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Executive Summary

Guideline Overview
This guideline provides recommendations for the therapeutic use of botulinum toxin to treat several common conditions in the ambulatory setting. Individual clinician experience may suggest stronger recommendations for some indications, however evidence based conclusions are based on the currently available evidence.

Key Revisions (2017 Periodic Review)
1. Clinical information is emphasized while operational information has been removed.
2. All recommendations are have been ranked by strength and include the quality ranking of the supporting evidence
3. Recommendations have been added for the management of: task-specific dystonia, palatal myoclonus, orofacial dyskinesia due to temporomandibular joint disorder, cricopharyngeal spasm, thyroid-associated orbitopathy, gustatory sweating, and gustatory lacrimation,
4. Evidence now suggests botulinum toxin may be considered for the treatment of essential hand tremor. Previously, insufficient evidence was available to recommend botulinum toxin for this use.

Key Practice Recommendations
1. Botulinum toxin should be administered in the ambulatory setting whenever possible
2. Botulinum toxin should not be considered for indications when there is documented lack of effect or available evidence is insufficient to support use.
3. Patients receiving botulinum toxin should be monitored regularly to ensure achievement of adequate therapeutic response. If initial and/or continuing response to the therapeutic effects of botulinum toxin is not documented, it should be discontinued.

Companion Documents
1. Assessment and Treatment of Migraine- Adult- Emergency/ Ambulatory Setting: https://uconnect.wisc.edu/clinical/cckm-tools/content/?path=/content/cpg/neurology/name-97600-en.cckm
**Scope**

**Disease/Condition(s):** Botulinum toxin is used to treat and prevent disorders from multiple organ systems including cutaneous disorders, endocrine disorders; ear, nose, and throat (ENT) disorders, gastroenterologic disorders, neurologic disorders, ophthalmologic disorders, and urologic disorders.

**Clinical Specialty:** Dermatology, Endocrinology, ENT/Otolaryngology, Gastroenterology, Neurology, Nursing, Ophthalmology, Pharmacy, Physical Medicine and Rehabilitation, Primary Care, Nursing, and Urology

**Intended Users:** Physicians, Advanced Practice Providers, Nurses, Pharmacists, Technical Support, Medication

**Objective(s):** To provide evidence-based guidelines to assist clinicians in determining the benefits of botulinum toxin use in patients with relevant disorders.

**Target Population:** All patients cared for within UW Health with a disorder for which botulinum toxin may be appropriate treatment

**Interventions and Practices Considered:** Botulinum toxin is the sole clinical intervention considered in the guideline, sometimes as a second or third line therapy

**Major Outcomes Considered:**
- Sustained relief or reversal of disorders addressed in the guideline.
- Avoidance/delay of surgical or other invasive procedures
- Decrease in effect due to formation of antibodies to botulinum toxin after prolonged use

**Methodology**

**Methods Used to Collect/Select the Evidence:**
PUBMED searches were conducted by the guideline author(s) and workgroup members to collect evidence for review. Expert opinion and clinical experience were also considered as a valuable source of evidence.

**Methods Used to Formulate the Recommendations:**
Through a collaborative process, the workgroup members agreed to adopt recommendations a consensus through discussion of the literature and expert experience. All recommendations endorsed or developed by the guideline workgroup were reviewed and approved by other stakeholders or committees.
Methods Used to Assess the Quality of the Evidence/Strength of the Recommendations:
Internally developed recommendations, or those adopted from external sources without an assigned evidence grade, were evaluated by the guideline workgroup using an algorithm adapted from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology (see Figure 1 in Appendix A).

Rating Scheme for the Strength of the Evidence/Recommendations:
See Appendix A for the rating scheme(s) used within this document.

Cost Analysis: The UW Health acquisition cost:
- OnabotulinumtoxinA 100 unit vial (Botox®) ~ $580
- RimabotulinumtoxinB 5000 unit vial (Myobloc®) ~ $530

Recognition of Potential Health Care Disparities: Botulinum toxin is a costly resource. Therefore there may be barriers to consistent access depending on financial circumstances.

