FDA Approves US WorldMeds' MYOBLOC® (rimabotulinumtoxinB) Injection for Chronic Sialorrhea

- MYOBLOC is the only approved botulinum toxin for chronic sialorrhea that provides significant results in as early as one week[1,2]

- One treatment with MYOBLOC significantly decreases symptoms of sialorrhea for up to 3 months[1]

LOUISVILLE, KY, August 26, 2019 -- US WorldMeds, LLC announced today that the U.S. Food and Drug Administration (FDA) approved the supplemental Biologics License Application (sBLA) for MYOBLOC® (rimabotulinumtoxinB) injection for the treatment of chronic sialorrhea in adults.[1]

Sialorrhea, or drooling, is defined as an excess spillage of saliva out of the mouth. Sialorrhea is a common and often problematic symptom of many neurological disorders, such as Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), cerebral palsy, stroke, and other conditions.[3,4] It affects up to 75% of people with PD and is considered one of the most bothersome non-motor symptoms of the disease.[5,6]

Stuart Isaacson, MD, Director of the Parkinson's Disease and Movement Disorder Center of Boca Raton, explains, "Sialorrhea can be highly distressing for patients and their caregivers and can have a significant, negative impact on quality of life. If left untreated, pooling of saliva can lead to irritation of the skin around the mouth, oral hygiene complications, speech difficulties, and sleep interruption. In some cases, pooling of saliva can lead to choking and aspiration pneumonia. In addition to the physical consequences, the social stigma associated with drooling can be severe enough to result in social withdrawal. These impacts can leave patients with compromised physical wellbeing, as well as feeling embarrassed by their condition, causing a lack of confidence and isolation." [3,5-8]

MYOBLOC, the first and only approved botulinum toxin type B, significantly decreases sialorrhea symptoms with a single treatment in as early as 1 week and lasts up to 3 months. The sBLA approval is supported by multiple clinical trials, including a multicenter, double-blind, placebo-controlled, efficacy and safety study of MYOBLOC. The co-primary efficacy endpoints, measured by decreases in salivary production and improvements in symptoms from baseline, were successfully achieved and statistically significant versus placebo. An open-label portion of this study demonstrated MYOBLOC's safety and efficacy over time at subsequent dosing sessions for over 1 year. The most common adverse reactions reported in all studies for chronic sialorrhea were dry mouth, dental caries, and dysphagia.[1,2]

"We are committed to helping patients who struggle with confidence due to their sialorrhea. This new indication for MYOBLOC offers a fast-acting and proven treatment," said P. Breckinridge Jones, CEO of US WorldMeds. "We are proud to support health care providers with an option that can have such a positive impact on the lives of patients and their caregivers."

MYOBLOC is currently available in three vial sizes to be prescribed and administered by a licensed healthcare provider and is the only botulinum toxin therapy available that requires no reconstitution.

MYOBLOC was first approved by the FDA in 2000 for the treatment of adults with cervical dystonia.

About MYOBLOC® (rimabotulinumtoxinB) injection
MYOBLOC is a prescription medicine that is:
- injected into neck muscles and used to treat the abnormal head position and neck pain that happens with cervical dystonia in adults.
- injected into the salivary glands (parotid and submandibular glands) and used to treat chronic sialorrhea in adults.

About US WorldMeds
US WorldMeds is a specialty pharmaceutical company whose products are making a difference in the lives of the patients and communities it serves. US WorldMeds takes an agile and personal approach to pharmaceuticals – pioneering research and product development in therapeutic areas that desperately need new solutions. Headquartered in Louisville, Kentucky, US WorldMeds has global presence and nearly 20 years of experience in the development, licensure, and commercialization of unique products. For more information about US WorldMeds, visit https://www.usworldmeds.com/. Follow US WorldMeds on Twitter, LinkedIn, and on Facebook.

Important Safety Information

WARNING: DISTANT SPREAD OF TOXIN EFFECT

See full prescribing information for complete boxed WARNING.

The effects of MYOBLOC® and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These symptoms have been reported hours to weeks after injection. Swallowing and breathing difficulties can be life threatening and there have been reports of death. The risk of symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults, particularly in those patients who have an underlying condition that would predispose them to these symptoms.

