Dysport® (abobotulinumtoxinA) is a prescription medicine that is injected into muscles and used to treat:

- increased muscle stiffness in elbow, wrist, and finger muscles in adults with upper limb spasticity
- cervical dystonia (CD) in adults

It is not known whether Dysport® is safe or effective in children under 18 years old or for the treatment of other types of muscle spasms.

Important Safety Information for Dysport®

Dysport® may cause serious side effects that can be life threatening, including problems breathing or swallowing, and spread of toxin effects. These problems can happen within hours, or days to weeks after an injection of Dysport®. Call your doctor or get medical help right away if you have any of these problems after treatment with Dysport®:

- **Problems swallowing, speaking, or breathing** after an injection of Dysport® if the muscles that you use to breathe or swallow become weak. If these problems are severe, death can happen as a complication. People with certain breathing problems may need to use muscles in their necks to help them breathe and may be at greater risk for serious breathing problems with Dysport®.
- Swallowing problems may last for several weeks; you may need a feeding tube to receive food or water. If swallowing problems are severe, food or liquids may go into your lungs. People who already have swallowing or breathing problems before receiving Dysport® have the highest risk of getting these problems.

Please see additional Important Safety Information throughout this brochure and accompanying Full Prescribing Information and Medication Guide.
The Facts About Adult Upper Limb Spasticity (ULS)

What is Upper Limb Spasticity?

ULS occurs when the nerve cells that carry messages from your brain to different parts of your body are damaged. When this happens, the affected muscles in the upper limbs receive the wrong signals. This can cause your muscles to contract or tense up, leading to continued stiffness and tightness in your elbow, wrist, and finger muscles.
What causes ULS?

ULS can result from different medical conditions or events, including a stroke or serious brain injury. ULS may develop right away or over a period of weeks, months, or years. ULS may also be caused by multiple sclerosis, cerebral palsy, or spinal cord injury. If left untreated, ULS may get worse over time, which is why identifying and treating ULS early is so important.

Developing ULS can be a turning point in a person’s life. The extreme stiffness and tightness caused by ULS can be painful. ULS can affect movement and the ability to perform simple tasks.

Know that you are not alone. In fact, more than 1.8 million adults have ULS in the United States. Managing ULS isn’t something you have to do on your own. Together, you and your healthcare team can create a treatment plan that is right for you.

Important Safety Information (continued)

Spread of toxin effects. In some cases, the effects of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include: loss of strength and muscle weakness all over the body, double vision, blurred vision and drooping eyelids, hoarseness or change or loss of voice, trouble saying words clearly, loss of bladder control, trouble breathing, or trouble swallowing. These problems could make it unsafe for you to drive a car or do other dangerous activities.
What You Should Know: About treatment

What is Dysport®?
Dysport® (pronounced DIS-port) (abobotulinumtoxinA) is a type of prescription medicine called a botulinum toxin type A that is injected into the muscles of adults with ULS. Dysport® works by helping to temporarily block signals from the nerves that tell the affected muscles to contract or tighten. This can help reduce muscle stiffness in the elbow, wrist, and finger muscles in people with ULS.

Although Dysport® was approved to treat ULS in the United States in 2015, it has been used to treat other medical conditions in the US for more than 6 years.

What are the potential benefits of treatment with Dysport®?
In a clinical study, Dysport® significantly reduced stiffness in the elbow, wrist, and finger muscles within 4 weeks of treatment. For some people, improvement was seen 1 week after treatment with Dysport®.

Important Safety Information (continued)

Do not take Dysport® if you are allergic to Dysport® or any of the ingredients in Dysport® (See Medication Guide for ingredients), or are allergic to cow’s milk protein; had an allergic reaction to any other botulinum toxin product, such as Myobloc® (rimabotulinumtoxinB), Botox® (onabotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); or have a skin infection at the planned injection site.

Botox®, Xeomin®, and Myobloc® are registered trademarks of their respective owners.

