policy Subject: Botulinum Toxin A	**Dates:**
Policy Number: SHS PBD32	**Effective Date:** August 23, 2012
Category: Neurotoxin	**Revision Date** May 7, 2018
Policy Type: ☒ **Medical** ☐ **Pharmacy**	**Approval Date:** June 6, 2017
Department: Pharmacy	**Next Review Date:** June 2018
Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	PHP: Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	PHP: Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover Botulinum Toxin [Abobotulinumtoxin (aboBoNT), incobulinumtoxin (incoBoNT), onabotulinumtoxin (onoBoTN)], through the Medical Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines.

Applicable Coding:

J-Code: J0585-87

Clinical Determination Guidelines:

Document the following with chart notes:

I. FDA approved indications
   A. Spasticity
      1. Upper extremity spasticity
         a. Age: ≥ 18 yrs.
         b. Diagnosis & severity:
            - ↑ muscle tone in elbow, wrist, finger & thumb flexors
            - Stroke or other non-stroke related upper extremity spasticity
            - Pain or abnormal hand/forearm position interfering w daily functioning
         c. Exclusions: Prior surgical treatment, infection at injection (inj.) site
      2. Lower extremity spasticity
         a. Age: ≥ 18 yrs.
         b. Diagnosis & severity:
            - ↑ muscle tone in ankle/toe flexors
            - Pain or ↑ muscle tone interfering w daily functioning

B. Chronic Migraine Headaches (HA)
1. Age: > 18yo
2. Diagnosis & severity:
   a. Neurologist evaluated: Established a dx of chronic migraine HA
   b. Frequency/duration: ≥ 15 days/month for > 4hrs/day (for ≥ 3 month)
   c. Severity: Interfering w routine daily functioning
3. Other therapies: Failed or had significant adverse events
   a. Abortive Treatment: Must try ≥ 2 agents from separate classes (≥10 days/mon)
      - Ergotamine derivatives: e.g ergotamine, dihydroergotamine (DHE)
      - Triptans: e.g. sumatriptan
      - Combination analgesic: opioids, acetaminophen, NSAIDS
   b. Preventive Treatment: Must try 2 agents from separate classes (3 mons.)
      - Valproic acid: divalproex (Depakote), valproate (Depacon)
      - Second generation anticonvulsant: topiramate (Topamax)
      - Beta blockers: metoprolol (Lopressor/Toprol XL), propranolol (Inderal), timolol

C. Cervical Dystonia (Spasmodic Torticollis)
1. Age: ≥18 years
2. Diagnosis & severity: Abnormal head position & neck pain interfering w daily functioning
3. Contraindications: Fixed contracture w ↓ ROM, prior surgical tx, infection at inj. site, neuro dx.

D. Blepharospasms, strabismus & hemifacial spasms
1. Age: ≥12 years
2. Diagnosis & severity:
   - Associated w dystonia
   - Benign essential blepharospasm or VII nerve disorders
3. Contraindications: Infection at injection site, neuromuscular disease (e.g. Myasthenia Gravis)

E. Bladder Dysfunction
1. Over active bladder
   a. Age: ≥18yo
   b. Diagnosis & severity:
      - Symptoms of urge urinary incontinence, urgency, & frequency
      - Identified from clinical evaluation
   c. Other therapies (1 each): Failed or had significant AE from anticholinergics & β-3 agonist
2. Neurogenic urinary incontinence
   a. Age ≥ 18 years
   b. Diagnosis & severity:
      - Due to neurological condition (e.g., MS, SCI)
      - Detrusor over-activity
   c. Other therapies:
      - Anticholinergics or β-3 agonist (1 of each): Failed or had significant adverse effects
      - Surgical treatment/balloon sphincter dilatation: Failed or not indicated
3. Contraindications: Acute UTI, acute urinary retention

II. Non-FDA approved indications
- A. Spasticity of Cerebral palsy
  - a. Age: Children (>18mons) & adolescents
  - b. Diagnosis & severity: Physical evidence of focal limb spasticity
  - c. Contraindication: Joint immobilization by a fixed contracture, severe weakness of opposing muscle in the limb for which the injection is intended, diffuse hypertonia
- B. Achalasia
  1. Diagnosis & severity
     - a. Esophageal manometry confirmation
     - b. Upper GI endoscopy: R/o other causes (peptic stricture, CA, lower esoph. compression)
     - c. Progressive dysphagia for liquids & solids
  2. Other therapies
     - a. Long-acting nitrates or Ca channel blockers: Failure or had significant adverse effects
     - b. Pneumatic dilation or surgical myotomy: Unless contraindicated/not indicated
- C. Anal Fissure
  1. Diagnosis & severity: ≥ 2 months of symptoms w ≥1 of the following:
     - a. Nocturnal pain & bleeding
     - b. Post-defecation pain
  2. Other therapies
     - a. Topical nitrates: Failure or significant adverse effects
     - b. Surgery: Unless contraindicated/not indicated
  3. Contraindication: Inflammatory bowel disease, HIV disease, hemorrhoids, anal fistula, perianal abscess, perianal cancer, previous perianal surgery

