[insert physician or practice letterhead]

Sample Letter of Medical Necessity
Submitted With Prior Authorization Form

[insert date]
[insert payer medical director/contact name]
[insert payer organization name]
[insert street address]
[insert city, state, zip]

Re: [insert patient name]
Date of birth: [insert patient DOB]
Policy ID/Group number: [insert policy ID/group number]
Policyholder: [insert policyholder name]

Dear [insert payer medical director/contact name]:

I am a(n) [insert physician practice area] writing on behalf of my patient, [insert patient name], to request prior authorization and to document the medical necessity of BOTOX® (onabotulinumtoxinA), which is reported under code J0585 ("injection, onabotulinumtoxinA, 1 Unit"), for the treatment of upper limb spasticity (ULS) in adult patients.

On March 9, 2010, BOTOX® for injection was approved by the FDA for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors (biceps), wrist flexors (flexor carpi radialis and flexor carpi ulnaris), and finger flexors (flexor digitorum profundus and flexor digitorum sublimis).

Important Limitations
Safety and effectiveness of BOTOX® have not been established for the treatment of other upper limb muscle groups, or for the treatment of lower limb spasticity. Safety and effectiveness of BOTOX® have not been established for the treatment of spasticity in pediatric patients under age 18 years. BOTOX® has not been shown to improve upper extremity functional abilities, or range of motion at a joint affected by a fixed contracture. Treatment with BOTOX® is not intended to substitute for usual standard of care rehabilitation regimens.

IMPORTANT SAFETY INFORMATION, INCLUDING BOXED WARNING

WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of BOTOX® and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, ptosis, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. 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 treated for spasticity and other conditions, particularly in those patients who have an underlying condition that would predispose them to these symptoms. In unapproved uses, including spasticity in children, and in approved indications, cases of spread of effect have been reported at doses comparable to those used to treat cervical dystonia and at lower doses.

Please see additional Important Safety Information about BOTOX® on following pages.

The efficacy and safety of BOTOX® (onabotulinumtoxinA) neurotoxin for the treatment of upper limb spasticity were evaluated in 3 randomized, multicenter, double-blind, placebo-controlled studies.

- Study 1 included 126 patients (64 BOTOX® and 62 placebo) with upper limb spasticity (Ashworth Scale score of at least 3 for wrist flexor tone and at least 2 for finger flexor tone) who were at least 6 months post stroke. BOTOX® (a total dose of 200 Units-240 Units) and placebo were injected intramuscularly (IM) into the flexor digitorum profundus, flexor digitorum sublimis, flexor carpi radialis, flexor carpi ulnaris, and, if necessary, into the adductor pollicis and flexor pollicis longus. Use of an EMG/nerve stimulator was recommended to assist in proper muscle localization for injection. Patients were followed for 12 weeks. The primary efficacy variable was wrist flexor muscle tone at week 6, as measured by the Ashworth Scale score. Key secondary end points included Physician's Global Assessment, finger flexor muscle tone, and thumb flexor muscle tone at week 6. At week 6, median change in muscle tone from baseline for the wrist and finger flexor was significantly greater in the BOTOX® group compared with placebo. Median response to treatment on the Physician's Global Assessment was significantly improved with BOTOX® compared with placebo at this time point. No significant difference from placebo was observed for thumb flexor muscle tone[1]

- Study 2 compared 3 doses of BOTOX® with placebo and included 91 patients (BOTOX® 360 Units [N = 21], BOTOX® 180 Units [N = 23], BOTOX® 90 Units [N = 21], and placebo [N = 26]) with upper limb spasticity (expanded Ashworth Scale score of at least 2 for elbow flexor muscle tone and at least 3 for wrist flexor muscle tone) who were at least 6 weeks post stroke. BOTOX® and placebo were injected with EMG guidance into the flexor digitorum profundus, flexor digitorum sublimis, flexor carpi radialis, flexor carpi ulnaris, and biceps brachii. The primary efficacy variable was the wrist flexor muscle tone at week 6, as measured by the expanded Ashworth Scale. Key secondary end points included Physician's Global Assessment, finger flexor muscle tone, and elbow flexor muscle tone at week 6. At week 6, median change in muscle tone from baseline at the wrist flexor was significantly greater with the BOTOX® treatment groups (90, 180, and 360 Units) compared with placebo. Median change in muscle tone from baseline at the elbow flexor was significantly greater than placebo for the 180 Unit dose group at week 6. Median response to treatment on the Physician's Global Assessment was also significantly improved in all 3 BOTOX® treatment groups compared with placebo at week 6[1]

