

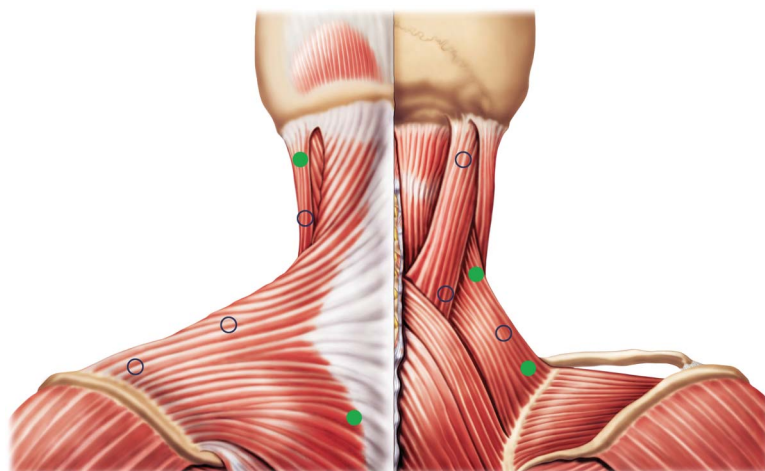
# Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache

## Payment policy perspectives

Raghav Govindarajan, MD; Katie M. Shepard; Constantine Moschonas, MD; Jack J. Chen, PharmD, BCPS, CGP

### Abstract

This article is presented as a companion to the American Academy of Neurology guideline update on the use of botulinum neurotoxin (BoNT) for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache. Whereas the guideline update provides clarity on the efficacy of different BoNT-branded preparations for the 4 listed indications, this companion piece identifies ambiguities in the evidence for efficacy among various brand names for a given clinical indication, their dosing equivalencies, as well as different clinical indications. This article provides guidance and background information to reduce obstacles for third party payment, especially when uncertainties exist and levels of evidence are lower. *Neurol Clin Pract* 2016;6:1-6



The first American Academy of Neurology (AAN) guideline on the use of botulinum toxin (BoNT), published in 2008, focused predominantly on the pharmacology and immunology of the toxin.<sup>1-3</sup> The guideline also reviewed a variety of clinical indications, with recommendations of efficacy based on the toxin as a whole. Furthermore, there was insufficient evidence to recommend the use of BoNT for chronic migraine.

Since then, there has been more evidence on the efficacy of different brand formulations for different indications as well greater understanding of the differences in pharmacology and immunology between the toxin A and B serotypes and branded formulations. However, there are

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*There are still multiple gaps in evidence for efficacy among various brand names for a given clinical indication, their dosing equivalencies, as well as different clinical indications.*

no consistent studies that establish dosing equivalencies among these brands. Further evidence has emerged on the efficacy of BoNT for chronic migraine.<sup>4,5</sup>

The newly revised AAN guideline<sup>6</sup> focuses on the use of BoNT in 4 clinical indications, including chronic migraine. Furthermore, for each of these indications, the guideline provides evidence of efficacy for each brand currently approved in the United States rather than the toxin class as a whole. Although traditionally payment policies covered BoNT A and B either separately or under a single policy, future policies might be more inclined to cover a specific brand for a given clinical indication. It is therefore prudent that providers be aware of BoNT brands, respective indications, and current payer policies.

Although the update to the original BoNT guideline does provide brand-specific evidence for the 4 described clinical indications, there are still multiple gaps in evidence for efficacy among various brand names for a given clinical indication, their dosing equivalencies, as well as different clinical indications. Although this could spur future research, payers still expect data and justification to satisfy current covered diagnoses (i.e., on-label and off-label indications). In this article, we discuss solutions to coverage situations that can result from incomplete evidence.

### **Blepharospasm**

Two Class I comparative effectiveness trials of onabotulinum toxin A with incobotulinum toxin A have provided evidence of equal efficacy between the 2 toxins.<sup>7</sup> Similarly, 1 Class II comparative effectiveness trial between abobotulinumtoxin A and onabotulinum toxin A has provided evidence of equal efficacy.<sup>7</sup> There are no data on the efficacy of rimabotulinum toxin B, so providers who choose to use it for this indication may need to be prepared to defend their BoNT choice in the event of a payer denial. If higher doses than those specified in the product insert are administered, the responsibility falls on providers to justify and clearly document the need in certain patient populations.