Introduction
Botulinum toxin (BoNT) is a potent neuroinhibitor that prevents the release of acetylcholine within the neuromuscular junction.\(^1,2\) Two different formulations, BoNT type A (Botox®, Dysport®, Xeomin®) and BoNT type B (Myobloc®), are FDA-approved. These formulations vary in their activity and intracellular targets; therefore, they are not considered interchangeable. Botulinum Toxin type A prevents acetylcholine release by cleavage of a synaptosome-associated protein of 25,000 daltons.\(^1\) Botulinum neurotoxin type B has been shown to inhibit neurotransmitter release by cleaving vesicle associated membrane protein.\(^2\)

Four botulinum toxin products are available on the US market:
- onabotulinumtoxinA (Botox®) – included on the UW Health formulary
- abobotulinum toxin A (Dysport®) - nonformulary
- incobotulinum toxin A (Xeomin®) - nonformulary
- rimabotulinum toxin B (Myobloc®) - included on the UW Health formulary

At this time, Botox® is the preferred formulary agent available at UW Health; however, Myobloc® is also available. Patients may develop antibodies to BoNT type A, but due to differing mechanisms of action may still respond to BoNT type B. One review by Yablon et al.\(^3\) found the overall prevalence of BoNT type A antibodies to be 0.5% in 191 patients treated for post-stroke spasticity. In these cases, it may be acceptable to treat patients with BoNT type B.

Botulinum toxin is used in the treatment of many spastic conditions, movement, and autonomic disorders. Since its’ FDA approval in the late 1980s, BoNT has been studied in many disease states. The American Academy of Neurology has published reports and recommendations that provide evidence and recommendations across a broad range of clinical uses.\(^4-7\) This guideline offers evidence-based recommendations for use of BoNT at UW Health.
Botulinum toxin should be administered in the ambulatory setting whenever possible. However, there are situations where it may be clinically appropriate to administer in the inpatient setting. For additional details regarding inpatient use of botulinum toxin, please refer to UWHC Policy 6.1.9 Restricted Primarily Ambulatory Administered Medications in Hospitalized Patients. Botulinum toxin use requires pharmacy department review as described in UWHC Policy 6.1.5 Formulary Restricted Clinic Administered Medication Pharmacy Department Review and Use of Non-UW Health Supplied Medications Administered in Clinics.
Recommendations
1. Indications for Use of Botulinum Toxin

1.1. Movement Disorders

1.1.1. Cervical dystonia (spasmodic torticollis) defined as clonic and/or tonic involuntary contractions of multiple neck muscles with sustained head torsion and/or tilt and limited range of motion in the neck with duration of at least 6 months. There are several high quality placebo-controlled trials and other evidence that support the use of BoNT for treatment of cervical dystonia\textsuperscript{1,2,8-24} and all four products are FDA approved for this indication. BoNT should be offered to patients. (UW Health High quality evidence; strong recommendation)

1.1.2. Spasticity –

1.1.2.1. Cerebral Palsy – High quality evidence supports the use of BoNT for treatment of spasticity due to cerebral palsy.\textsuperscript{25-38} BoNT should be offered to patients in the setting of cerebral palsy with spasticity or dystonia in addition to physical/occupational therapy, conventional therapies (e.g., baclofen), or splinting. (UW Health High quality evidence; strong recommendation)

1.1.2.2. Upper and lower extremity spasticity – High quality evidence supports the use of BoNT for treatment of upper and lower extremity spasticity.\textsuperscript{39-55} BoNT should be offered to treat spasticity resulting from a stroke, traumatic or non-traumatic spinal cord injury, multiple sclerosis or other demyelinating disease of the central nervous system, traumatic brain injury or other central process with BoNT injections as a component of a documented rehabilitation and strengthening program. (UW Health High quality evidence; strong recommendation)