- Study 3 compared 3 doses of BOTOX® (onabotulinumtoxinA) with placebo and included 88 patients (BOTOX® 360 Units [N = 23], BOTOX® 180 Units [N = 23], BOTOX® 90 Units [N = 23], and placebo [N = 19]) with upper limb spasticity (expanded Ashworth Scale score of at least 2 for elbow flexor muscle tone and at least 3 for wrist flexor muscle tone and/or finger flexor muscle tone) who were at least 6 weeks post stroke. BOTOX® and placebo were injected with EMG guidance into the flexor digitorum profundus, flexor digitorum sublimis, flexor carpi radialis, flexor carpi ulnaris, and biceps brachii. The primary efficacy variable was wrist and elbow flexor muscle tone, as measured by the expanded Ashworth Scale score. A key secondary end point was assessment of finger flexor muscle tone. At week 4, median change from baseline in muscle tone at the wrist, finger, and elbow flexor was significantly greater for the BOTOX® 360 Unit dose group compared with placebo. Significant changes were not observed with the other dose groups[1]

Adverse reactions reported by ≥ 2% of BOTOX® treated patients and more frequent than in placebo-treated patients in double-blind, placebo-controlled clinical trials in upper limb spasticity included: nausea, fatigue, bronchitis, pain in extremity, and muscular weakness.[1]

Please see additional Important Safety Information about BOTOX® on following pages.

[Mr./Mrs./Ms.] [insert patient's last name] is a [insert age]-year-old [male/female] who has [insert name of condition(s) and primary and secondary *ICD-9-CM* codes]. [Mr./Mrs./Ms.] [insert patient's last name] presented to me on [insert date] with [details such as physical exam results and clinical impressions]. This condition impacts [Mr./Mrs./Ms.] [insert patient's last name] ability to [(if appropriate) describe how condition affects hygiene, activities of daily living, or other outcome measures]. [If other treatments were used prior to BOTOX® (onabotulinumtoxinA), would add: Other therapies tried, as part of the treatment of [Mr./Mrs./Ms.] [insert patient's last name] upper limb spasticity, included [describe treatment]. Despite these treatments, [Mr./Mrs./Ms.] [insert patient's last name] remained significantly impaired due to upper limb spasticity].

[Mr./Mrs./Ms.] [insert patient's last name] is a candidate for BOTOX® for the treatment of [his/her] upper limb spasticity. To treat [Mr./Mrs./Ms.] [insert patient's last name], I will inject BOTOX® into the muscles of the [list areas] on the [insert "right," "left," or "both" side(s)]. The BOTOX® dose required for this patient will range from [insert estimated dose range] based upon current evaluation of the patient's symptoms and examination findings [and, if appropriate, may add: outcomes from previous treatment with BOTOX®].

[If the patient has received BOTOX® previously, would include: This patient's response to the initial dose of BOTOX® has been [indicate the status, if applicable]. Based on this outcome], I plan to treat [Mr./Mrs./Ms.] [insert patient's last name] with BOTOX® [indicate the planned course of treatment and duration]. My clinical expectations for treatment with BOTOX® are [indicate expectations]. Follow-up is expected to involve [include expected additional evaluations and treatments].

I request confirmation that this therapy is a covered benefit based on medical necessity and that associated fees will be covered. Thank you for your review of this information and for your coverage consideration. If you have any questions or require additional information, please contact me at [insert physician's contact information].

IMPORTANT SAFETY INFORMATION (continued)
CONTRAINDICATIONS
BOTOX® is contraindicated in the presence of infection at the proposed injection site(s) and in individuals with known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation.