### **Chronic migraine**

Two Class I studies comparing onabotulinumtoxin A with placebo have provided evidence of efficacy by reducing the number of headache days in patients with chronic migraine.<sup>4,5</sup> There have been no comparative effectiveness trials between BoNT and oral prophylactic drugs used to treat chronic migraine. Given the high costs of BoNT and the high prevalence of chronic migraine, some payers (e.g., Anthem, BCBS, Highmark) have instituted a step therapy in their treatment (e.g., oral prophylactic would have to be tried and fail before onabotulinumtoxinA could be offered as a treatment option). In such cases, it is imperative that providers clearly document compliance with step therapy criteria and obtain prior authorization before they start using onabotulinumtoxinA for treatment of chronic migraine.<sup>8</sup> It is also prudent that a headache diary be maintained by the patient to show efficacy in case payers question its benefit and ultimately deny coverage. Data for other BoNT formulations in the treatment of chronic migraine did not meet inclusion criteria for the updated guidelines; before using other BoNT brands, providers should check with payers for migraine coverage.

For episodic migraine, the guideline clearly states that use of onabotulinumtoxinA is ineffective. Providers should not be surprised if payers do not cover BoNT for treatment of episodic

## Payers often adopt BoNT package insert statements on maximum allowable doses and injection frequency for determination of coverage.

migraine. It is important to clearly document that the patient's headache symptoms meet the *International Classification of Headache Disorders* definition of chronic migraine (e.g.,  $\geq 15$  days per month) to prevent denials.<sup>9</sup>

### Cervical dystonia

Based on the guideline findings, all brands of BoNT should enjoy payer coverage for the treatment of cervical dystonia. Although comparative dosing efficacies and equivalencies among different brands are not clearly established, we do not foresee any payer denials when there is a medical indication to change from 1 brand to another given the extensive evidence of efficacy of BoNTs for this indication. Additional research in this area using meta-analytical methods, such as mixed-treatment comparisons, will introduce additional data for evidence-based statements on the comparative efficacy of the BoNT brands.

### Adult spasticity

Abobotulinumtoxin A and onabotulinumtoxin A have been shown to reduce upper-limb hypertonia with improvement of passive function.<sup>10,11</sup> Onabotulinumtoxin A was found through comparative effectiveness studies to be superior to tizanidine in improving wrist flexor tone.<sup>12</sup> Some payers may have a step therapy requirement or require documentation of failure of other standard medical therapies. Providers should periodically keep up with local payer policies and reimbursement changes.<sup>13</sup> For reduction of lower-limb hypertonia, abobotulinumtoxin A and onabotulinumtoxin A can be offered as treatment options.<sup>14,15</sup>

### Dosing

Dosing for BoNT drugs, as listed on the product insert, may not be sufficient for patients with cervical dystonia for their initial—and especially subsequent—injections. Dosing should be based on provider experience and the patient's functional goals for initial and subsequent treatments. Payers often adopt BoNT package insert statements on maximum allowable doses and injection frequency for determination of coverage. To reduce likelihood of denials, providers should be familiar with branded product labeling parameters for dosage and intervals. Documenting responsiveness or lack of responsiveness to make dosing changes including escalation is good clinical practice and will demonstrate medical necessity, especially if doses or injection intervals fall outside the payer's allowable parameters. Payers may appreciate a written procedure note that indicates the injected sites and notes the specific dosages injected at each site. This is also good clinical practice, as it will better enable reproduction of injections at future visits.

### What if my payer doesn't have a coverage policy on botulinum toxins?

Correct coding (using Current Procedural Terminology [CPT] and ICD-10-CM) is essential for successful integration of BoNT therapy into clinical practice, and it is important for providers to periodically keep up with policies and reimbursement changes.<sup>13</sup> Each of the BoNT manufacturers has specialists to assist in reimbursement issues (e.g., prior authorization, billing and coding, insurance verification, local coverage policy support, claims denials and appeals). Medicare, Medicaid, and private insurances cover BoNT treatment for on- and off-label uses that are considered medically necessary. Based on a review of current payer policies and anecdotal experience, if BoNT is used for an off-label condition in which it is considered