1.1.3. Hemifacial spasm- Moderate quality evidence supports the use of BoNT for treatment of hemifacial spasm.\textsuperscript{56-67} BoNT is a reasonable treatment and should be considered for patients before administration of oral medications. (UW Health Moderate quality evidence; strong recommendation)

1.1.4. Task specific dystonia- Moderate quality evidence supports the use of BoNT for treatment of task specific dystonias,\textsuperscript{68-72} including writer’s and musician’s cramp. BoNT is a reasonable treatment and should be considered as first line therapy. (UW Health Moderate quality evidence; strong recommendation)

1.1.5. Essential hand tremor- Moderate quality evidence supports the use of BoNT for treatment of essential hand tremor.\textsuperscript{73,74} Treatment with BoNT is reasonable and should be considered in selected patients after oral medications are documented to be ineffective or when the patient is at high risk of experiencing adverse effects. (UW Health Moderate quality evidence; strong recommendation)

1.1.6. Facial synkinesia– Moderate quality evidence supports the use of BoNT for treatment of facial synkinesia resulting from Bell’s palsy or injury.\textsuperscript{75-82} Treatment with BoNT is reasonable and should be considered as part of a documented comprehensive plan for physical rehabilitation such as occupational therapy. (UW Health Moderate quality evidence; strong recommendation)

1.1.7. Torsion dystonia – Low quality evidence supports the use of BoNT for treatment of torsion dystonia.\textsuperscript{83-86} Treatment with BoNT may be considered after oral therapies are documented to be ineffective or when the patient is documented to be at high risk for experiencing adverse effects. (UW Health Low quality evidence; strong recommendation)

1.1.8. Congenital muscular torticollis– Low quality evidence supports the use of BoNT for treatment of congenital muscular torticollis.\textsuperscript{87-92} Treatment with BoNT may be considered after conservative treatment, including physical therapy or stretching, is documented to be ineffective. (UW Health Low quality evidence; strong recommendation).
1.1.9. Essential head tremor- Low quality evidence supports the use of BoNT for treatment of essential head tremor. Treatment with BoNT may be considered in patients after oral medications are documented to be ineffective or when the patient is documented to be at high risk for experiencing adverse effects. (UW Health Low quality evidence; strong recommendation)

1.1.10. Palatal myoclonus- Low quality evidence supports the use of BoNT for treatment of palatal myoclonus. Treatment with BoNT may be considered in this population. Benefit is modest; however there are few treatment options for this disorder. (UW Health Low quality evidence; weak/conditional recommendation)

1.1.11. Cervical or facial tic disorder (not including ocular tics)- Low quality evidence supports the use of BoNT for treatment of tics. Treatment with BoNT may be considered for patients after oral medications are documented to be ineffective or when patients are documented to be at high risk for adverse effects. (UW Health Low quality evidence; strong recommendation)

1.1.12. Orofacial dyskinesia due to temporomandibular joint disorder- Low quality evidence supports the use of BoNT for treatment of temporomandibular joint disorders. Treatment with BoNT may be considered after splints, physical therapy, or orally administered medications are documented to be ineffective or when patients are documented to be at high risk of adverse effects. (UW Health Low quality evidence; strong recommendation)

1.2. Throat Disorders

1.2.1. Laryngeal spasm (spasmodic dysphonia/ voice tremor, refractory chronic cough, refractory laryngospasm/paradoxical vocal fold motion [PVFM], refractory muscle tension dysphonia)- Moderate quality evidence supports the use of BoNT for treatment of spasmodic dysphonia or voice tremor. Treatment with BoNT is reasonable and should be considered for patients. There is a distinct lack of alternative pharmacologic therapies established as effective for this indication. (UW Health Moderate quality evidence; strong recommendation)

1.2.2. Cricopharyngeal spasm- Low quality evidence supports the use of BoNT for treatment of cricopharyngeal spasm. Treatment with BoNT may be considered in selected patients who wish to avoid mechanical dilation or surgery. (UW Health Low quality evidence; weak/conditional recommendation)