WARNINGS AND PRECAUTIONS
Lack of Interchangeability Between Botulinum Toxin Products
The potency Units of BOTOX® are specific to the preparation and assay method utilized. They are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of BOTOX® cannot be compared to nor converted into units of any other botulinum toxin products assessed with any other specific assay method.

Spread of Toxin Effect
See Boxed Warning.

Injections In or Near Vulnerable Anatomic Structures
Care should be taken when injecting in or near vulnerable anatomic structures. Serious adverse events including fatal outcomes have been reported in patients who had received BOTOX® injected directly into salivary glands, the oro-lingual-pharyngeal region, esophagus, and stomach. Some patients had pre-existing dysphagia or significant debility. (Safety and effectiveness have not been established for indications pertaining to these injection sites.) Pneumothorax associated with injection procedure has been reported following the administration of BOTOX® near the thorax. Caution is warranted when injecting in proximity to the lung, particularly the apices.

Please see additional Important Safety Information about BOTOX® on following pages.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS (continued)

Hypersensitivity Reactions

Serious and/or immediate hypersensitivity reactions have been reported. These reactions include anaphylaxis, serum sickness, urticaria, soft-tissue edema, and dyspnea. If such a reaction occurs, further injection of BOTOX® (onabotulinumtoxinA) should be discontinued and appropriate medical therapy immediately instituted. One fatal case of anaphylaxis has been reported in which lidocaine was used as the diluent, and consequently the causal agent cannot be reliably determined.

Pre-Existing Neuromuscular Disorders

Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis, or neuromuscular junctional disorders (eg, 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 therapeutic doses of BOTOX®.

Pulmonary Effects of BOTOX® in Patients With Compromised Respiratory Status Treated for Spasticity

Patients with compromised respiratory status treated with BOTOX® for upper limb spasticity should be monitored closely.

Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity

Bronchitis was reported more frequently as an adverse reaction in patients treated for upper limb spasticity with BOTOX® (3% at 251-360 Units total dose) compared to placebo (1%). In patients with reduced lung function treated for upper limb spasticity, upper respiratory tract infections were also reported more frequently as adverse reactions in patients treated with BOTOX® (11% at 360 Units total dose; 8% at 240 Units total dose) compared to placebo (6%).

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. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered extremely remote. No cases of transmission of viral diseases or CJD have ever been reported for albumin.

ADVERSE REACTIONS

The following adverse reactions to BOTOX® for injection are discussed in greater detail in the following sections: Spread of Toxin Effect (see Boxed Warning); Hypersensitivity Reactions (see *Contraindications* and *Warnings and Precautions*); Bronchitis and Upper Respiratory Tract Infections in Patients Treated for Spasticity (see *Warnings and Precautions*).

Upper Limb Spasticity

The most frequently reported adverse reactions following injection of BOTOX® for upper limb spasticity include pain in extremity, muscle weakness, fatigue, nausea, and bronchitis.

Post Marketing Experience

There have been spontaneous reports of death, sometimes associated with dysphagia, pneumonia, and/or other significant debility or anaphylaxis, after treatment with botulinum toxin. There have also been reports of adverse events involving the cardiovascular system, including arrhythmia and myocardial infarction, some with fatal outcomes. Some of these patients had risk factors including cardiovascular disease. The exact relationship of these events to the botulinum toxin injection has not been established.

Please see additional Important Safety Information about BOTOX® on following page.

IMPORTANT SAFETY INFORMATION (continued)
DRUG INTERACTIONS
Co-administration of BOTOX® (onabotulinumtoxinA) and aminoglycosides or other agents interfering with neuromuscular transmission (eg, 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 BOTOX® may potentiate systemic anticholinergic effects. The effect of administering different botulinum neurotoxin 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 BOTOX®.

Please see accompanying full Prescribing Information including Boxed Warning and Medication Guide.

Sincerely,

[insert physician's signature]
[insert physician's full name]
[insert address]
[insert telephone number]

Enclosures

1. BOTOX® Prescribing Information, January 2013.

ALLERGAN

www.BOTOXMedical.com/HCP www.BOTOXReimbursementSolutions.com
1-800-44-BOTOX APC55HY13 131493