Please see additional Important Safety Information throughout this brochure, including Boxed Warning regarding distant spread of toxin effect.
What You Should Know: About receiving treatment

How is Dysport® treatment given?

Dysport® is given as an injection into your muscles by your doctor. Depending on how many muscles are affected, your doctor may give you injections in a few different muscles. Your doctor will tailor the amount of Dysport® given and the locations of the injections to your own individual needs. Your doctor may change your dose of Dysport® until you and your doctor find the best dose for you.

How long before my symptoms come back?

Dysport® injections should be given at least 3 months apart, as needed, when your symptoms return. In a Dysport® clinical study, most patients needed treatment again between 3 and 4 months. Some had a longer response and were treated again at 5 months.

MOST PATIENTS HAD 3 to 4 months BEFORE TREATMENT WAS NEEDED AGAIN*

*Based on the return of symptoms.
What You Should Know: About side effects

What are the possible side effects with Dysport®?

Serious side effects

Dysport® (abobotulinumtoxinA) may cause serious side effects that can be life threatening, including problems breathing or swallowing and spread of toxin effect. These problems can happen within hours, or days to weeks, after an injection of Dysport®. Deaths due to these problems have occurred. Call your doctor or get medical help right away if you have any of these problems after treatment with Dysport®. Please see the front cover of this brochure for additional information about these serious side effects.

Common side effects

The most common side effects of Dysport® in people with upper limb spasticity include: urinary tract infection, muscle weakness, musculoskeletal pain, fall, depression, stuffy or runny nose and sore throat, and dizziness.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Dysport®.

Important Safety Information (continued)

Before you take Dysport®, tell your doctor about all your medical conditions, including if you have a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig’s disease], myasthenia gravis, or Lambert-Eaton syndrome), as you may be at increased risk of serious side effects, including difficulty swallowing or breathing.

Please see additional Important Safety Information throughout this brochure, including Boxed Warning regarding distant spread of toxin effect.
What You Should Know: About prior treatment

Can I still use Dysport® if I’ve already used another botulinum toxin?

You can receive treatment with Dysport® even if you have been treated with another botulinum toxin in the past, such as Botox® (onabotulinumtoxinA), Xeomin® (incobotulinumtoxinA), or Myobloc® (rimabotulinumtoxinB).*

Dysport® was studied in adults with ULS, including those who had:
- Already used another botulinum toxin
- Never used any botulinum toxin

Tell your doctor if you have received any botulinum toxin product in the last 4 months and also which product you received. Do not take Dysport® if you had any allergic reaction to any of these other botulinum toxin products.

Dysport® should be given at least 12 weeks after the last injection. Also inform your doctor if you are allergic to any of the inactive ingredients in Dysport®, including human albumin, or cow’s milk protein.

Important Safety Information (continued)

Before you take Dysport®, tell your doctor if you have or have had any of the following: a side effect from any botulinum toxin in the past; breathing problems such as asthma or emphysema; swallowing problems; bleeding problems; diabetes; and slow heartbeat, or other problems with your heart rate or rhythm.

*Botox®, Xeomin®, and Myobloc® are registered trademarks of their respective owners.
What Your Doctor Needs to Know: About your medical history

What should I tell my doctor?

Before starting treatment with Dysport® (abobotulinumtoxinA), you should tell your doctor about all of your medical conditions, especially any that may affect your muscles and nerves. You should also inform your doctor of all other medical conditions, including if you have or have had:

- Any problems with breathing, swallowing, or bleeding
- A slow or irregular heartbeat or rhythm
- Diabetes
- Any side effect or allergy to any botulinum toxin product

Also, let your doctor know if you are:

- Planning to have surgery
- Pregnant or plan to become pregnant; it is not known if Dysport® can harm your unborn baby
- Breast-feeding or planning to breast-feed; it is not known if Dysport® can pass into breast milk

Important Safety Information (continued)

Tell your doctor if you have plans to have surgery, had surgery on your face, have weakness of your forehead muscles (such as trouble raising your eyebrows), have drooping eyelids, or have any other change in the way your face normally looks.