1.3. Ophthalmic Disorders

1.3.1. Blepharospasm- High quality evidence supports the use of BoNT A for the treatment of blepharospasm. It should be offered to patients especially when associated with dystonia. (UW Health High quality evidence; strong recommendation)

1.3.2. Strabismus- Low quality evidence supports the use of BoNT for the treatment of strabismus. A meta-analysis confirms that the majority of evidence is based on retrospective studies, prospective cohorts, or case reviews. Randomized controlled trials show varying responses to BoNT administration. Treatment with BoNT may be considered in these patients. (UW Health Low quality evidence; weak/conditional recommendation)

1.3.3. Thyroid associated orbitopathy- Low quality evidence supports the use of BoNT for the treatment of orbitopathy associated with Grave’s Disease. Treatment with BoNT may be considered in patients that wish to avoid surgery. (UW Health Low quality evidence; weak/conditional recommendation)

1.4. Gastrointestinal Disorders

1.4.1. Esophageal achalasia- Moderate quality evidence supports the use of BoNT for the treatment of esophageal achalasia. Although the initial esophageal relaxation success rate with BoNT is high and comparable to surgical myotomy and pneumatic dilation, the effect is temporary and requires repeated administration. Treatment with BoNT is reasonable and should be considered for patients who are at high risk of adverse effects as a result of pneumatic balloon dilation or surgical myotomy. (UW Health Moderate quality evidence; weak/conditional recommendation).
1.4.2. Chronic anal fissures- Moderate quality evidence supports the use of BoNT for the treatment of anal fissures.\textsuperscript{175-183} Lateral internal sphincterotomy has better long term results, however it presents a risk of incontinence.\textsuperscript{177} Treatment with BoNT is reasonable and should be considered for patients with documentation of therapeutic failure, contra-indication, or intolerance to conventional therapy, including topical nitrates and calcium channel blockers, and who wish to avoid surgery. (UW Health Moderate quality evidence; strong recommendation).

1.5. \textbf{Hypersecretory Disorders-}

1.5.1. Axillary hyperhydrosis - High quality evidence supports the use of BoNT for the treatment of axillary hyperhydrosis in patients inadequately managed with topical antiperspirants.\textsuperscript{184-197} Treatment with BoNT should be offered to these patients. While BoNT is effective, only patients with a documented failure of topical antiperspirants should receive it because topical antiperspirants are readily available, inexpensive, and associated with few adverse effects. (UW Health High quality evidence; strong recommendation).

1.5.2. Palmar/ plantar hyperhydrosis- Moderate quality evidence supports the use of BoNT for the treatment of palmar/ plantar hyperhydrosis.\textsuperscript{198-211} Treatment with BoNT is reasonable and should be considered for patients with documented therapeutic failure, contra-indication, or intolerance to systemic (i.e. anticholinergics) or topical therapy. BoNT should also be considered for those seeking an alternative to iontophoresis. Injections can be painful on the hands/ feet and there is risk of temporary local muscle weakness. (UW Health Moderate quality evidence; strong recommendation).

1.5.3. Sialorrhea- Moderate quality evidence supports the use of BoNT for the treatment of sialorrhea in patients with Parkinson’s Disease, cerebral palsy, amyotrophic lateral sclerosis, and other motor neuron disorders.\textsuperscript{212-235} Treatment with BoNT is reasonable and should be considered for patients whose quality of life is significantly negatively impacted by sialorrhea. Caution should be used, as BoNT may worsen symptoms of dysphagia. The efficacy of BoNT B is better supported by evidence. (UW Health Moderate quality evidence; strong recommendation).

1.5.4. Gustatory sweating (Frey’s Syndrome)- Low quality evidence supports the use of BoNT for the treatment of gustatory sweating.\textsuperscript{236} Treatment with BoNT may be considered for patients. (UW Health Low quality evidence; weak/ conditional recommendation)

1.5.5. Gustatory lacrimation (crocodile tears)- Low quality evidence supports the use of BoNT for the treatment of gustatory lacrimation.\textsuperscript{237,245} Treatment with BoNT may be considered as few treatment options are available for this indication. (UW Health Low quality evidence; weak/ conditional recommendation).