III. Approval
- A. Initial: 7 months
- B. Re-approval: 1 yr.
  1. Continue to meet criteria for diagnosis as applicable w significant improvement in symptoms:
     - a. Migraine: 50% ↓ in HA frequency/severity (documented in chart notes)

IV. Exclusions:
- A. Movement disorders/spasticity: Spasticity from conditions other than stroke/CP; tremor (essential, head/voice); TD; Motor Tics; Laryngeal dystonia; fixed contracture of joint
- B. Chronic Pain: Myofascial, inflammatory, musculoskeletal, neuropathic, postop., post-herpetic, neck/shoulder pain; HA (acute, episodic, tension, cranial neuralgia, acute, med-overuse, NM dx HA's); plantar fasciitis; brachial plexus injury; trigeminal neuralgia; gynecologic pain syndromes
- C. GI Disorders: Anal sphincter; achalasia; chronic idiopathic constipation (children); gastroparesis; upper esophageal sphincter disorder; sialorrhea
- D. Other: BPH w lower urinary tract sx; clubfeet; gustatory sweating (Frey's); obesity; depression; hyper-lacrimation; masseter hypertrophy; refractory interstitial cystitis; hyperhidrosis

Appendix I: Dosage Regimens

FDA-Approve Indications			
Condition	**Recommended product (Level A-B*)[6]**	**Average Dose**	**Duration of effect**
Upper limb spasticity	A-Dysport (aboBoTN) A-Xeomin (incoBoTN) A-Botox (onoBoTN)	≤ 400 units total given 12.5 - 50 units/site	12 weeks
Lower limb spasticity	A-Botox (onoBoTN) A-Dysport (aboBoTN)	≤ 500 units total given in multiple sites	3 months
Migraine	A-Botox (onoBoTN)	≤ 200 units total given in multiple sites	12 weeks
Neurogenic bladder	NA	200 units total given in multiple sites	8-12 weeks
Overactive bladder	NA	100 units total given in multiple sites	12 weeks
Cervical Dystonia	A-Dysport (aboBoTN) B-Xeomin (incoBoTN) B-Botox (onoBoTN)	200-300 units total given in multiple sites	4 weeks - 3 months
Strabismus	NA	25 units total; 2.5-5 units/site	6-8 weeks to 6-12 months
blepharospasm	B-Xeomin (incoBoTN) B-Botox (onoBoTN)	5 units/site	12.5 weeks
Non-FDA Approved Indications			
Condition		**Average dose**	**Duration of effect**
Spasticity of CP	NA	3-6 units/Kg (max 12 units/Kg); 82-220 total units given in multiple sites	1-6 months
Achalasia	NA	15-25 units/quadrant or ≤ 50units on either side of IAS	Single treatment; may repeat
Anal fissure	NA	20 units both sides	Single injection

**A-Intervention should be offered; B- Intervention should be considered; NA - rating not available*

Appendix II Monitoring and Patient Safety

Drug	Adverse Reactions*	Monitoring	REMS
Dysport abobotulinum toxin Xeomin Incobotulinum Toxin Botox Onabotulinmum Toxin	• Cervical Dystonia: Dysphagia (19%), URI (12%), HA/neck pain (11%) • Blepharospasm: Ptosis (21%), eye dryness, superficial punctate keratitis (6%) • Chronic Migraine: Muscular weakness (4%), Neck pain (9%) • Urinary Incontinence: Urinary retention (17%), UTI (24%) • Upper limb spasticity: Pain in extremity (6-9%) • Strabismus: Ptosis (16-38%)) • Black Box: Dysphagia, breathing difficulties • Pregnancy category C	• Monitor those with motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junction disease (myasthenia gravis, Lambert-Eaton Syndrome)	• No longer required

**Reported by indication*

References and Resources:

1. Onabotulinumtoxin A Milliman Care Guidelines® Ambulatory Care are19th Edition. assessed May 16, 2016
2. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology 2012;78:1337-45.
3. Botox, Migraine, and the American Academy of Neurology: An Antidote to Anecdote. JMCP June 008;14(5); 465-467.
4. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Onbotulinumtoxina injection accessed May 2018.
5. *Clin-eguide Drug Facts and Comparisons eAnswers.* Onbotulinumtoxina [database online]: Wolters Kluwer Health Inc; 2016
6. Practice guideline update summary: Botulinum neurotoxin for the treatment blepharospasm, cervical dystonic, adult spasticity and headache. Neurology 2016;86:818-1826.

Approved By:

	6/27/18
Peter Graham, MD – PHP Executive Medical Director	Date
	6/27/18
Human Resources (Kurt Batteen)	Date