Contraindications
MYOBLOC is contraindicated in patients with:

- A known hypersensitivity to any botulinum toxin product or to any of the components in the formulation
- Infection at the proposed injection site(s)

Warnings and Precautions

Lack of Interchangeability Between Botulinum Toxin Products
The potency units of MYOBLOC are specific to the preparation and biological activity assay method utilized. Due to differences in the aspects of this assay such as the vehicle, dilution scheme, and laboratory protocols for various potency assays, potency units are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of MYOBLOC cannot be compared to or converted into units of any other botulinum toxin products assessed with any other specific assay method.

Hypersensitivity Reactions
Serious hypersensitivity reactions have been reported with botulinum toxin products. Angioedema, urticaria, and rash have occurred with MYOBLOC treatment. Hypersensitivity reactions can also include anaphylaxis, serum sickness, soft tissue edema, and dyspnea. If serious and/or immediate hypersensitivity reactions occur, discontinue further injection of MYOBLOC and institute appropriate medical therapy immediately. The use of MYOBLOC in patients with a known hypersensitivity to any botulinum neurotoxin or to any of the excipients (human albumin, sucrose), could lead to a life-threatening allergic reaction.

Dysphagia and Breathing Difficulties
Treatment with MYOBLOC and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or swallowing. When distant effects occur, additional respiratory muscles may be involved. Deaths as

a complication of severe dysphagia have been reported after treatment with botulinum toxin. Dysphagia may persist for several months and require use of a feeding tube to maintain adequate nutrition and hydration. Aspiration may result from severe dysphagia and is a particular risk when treating patients in whom swallowing or respiratory function is already compromised.

Cervical Dystonia: Treatment of cervical dystonia with botulinum toxins may weaken neck muscles that serve as accessory muscles of ventilation. This may result in a critical loss of breathing capacity in patients with respiratory disorders who may have become dependent upon these accessory muscles. There have been postmarketing reports of serious breathing difficulties, including respiratory failure, in cervical dystonia patients. Patients treated with botulinum toxin may require immediate medical attention should they develop problems with swallowing, speech or respiratory disorders. These reactions can occur within hours to weeks after injection with botulinum toxin.

Pre-Existing Neuromuscular Disorders
Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (e.g., myasthenia gravis or Lambert-Eaton syndrome) should be monitored particularly closely when given botulinum toxin. Patients with neuromuscular disorders may be at increased risk of clinically significant effects including severe dysphagia and respiratory compromise from typical doses of MYOBLOC.

Human Albumin and Transmission of Viral Diseases
This product contains albumin, a derivative of human blood. Based on effective donor screening and product manufacturing processes, it carries an extremely remote risk for transmission of viral diseases and variant Creutzfeldt-Jakob disease (vCJD). There is a theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD), but if that risk actually exists, the risk of transmission would be considered extremely remote. No cases of transmission of viral diseases, CJD, or vCJD have ever been identified for licensed albumin or albumin contained in other licensed products.

Most Common Adverse Reactions (>5% of patients and >5% more than placebo)
Cervical Dystonia: dry mouth, dysphagia, injection site pain, headache
Sialorrhea: dry mouth, dysphagia

Drug Interactions
Co-administration of MYOBLOC and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like compounds) should only be performed with caution as the effect of the toxin may be potentiated. Use of anticholinergic drugs after administration of MYOBLOC may potentiate systemic anticholinergic effects. The effect of administering different botulinum toxin products at the same time or within several months of each other is unknown. Excessive neuromuscular weakness may be exacerbated by administration of another botulinum toxin prior to the resolution of the effects of a previously administered botulinum toxin. Excessive weakness may also be exaggerated by administration of a muscle relaxant before or after administration of MYOBLOC.

Indications
MYOBLOC® (rimabotulinumtoxinB) injection is indicated for:

- the treatment of cervical dystonia (CD) to reduce the severity of abnormal head position and neck pain associated with CD in adults
- the treatment of chronic sialorrhea in adults

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact US WorldMeds at 1-888-461-2255. You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the full Prescribing Information, including Boxed WARNING and Medication Guide.

References:

1. MYOBLOC® US Prescribing Information. Solstice Neurosciences, LLC; Louisville, KY:2019.
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5. Hockstein NG, et al. Sialorrhea: a management challenge. *Am Fam Physician.* 2004;69(11):2628-2634.
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7. Ozdilek B, Gunal DI. Motor and non-motor symptoms in Turkish patients with Parkinson's disease affecting family caregiver burden and quality of life. *J Neuropsychiatry Clin Neurosci.* 2012;24:478-483.
8. Benson J, Daugherty KK. Botulinum toxin A in the treatment of sialorrhea. Ann Pharmacother. 2007;41:79-85.

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