1.6. \textbf{Urinary incontinence-}

1.6.1. Neurogenic detrusor overactivity- High quality evidence supports the use of BoNT for the treatment of neurogenic detrusor overactivity.\textsuperscript{246,256} Treatment with BoNT should be offered to patients who use clean, intermittent catheterization and who have a documented therapeutic failure of behavior modifications or physical therapy, Documentation of therapeutic failure, contra-indication, or intolerance to anticholinergic medications is also required. (UW Health High quality evidence; strong recommendation)

1.6.2. Overactive (idiopathic, non-neurogenic) bladder- High quality evidence supports the use of BoNT for the treatment of idiopathic overactive bladder.\textsuperscript{257,275} Treatment with BoNT should be offered to carefully selected patients who are documented to be refractory to first line (behavioral) and second line (anticholinergic) overactive bladder therapies. Transient post void residual (PVR) may be high after BoNT administration. Therefore patients should be willing to have the PVR monitored closely and be willing and able to perform self-catheterization if necessary. (UW Health High quality evidence; strong recommendation)
1.6.3. Detrusor sphincter dyssynergia—Moderate quality evidence supports the use of BoNT for the treatment of detrusor sphincter dyssynergia resulting from spinal cord injury. Treatment with BoNT is reasonable and should be considered for these patients. (UW Health Moderate quality evidence; strong recommendation)

Low quality evidence supports the use of BoNT for the treatment of detrusor sphincter dyssynergia resulting from multiple sclerosis when confirmed by urodynamic testing. Treatment with onabotulinumtoxin A may be considered as it may increase voiding volume, decrease detrusor pressures, and/or improve bladder emptying in a population with few treatment options. (UW Health low quality evidence; weak/conditional recommendation)

1.7. Headache

1.7.1. Chronic migraine headache—High quality evidence supports the use of BoNT for the prevention of chronic migraine headache. Treatment with BoNT should be offered to disabled (significantly limited in ability to work, attend school, maintain household, or participate in social/leisure activities) patients who experience chronic migraines; headaches lasting at least 4 hours per day at least 15 days per month for at least 3 months. Criteria for migraine must be met at least 8 days out of the month. Patients should have documentation of therapeutic failure, contra-indication, or intolerance to conventional migraine prophylactic medications such as beta adrenergic blockers (propranolol) and tricyclic antidepressants (amitriptyline) or neuromodulators (divalproex). BoNT should be prescribed by a headache specialist as part of a comprehensive headache management plan to decrease the number of days the patient experiences migraines. Patient should report improvements with successful use of BoNT, including less medication use, fewer visits to the emergency department, urgent care center, clinic, or fewer work/school days missed. Currently only onabotulinum toxin A is FDA approved for preventing chronic migraine headache. (UW Health High quality evidence; strong recommendation)

2. Indications for Which Insufficient Data Exist to Warrant Use

Treatment with BoNT should not be considered when lack of effect is documented or available evidence is insufficient to support use.

2.1. Benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) High quality evidence does not support use of BoNT for this indication. Results of clinical studies do not provide adequate evidence of clinical benefit. (UW Health high quality evidence; strong recommendation)

2.2. Chronic neck (cervicalgia)/back pain: Moderate quality evidence does not support use of BoNT for treatment of cervicalgia or low back pain. Results from clinical studies do not provide adequate evidence of clinical benefit. (UW Health low quality evidence; strong recommendation)

2.3. Raynaud’s Disease- Low quality evidence does not support use of BoNT for the treatment of Raynaud’s Disease. Results from clinical studies do not provide adequate evidence of clinical benefit. (UW Health low quality evidence; strong recommendation)

2.4. Acute/episodic migraine—High quality evidence does not support use of BoNT for the prophylaxis of acute migraine. Results from clinical studies do not provide adequate evidence of clinical benefit. (UW Health high quality evidence; strong recommendation)