**Table CPT codes for botulinum toxin injections**

|                          |                                                                                                                                                               |
|--------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>64615</b>             | Chemodenervation of muscle(s); muscle(s) innervated by facial, trigeminal, cervical spinal and accessory nerves, bilateral (e.g., for chronic migraine)       |
| <b>64616</b>             | Chemodenervation of muscle(s); neck muscle(s), excluding muscles of the larynx, unilateral (e.g., for cervical dystonia, spasmodic torticollis)               |
| <b>64617</b>             | Chemodenervation of muscle(s); larynx, unilateral, percutaneous (e.g., for spasmodic dysphonia), includes guidance by needle electromyography, when performed |
| <b>64642</b>             | Chemodenervation of one extremity; 1–4 muscle(s)                                                                                                              |
| <b>64643<sup>a</sup></b> | Chemodenervation of one extremity; each additional extremity, 1–4 muscle(s), (Use 64613 in conjunction with 64642, 64644)                                     |
| <b>64644</b>             | Chemodenervation of one extremity; 5 or more muscle(s)                                                                                                        |
| <b>64645<sup>a</sup></b> | Chemodenervation of one extremity; each additional extremity, 5 or more muscle(s), (Use 64645 in conjunction with 64644)                                      |
| <b>64646</b>             | Chemodenervation of trunk muscle(s); 1–5 muscle(s)                                                                                                            |
| <b>64647</b>             | Chemodenervation of trunk muscle(s); 6 or more muscle(s)                                                                                                      |
| <b>76942</b>             | Ultrasonic guidance for needle placement (e.g., biopsy, aspiration, injection, localization device), imaging supervision and interpretation                   |
| <b>95873<sup>a</sup></b> | Electrical stimulation for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)                          |
| <b>95874<sup>a</sup></b> | Needle electromyography for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)                         |

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<sup>a</sup>Add-on code, report in conjunction with an appropriate base code.

standard of care (i.e., a covered diagnosis), it will generally be approved. Although private insurance policies are generally universal, Medicare policies can vary from state to state. Providers should keep up-to-date with their state Medicare policies.

Novitas Solutions—the Part B Medicare administrative contractor for several states—announced in July 2013 that it had retired its coverage policy on BoNTs retroactively effective to January 18, 2013.<sup>16</sup> It is also possible that some payers might not have updated their policies and in rare cases not even have a policy in place on the use of BoNT. It is imperative that providers check their patients' payer policies periodically.

With traditional Medicare, no prior authorization is needed for BoNT, and payment will occur if the procedure is covered on the state's policy and if proper linkage between ICD-10-CM code and CPT code (table) is documented. For patients with private insurance or Health Maintenance Organization Medicare/Medicaid, prior authorization for BoNT should be obtained, even for on-label indications. A letter of medical necessity should be included with the prior authorization request. Clear and consistent documentation of medical necessity and therapeutic benefit is necessary, especially in cases in which BoNT is needed long-term or should a payer audit occur.

### Other considerations

**Improvements in muscle hypertonicity and functional improvement** For some indications in the guideline, the studies included are characterized by dissimilar endpoint assessments for muscle hypertonicity and functional outcomes, which can make direct comparisons of BoNT brands challenging. Future studies and methodologies (e.g., mixed-treatment comparison) will have to be designed to address this important question. From a practice perspective, documentation of medical necessity for BoNT treatment in the 4 indications is essential. For instance, for initiation and long-term treatment of spasticity and muscle hypertonicity, providers should

document BoNT use for reduction in hypertonicity and/or functional gains (e.g., pain relief, to assist in posturing and walking, to prevent joint contracture or future growth, to allow better range of motion, to permit better physical therapy or use of other therapeutic modalities, and to reduce severe spasm in order to provide adequate perineal hygiene). Evidence of such documentation will also avoid issues should a payer audit occur.

**Using EMG or ultrasound for guided injections** EMG, muscle stimulation, and ultrasound can be used independently or together based on clinical necessity and are reimbursable. For example, Medicare allows for EMG or electrical stimulation to be performed with ultrasound guidance. Use of these techniques can optimize clinical efficacy. Although studies have shown that EMG- and ultrasonography-guided injection of BoNT is more likely to reach the targeted muscle as well as its endplate in treatment of spasticity,<sup>17,18</sup> it remains unclear whether injections using EMG or ultrasonography guidance result in greater functional improvement than nonguided injections. Although generally payers will not question EMG or ultrasound for BoNT, there are no clear payer policies on the use of guided injections, and their use depends on the experience and comfort level of the individual providers.

## CONCLUSION

Many providers are adding or already offer BoNT procedures to their practice. With the updated guidelines, providers are now current with the latest evidence base for use of each BoNT formulation for various neurologic indications. Once a clinically appropriate patient has been identified, knowledge of reimbursement elements is essential for successful integration of BoNT procedures into clinical practice. The BoNT therapeutic space is evolving at a rapid pace and providers are encouraged to stay up-to-date with changes in the scientific literature and reimbursement landscape.

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## AUTHOR CONTRIBUTIONS

Raghav Govindarajan: study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content. Katie Shepard: study concept and design, critical revision of the manuscript for important intellectual content. Constantine Moschonas: critical revision of the manuscript for important intellectual content. Jack J. Chen: study analysis and interpretation, critical revision of the manuscript for important intellectual content.

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