Chapter 16
Cost and Insurance Issues in Botulinum Toxin Therapy

Introduction

All pharmaceutical companies that produce FDA approved Botulinum toxin products is the US have established patient assistance programs. Through these programs, help is offered to needy patients with their- out of pocket- payments. The four FDA approved botulinum toxins in the US are distributed under the trade names of Botox (Allergan Inc), Xeomin (Merz Pharmaceutical), Dysport (Ipsen) and Myobloc.(Solstice Neuroscience). The propriety names given to these toxins by FDA is onabotulinum toxin A, incobotulinumtoxinA, aboboyulinumtoxinA and rimabotulinumtoxinB, respectively. The first three, are a type A and the fourth one is a type B Toxin. Of seven distinctly defined types of botulinum toxins in nature, only types A and B can be used clinically. The reader is referred to Chaps. 2 and 3 of this book for further definition of these toxins including their molecular structure, physical properties and mechanisms of action. There are two other well known toxins (both type A) with trade names of Prosigne (Lanzhou Institute-China) and Meditox (Korea) that are widely used in Asia, but are not approved by FDA for use in the US.

For enrollment into botulinum toxin patient assistant programs, patients have to meet certain eligibility criteria. These eligibility criteria are more or less the same for all companies that produce the FDA approved toxins. The eligibility criteria consist of:

1. Age 18 years or older
2. Medical condition must be FDA approved for botulinum toxin therapy.
3. The Patient should have either no insurance or a private insurance coverage.
4. The patient should not be enrolled in a federally insured program such as Medicare, Medicaid or Tricare

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The total amount of medical aid ranges from $4000 (for Xeomin and Dysport and Botox) to $5000 per year. The limit for each treatment is up to $500 per session and it can be repeated several times per year as repeat injection sessions are indicated. The aid covers both cost of the vials and payment to doctor's office for medical assessment and botulinum toxin injection. It may cover the cost of ancillary diagnostic techniques such as ultrasound that visualizes the targeted muscle (for instance in spasticity), or electromyography that locates muscle activity by recording the electrical activity of the muscle or the nerve stimulation that identifies the muscle to be targeted for injecting by moving it.

In case of patients who have insurance, the patient informs the physician's office regarding being enrolled in the patient- assisted program. The physician's office then submits a bill to the insurance company for patient assessment and procedure cost. If the patient receives an invoice asking payment for part of the bill not covered by patient's insurance, he/she can submit a copy of that bill to the patient assisted program that is geared to cover up to $500 of the unpaid bill for each treatment.

The cost of botulinum toxins varies among the states. In 2005 the price was higher in the northern states compared to western states in pharmacies and hospitals provided the toxin by the whole sale organizations. The current whole sale acquisition cost (WAC) for the three widely used botulinum toxins in US are as follows:

Botox, 100 unit vial: $ 601
Xeomin, 100 unit vial: $ 482
Dysport, 300 unit vial: $ 491

The price for 50 and 200 unit vials of Xeomin is $253 and $964, respectively. Although the units of the toxins are not truly interchangeable, each one unit of Botox approximates one unit of Xeomin and 2.5 units of Dysport.

Various strategies are used by physicians to lower the price of toxin used per patient. Some of these practices are inappropriate such as an injection arrangement called "Botox parties." Usually, practiced for cosmetic purposes that require fewer units of Botox than that used for spasticity or dystonia; a physician injects a large number of patients (20 or more) in a rapid sequence. Although somewhat cheaper for the patient, such a practice is not sound and safe since rushed injections may jeopardize the accuracy of the procedure and could potentially interrupt maintenance of full sterility.