2.5. Tension headache—Moderate quality evidence does not support use of BoNT for the prophylaxis of tension headaches. Results from clinical studies do not provide adequate evidence of clinical benefit. (UW Health moderate quality evidence; strong recommendation)

2.6. Restless leg syndrome—Low quality evidence does not support use of BoNT for the treatment of restless leg syndrome. Results from clinical studies do not provide adequate evidence of clinical benefit. (UW Health low quality evidence; strong recommendation)
3. **Aesthetic/ Cosmetic Uses**

3.1. Glabellar lines
3.2. Horizontal facial rhytids
3.3. Crow’s feet
3.4. Bunny lines
3.5. Perioral area
3.6. Dimpled chin
3.7. Platysmal bands

4. **Assessment for Allowance and Coverage**

All patients will undergo insurance screening for coverage prior to receipt of botulinum toxin therapy. Insurance company-specific prior authorization criteria will be reviewed, coverage will be verified, and authorization will be documented in the EMR prior to receipt of the first dose of botulinum toxin therapy. Not all insurance companies will cover botulinum toxin for all indications or doses, especially when the recommendation strength is weak or conditional. For cosmetic uses, a payment plan is established prior to administration of botulinum toxin. Additionally, continued coverage is reviewed prior to each subsequent administration of botulinum toxin.

5. **Usual Dosing**

Dosing of BoNT is highly individualized based on condition, patient characteristics, affected muscle groups, and patient response. It is recommended to use the lowest effective dose and to separate treatments by the longest interval tolerated to avoid adverse effects and minimize antibody formation. Three months is generally recommended between injections for spastic conditions. Various methods, such as electromyography and electrical stimulation, are used to localize the involved muscle groups. The following represent usual or starting doses of onabotulinumtoxin A (Botox) for common conditions. Specific patient doses may vary. Please note that insurers may not provide coverage for doses higher than those presented in package inserts or generally recognized drug information databases.

5.1. **Movement Disorders**

5.1.1. Cervical dystonia

5.1.1.1. Dose and location of injections should be individualized for each patient and is dependent on previous exposure

5.1.1.2. Previously untreated: The mean dose should be less than 236 units.

5.1.1.3. Previously treated: dose is dependent on head/neck position, localization of pain, muscle hypertrophy, patient response; and previous adverse reactions. The mean dose is 236 units divided among affected muscles

5.1.2. Spasticity and non-cervical dystonia in adult and pediatric patients

5.1.2.1. 0.5 – 20 units/kg with a maximum dose of 400 – 600 units; initiate therapy at the lower end of the dose range

5.1.3. Hemifacial spasm

5.1.3.1. Mean dose per treatment session = 25 units divided (range = 7.5 – 100 units). Start at low end of range and titrate based on effectiveness and adverse effects. Higher doses are reserved for patients refractory to lower doses. The cumulative dose for treatment of hemifacial spasm in a 30 day period should not exceed 200 units.

5.2. **Throat Disorders**

5.2.1. Laryngeal spasm (spasmodic dysphonia/tremor): 0.1-7.5 units

5.3. **Ophthalmic Disorders**

5.3.1. Blepharospasm: typical initial dose is 2.5 units per injection in 5-6 sites around each eye. Subsequent doses can be increased to 7.5-10 units per injection in six or more sites around each eye.
eye. The cumulative dose for treatment of blepharospasm in a 30-day period should not exceed 200 units.

5.3.2. Strabismus: 1.25-5 units per muscle initially

5.4. Gastrointestinal Disorders

5.4.1. Esophageal achalasia: 100 units divided in at least 4 quadrants (maximum dose = 100 units)

5.4.2. Chronic anal fissure: 20-30 units

5.5. Hypersecretory Disorders

5.5.1. Axillary hyperhidrosis: 50-75 units per axilla divided

5.5.2. Palmar hyperhidrosis: 50-100 units per palm divided

5.5.3. Sialorrhea: 10-50 units per gland

5.6. Urinary incontinence

5.6.1. Detrusor sphincter dyssynergia: 100 units

5.6.2. Neurogenic detrusor overactivity: 200-300 units

5.6.3. Nonneurogenic detrusor overactivity: 100 units administered no more frequently than every 12 weeks

5.7. Migraine Headache: 155 units divided into 31 sites administered every 12 weeks. Up to 40 units may be added if necessary after the second administration (total should not exceed 195 units).