Please see additional Important Safety Information throughout this brochure, including Boxed Warning regarding distant spread of toxin effect.
What Your Doctor Needs to Know: About prior treatment

It is important to inform your doctor if you have ever received any other botulinum toxin products in the past or had an allergic reaction to Botox®, Xeomin®, or Myobloc® or had treatment with any of these products in the last 4 months.

Also, let your doctor know if you have recently received an antibiotic by injection or are currently taking any prescription or nonprescription medications, muscle relaxants, sleep medicines, allergy/cold medicines, vitamins, or herbal supplements.

Before starting any new medicines, be sure to tell your doctor if you have ever had treatment with Dysport®.

*Botox®, Xeomin®, and Myobloc® are registered trademarks of their respective owners.
Support When You Need It

DYSPORT COPAY ASSISTANCE PROGRAM

Eligible* patients can receive Dysport® for little or no copay

You can save up to $2,000 in out-of-pocket expenses every year. Here is how the Dysport® (abobotulinumtoxinA) Copay Assistance Program works:

- Visit IpsenCares.com to complete a Patient Authorization form, and have your HCP complete an enrollment form on your behalf
- An IPSEN CARES™ Patient Access Specialist will contact you to let you know about your eligibility
- If you are eligible,* you will receive a MasterCard® covering up to $500 of your out-of-pocket costs for up to 4 treatments per year
- After each injection, send the IPSEN CARES™ team your Explanation of Benefits (EOB) or pharmacy receipt and your card will be loaded with money
- The MasterCard can only be used at your doctor’s office or at your specialty pharmacy to cover your out-of-pocket costs† for Dysport®

To learn more about the Dysport® Copay Assistance Program, visit Dysport.com/co-pay-assistance.

Eligible* patients may save up to $2,000 annually in out-of-pocket expenses for Dysport®.

*You may be eligible if your Dysport® therapy is covered by a commercial insurance company and you are not covered by a federal- or state-funded insurance program. Additional eligibility rules apply and can be found at IpsenCares.com.

†The Dysport® Copay Assistance Program MasterCard® must be used within 60 days.

Please see additional Important Safety Information throughout this brochure, including Boxed Warning regarding distant spread of toxin effect.
IPSEN CARES™ is dedicated to helping you receive your treatment with Dysport®

IPSEN CARES™ can help:

- Navigate the insurance coverage process
- Provide copay assistance for eligible* patients
- Provide free medication to financially eligible patients through the Patient Assistance Program
- Avoid delays or interruptions in therapy

To learn more about IPSEN CARES™, visit IpsenCares.com, or call an IPSEN CARES™ Patient Access Specialist at (866) 435-5677.

Representatives are available from 8:00 AM to 8:00 PM ET (5:00 AM to 5:00 PM PT) Monday through Friday.

Important Safety Information (continued)

Tell your doctor if you are pregnant, plan to become pregnant, or are breast-feeding or planning to breast-feed. It is not known if Dysport® can harm your unborn baby. It is not known if Dysport® passes into breast milk.

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins, and herbal products. Using Dysport® with certain other medicines may cause serious side effects. Do not start any new medicines until you have told your doctor that you have received Dysport® in the past.
More Support for Patients and Caregivers

Reach for additional help when you need it

Living with ULS can be challenging. You are not alone—support and additional resources are available for you and those who care for you:

**Caregiver Action Network**  
1-202-454-3970  
caregiveraction.org

**Alliance for Patient Access**  
1-202-499-4114  
allianceforpatientaccess.org

**American Stroke Association**  
1-888-4-STROKE (1-888-478-7653)  
strokeassociation.org

**National Stroke Association**  
1-800-STROKES (1-800-787-6537)  
stroke.org

**Brain Injury Association of America**  
1-800-444-6443  
biausa.org

**Paralyzed Veterans of America**  
1-800-424-8200  
pva.org

Please see additional Important Safety Information throughout this brochure, including **Boxed Warning** regarding distant spread of toxin effect.
Important Safety Information (continued)

**Especially tell your doctor if you have received** injections of botulinum toxin in the last four months or in the past. Be sure your doctor knows exactly which product you received such as Myobloc® (rimabotulinumtoxinB), Botox® (onabotulinumtoxinA), or Xeomin® (incobotulinumtoxinA); have recently received an antibiotic by injection; take muscle relaxants; take an allergy or cold medicine; or take a sleep medicine.

**Most common side effects of Dysport® (abobotulinumtoxinA) in people with upper limb spasticity include:** urinary tract infection, muscle weakness, musculoskeletal pain, fall, depression, stuffy or runny nose and sore throat, and dizziness.

**Most common side effects of Dysport® in people with cervical dystonia include:** muscle weakness, dry mouth, feeling of tiredness, neck pain or muscle pain, problems speaking, eye problems, difficulty swallowing, injection site pain, and headache.

**Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of Dysport®. For more information, ask your doctor or pharmacist.**

Please see Dysport® Full Prescribing Information including **Boxed Warning** and Medication Guide.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Botox®, Xeomin®, and Myobloc® are registered trademarks of their respective owners.
Treatment for Adults With Upper Limb Spasticity (ULS)

Dysport®—Proven to reduce stiffness in the elbow, wrist, and finger muscles in adults with ULS

- In a clinical study, Dysport® (abobotulinumtoxinA) reduced muscle stiffness in elbow, wrist, and finger muscles within 4 weeks of treatment.
  - Improvement may be seen 1 week after treatment.
- Most patients had treatment again within 3 to 4 months after their first treatment.

The most common side effects of Dysport® in people with upper limb spasticity include urinary tract infection, muscle weakness, musculoskeletal pain, fall, depression, stuffy or runny nose and sore throat, and dizziness.

The Copay Program can help eligible* patients save up to $2,000 in out-of-pocket expenses for Dysport® every year.

- To learn more about the Dysport® Copay Assistance Program:
  - Visit Dysport.com/co-pay-assistance
  - Or call an IPSEN CARESTM Patient Access Specialist at (866) 435-5677.
    - Representatives are available from 8:00 AM to 8:00 PM ET (5:00 AM to 5:00 PM PT) Monday through Friday.

*You may be eligible if your Dysport® therapy is covered by a commercial insurance company and you are not covered by a federal- or state-funded insurance program. Additional eligibility rules apply and can be found at IpsenCares.com.

Important Safety Information

Dysport® may cause serious side effects that can be life threatening, including problems breathing or swallowing, and spread of toxin effects. These problems can happen within hours, or days to weeks after an injection of Dysport®. Call your doctor or get medical help right away if you have any of these problems after treatment with Dysport®.

Please see additional Important Safety Information throughout this brochure, including Boxed Warning regarding distant spread of toxin effect, and the accompanying Medication Guide.
WARNING: DISTANT SPREAD OF TOXIN EFFECT
See full prescribing information for complete boxed warning
The effects of DYSPORT® and all boturnin 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 underlying conditions that would predispose them to these symptoms.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DYSPORT® safely and effectively. See full prescribing information for DYSPORT®.

DYSPORT® (abobotulinumtoxinA) for injection, for intramuscular use
Initial U.S. Approval: 2009

RECENT MAJOR CHANGES

2 DOSAGE AND ADMINISTRATION

2.1 Instructions for Safe Use
• Once reconstituted, store in original container in a refrigerator (2–8°C) and use within 24 hours (2.1, 16)
• Do not freeze after reconstitution (2.1, 16)
• Protect from light (16)
• Reconstitution instructions are specific for the 300 Unit and 500 Unit vials (2.1)
• Reconstituted DYSPORT® is intended for intramuscular injection only. After reconstitution, DYSPORT® should be used for only one injection session and for only one patient.