Patients and Insurance Companies

Insurance companies use a list of different diagnoses with designated diagnostic codes that illustrate indications that a particular company has approved for botulinum toxin therapy. This list varies somewhat among different companies. In consultations with experts in the field, the companies often update this list annually or biannually. Although the list(s) are somewhat rigid, there is often some room for negotiation. In each region of the country, insurance companies have physicians in

their payroll who deal with insurance issues with medical providers. If your insurance company refuses to approve you for botulinum toxin treatment of your condition, you should ask your physician if he can call the insurance company and argue your case for you. Sometimes, a very informed nurse can do as well as the treating physician but usually the process works better when the issue is discussed by the treating and company physician. The medical conditions considered for insurance approval do not always have to be FDA approved indications. For several non-approved clinical conditions, there is now ample literature to support effectiveness of botulinum toxin therapy. Some of these off-label conditions include injection of Botox and other neurotoxins into the skin for alleviating the pain associated with shingles (post-herpetic neuralgia) or the pain in the distal part of the limbs resulting from nerve damage from diabetes or local trauma. Your treating physician can provide the company's physician, before their telephonic communication, the relevant literature that strongly supports the use of botulinum toxin injection for your medical condition. In busy practices, many physicians may not find the time to do this but I know, from personal experience, that treating physicians' calls to insurance company's physician, often succeeds in gaining treatment approval for patients.

One of the reasons for disapproval for some disorders is an insurance company policy that requires evidence for failure of other medications before botulinum toxin therapy. A brief request for approval submitted to the insurance company by the clinic staff may not provide convincing information on this issue. Again, a call from treating physician is helpful. In many instances, specific medications asked by insurance companies to be used before botulinum toxin therapy may not be compatible with the patient's age or it may interfere with other medications essential for patient's health. It is the treating physician who can best discuss and document these issues or, even better, explain it over the phone.

Contact Information for Patient Support and Co–Pay Programs in US

Dysport (Ipsen Inc): Ipsen Care Program

Telephone: 1–866–435-5677- 8 am to 8 pm. Website: Ipsencares.com

Botox (Allergan Inc): Reimbursement Solutions Patient Assistance Programs

The programs assist uninsured and underinsured patients with their treatment through the donation of Botox.

https://www.botoxone.com/ Down load program application instructions. Out of pocket costs of patients' for treatment of cervical dystonia may be covered through National Organization of Rare Diseases (NORD-rarediseases.org).

Telephone: 1–855–864-4024. Website: Cervicaldystonia@rarediseases.org

Xeomin (Merz Pharma): Xeomin Patient Co–Pay Program

Telephone: 1–888–493-6646- 8 am to 8 pm ET. Website: Xeomin.com

Myobloc (Solstice Neuroscience): Myobloc Co-Pay Program

Telephone: 1–888–461-2255- 8 am to 8 pm ET.
Website: www.myobloc-reimbursement.com

Cost Effectiveness

Botulinum toxin therapy is an expensive commodity. Depending on the indications the effect of botulinum toxin injection into the muscle lasts 3 to 9 months. The need for repeat injections to maintain long-term efficacy adds to long-term expense of botulinum toxin therapy over time. Table 16.1 shows current FDA approved indications for each of the four FDA approved botulinum toxins currently used in the US.

The high cost of botulinum toxin therapy is balanced by its long-term effect that reduces the need for daily medications. Furthermore, it has been shown that utilization of botulinum toxin therapy for its numerous indications (chronic migraine, spasticity, bladder dysfunction) clearly reduces emergency room visits and the frequency of hospitalizations. For this reason, investigators began to assess the cost efficacy of botulinum toxin therapy compared with other modes of treatment. They also studied the cost effectiveness of botulinum toxin therapy, comparing some of the four FDA approved toxins with each other. The cost efficacy studies have been published for both adult and childhood indications of botulinum toxin therapy. The results of some of these studies are presented below.

Dr. Visco and his colleagues compared the cost of Botox treatment with standard oral medications (anticholinergics) in 231 women with bladder dysfunction. Botox injection of the bladder (see Chap. 8) was as effective as the use of oral medications. The cost for Botox treatment was cheaper after six months of treatment, averaging $207/month versus $305/month for oral medications [1]. These findings were supported by a subsequent British study of 101 patients with bladder problems, in whom the cost savings in favor of Botox treatment was found to be 617 pounds per patients per year [2].