5.8. Cosmetic use

5.8.1. Glabellar lines: 20-30 units total for women and 30-40 total units for men

5.8.2. Horizontal forehead rhytids: 10-20 total units for women and 20-30 total units for men

5.8.3. Crow’s feet: 12-30 units total

5.8.4. Bunny lines: 2-5 units total

5.8.5. Perioral area: 4-10 units total

5.8.6. Dimpled chin: 2-6 units total for women and 2-8 units total for men

5.8.7. Platysmal bands: highly variable

6. Patient Monitoring

6.1. Patients should be monitored for efficacy and toxicity throughout treatment. Goals of therapy may vary depending on condition and patient specific variables. However goals should be established prior to initiation of treatment for all patients. After 6-12 months of treatment, if adequate response is not achieved, consideration should be given to alternative treatments which may include use of a different serotype or discontinuation of botulinum toxin.

7. Contraindications

7.1. If active infection is present at the site of injection, botulinum toxin is contraindicated.

7.2. If a patient has a known reaction or hypersensitivity to botulinum toxin or any ingredients use is contraindicated.

UW Health Implementation

Potential Benefits: Botulinum toxin will be used in a consistent, evidence-based, cost-effective manner throughout UW Health.
Potential Harms: Patients may experience adverse effects to botulinum toxin, even when receiving it for an approved indication and at a recommended dose.

Pertinent UW Health Policies & Procedures
1. UW Health Policy 8.30: Management of Clinic Administered Medications with Internal Pharmacy Prior Authorization
2. UW Health Policy 8.95: Restricted Clinic Administered Medications in Hospitalized Patients.

Patient Resources
1. UW Health Botulinum Toxin Consent Form
2. Health Facts for You #6370 Trigger Point Injections
3. UW Health Facial Nerve Paralysis Questionnaire
4. Medication guides are available for each specific product. Health professionals should urge patients, their families, and caregivers to review it carefully.


Guideline Metrics
1. Periodic medication use evaluation of botulinum toxin

Implementation Plan/Clinical Tools:
The restriction of botulinum toxin to appropriate, evidence-based indications will be operationalized by pharmacist review for appropriate indication. Applicable paper orders will reflect current recommendations in the guideline. Prescribers, pharmacists, and nursing staff will be educated about the guideline through electronic distribution.

Disclaimer: This Clinical Practice Guideline provides an evidence-based approach for the use of botulinum toxin. It is understood that occasionally patients will not match the conditions addressed in the guideline.
Appendix A. Evidence Grading Scheme(s)

Appendix A. GRADE Methodology adapted by UW Health

<table>
<thead>
<tr>
<th>GRADE Ranking of Evidence</th>
<th>Description</th>
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<tbody>
<tr>
<td>High</td>
<td>We are confident that the effect in the study reflects the actual effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>We are quite confident that the effect in the study is close to the true effect, but it is also possible it is substantially different.</td>
</tr>
<tr>
<td>Low</td>
<td>The true effect may differ significantly from the estimate.</td>
</tr>
<tr>
<td>Very Low</td>
<td>The true effect is likely to be substantially different from the estimated effect.</td>
</tr>
</tbody>
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<table>
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<tr>
<th>GRADE Ratings for Recommendations For or Against Practice</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>The net benefit of the treatment is clear, patient values and circumstances are unlikely to affect the decision.</td>
</tr>
<tr>
<td>Weak/conditional</td>
<td>Recommendation may be conditional upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented.</td>
</tr>
</tbody>
</table>
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