Table 16.1 Clinical indications approved by FDA for 4 types of botulinum toxin FDA approved for use in the US

Trade name	Abbreviation or Type	Manufacturer	Approved indication (FDA)	Year of FDA approval
Botox	onaBoNT-A	Allergan -Inc	Blepharospasm	1989
			Hemifacial spasm	1989
			Strabismus	1989
			Cervical dystonia	2000
			Excessive armpit sweating	2004
			Migraine	2010
			Upper limb spasticity	2010
			Lower limb spasticity (adult)	2014
			Bladder (NDO)*	2011
			Bladder (OAB)**	2013
			Forehead wrinkles	2017
Xeomin	oncoBoNT-A	Merz Pharma	Cervical dystonia	2010
			Blepharospasm	2010
			Frown lines (aesthetics)	2011
			Upper limb spasticity	2015
			Sialorrhea	2018
Dysport	AboBoNT-A	Ipsen -Limited	Cervical dystonia	2009
			Upper limb spasticity (adult)	2015
			Lower limb spasticity (children)	2016
			Lower Limb Spasticity (adult)	2017
			Wrinkles	2009
Myobloc, Neurobloc in Europe	rimaBoNT-B	Solstice, Neuroscience	Cervical dystonia	2009

*NDO: Neurogenic detrusor over-activity
**OAB: Overactive bladder (See Chap. 8)

Dr. Squenazi, a knowledgeable and well published physiatrist, in a relatively recent publication [3], discusses why intramuscular botulinum toxin injections, in the long-term, are more cost effective for patients suffering from stroke, spinal cord injury and multiple sclerosis. Such patients are affected by spasticity, a condition of heightened muscle tone and stiffness and jerkiness of the limbs, that limits their daily activities and impairs their quality of life. Botulinum toxin injection into the muscle reduces the muscle tone and improves spasticity. This allows patients to reduce, and in many instances, stop anti-spasticity medications which in many cases are poorly tolerated by elderly patients. Furthermore, relief from spasticity reduces associated muscle pain, and in some patients prevents falls resulting from poor

balance due to stiff and jerky legs. Hip fractures are costly and often incapacitating in elderly patients. A very recent review (2018), found 18 articles in the literature that specifically studied cost effectiveness of botulinum toxin therapy for treatment of spasticity in children with cerebral palsy. The review concluded that Botulinum toxin therapy was cost effective in these children but suggested studies with longer follow ups are required to see if the savings persist over years.

In a study of a large cohort of patients from US based hospitals, Dr.Hepp and coworkers found positive gains in patients with chronic migraine after Botox treatment [4]. The Botox treated group had significantly lower visits to emergency room at 6, 9 and 12 months; the visits were 21%, 10% and 20% less, respectively. The figures for reduced hospitalizations over those three time lines were 47%, 48% and 56%, respectively.

Few studies have compared two or more toxins for cost effectiveness. Drs Kazerooni and Broadhead compared cost effectiveness of Botox, Dysport and Xeomin in Cervical dystonia [5]. Cervical dystonia is a late onset movement disorder characterized by posturing and twisting of the neck as well as neck pain. It responds very well to Botox or other toxin injection into the neck and shoulder muscles (see Chap. 11 of this book). Kazerooni and Broadhead found Xeomin to be the most cost effective of the three toxins followed by Dysport. In another study of patients with dystonias (blepharospasm and cervical dystonia- see Chap. 11), Dysport was associated with the lowest possible waste (2.2%) compared to10% waste for Xeomin and 22.9% waste for Botox [6]. Drs Tilden and Guanierie also found Xeomin superior to Botox in terms of cost effectiveness when they studied patients in the Australian Health System [7]. In a recently (2018) published article, Swedish authors compared the cost effectiveness of Dysport with Botox in 159 children with cerebral palsy and spasticity; the 159 children had received a total of 341 injections. Both botulinum toxins were equally effective for this indication, but Dysport was 41% cheaper than Botox. Further studies are necessary to substantiate the results of these preliminary data.

Conclusion

Cost issues are important to the patients who receive expensive botulinum toxin therapy for management of their symptom(s). Patient co-pay programs are available through manufacturers of botulinum toxins to defray some of patients' out of pocket costs. There is evidence from published literature that despite the apparent high cost, botulinum toxin therapy is cost effective compared to other modes of therapy in management of chronic migraine, spasticity associated with stroke, multiple sclerosis, spinal cord injury and chronic bladder disorders. A limited published literature from comparative studies suggests that Botox is the least cost effective compared to Dysport and Xeomin when used for the same indications.

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