2.2 Cervical Dystonia
• Initial dose is 500 Units given intramuscularly as a divided dose among the affected muscles
• Re-treatment every 12 to 16 weeks or longer, as necessary, based on return of clinical symptoms with doses administered between 250 and 1000 Units to optimize clinical benefit
• Re-treatment should not occur in intervals of less than 12 weeks
• Titrate in 250 Unit steps according to patient’s response

2.3 Glabellar Lines
• Administer a total dose of 50 Units, divided in five equal aliquots of 10 Units each, intramuscularly to affected muscles to achieve clinical effect
• Re-treatment should be administered no more frequently than every 3 months

2.4 Upper Limb Spasticity
• Select dose based on muscles affected, severity of muscle spasticity, prior response and adverse reaction history following treatment with DYSPORT®
• Re-treatment every 12 to 16 weeks or longer, as necessary, based on return of clinical symptoms with doses administered between 500 to 1000 Units.
• Re-treatment in less than 12 weeks has not been studied.

7 DRUG INTERACTIONS

8 USE IN SPECIFIC POPULATIONS

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8.2 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Ethnic Groups

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

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16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

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WARNING: DISTANT SPREAD OF TOXIN EFFECT

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1.1 Cervical Dystonia
1.2 Glabellar Lines
1.3 Upper Limb Spasticity

2 DOSAGE AND ADMINISTRATION

2.1 Instructions for Safe Use
2.2 Dosing in Cervical Dystonia
2.3 Dosing in Glabellar Lines
2.4 Dosing in Upper Limb Spasticity

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

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5.2 Spread of Toxin Effect
5.3 Dysphagia and Breathing Difficulties in Treatment of Cervical Dystonia
5.4 Facial Anatomy in the Treatment of Glabellar Lines
5.5 Pre-existing Neuromuscular Disorders
5.6 Human Albumin
5.7 Intradermal Immune Reaction

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience
6.2 Postmarketing Experience
6.3 Immunogenicity

DOSAGE FORMS AND STRENGTHS

• For Injection: 300 Units or 500 Units lyophilized powder in a single-use vial for reconstitution with preservative-free 0.9% Sodium Chloride Injection, USP (3)

CONTRAINDICATIONS

• Hypersensitivity to any botulinum toxin product or excipients (4, 6.1, 6.2)
• Allergy to cow’s milk protein (4)
• Infection at the proposed injection site(s) (4)

WARNINGS AND PRECAUTIONS

• The potency Units of DYSPORT® are not interchangeable with other preparations of botulinum toxin products and, therefore, units of biological activity of DYSPORT® cannot be compared to or converted into units of any other botulinum toxin products (5.1)
• Recommended dose and frequency of administration should not be exceeded (5.4)
• Immediate medical attention may be required in cases of respiratory, speech or swallowing difficulties (5.3)
• Concomitant neuromuscular disorder may exacerbate clinical effects of treatment (5.5)
• DYSPORT® contains human albumin. There is a risk for transmission of Creutzfeldt-Jakob disease (CJD) however, no cases of transmission of viral diseases or CJD have ever been identified for albumin (5.6)

CLINICAL STUDIES

15 See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 07/2015

* Sections or subsections omitted from the full prescribing information are not listed.
**INDICATIONS AND USAGE**

1.1 **Cervical Dystonia**

DYSPORT® is indicated for the treatment of adults with cervical dystonia.

1.2 **Glabellar Lines**

DYSPORT® is indicated for the temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients less than 65 years of age.

1.3 **Upper Limb Spasticity**

DYSPORT® is indicated for the treatment of upper limb spasticity in adult patients, to decrease the severity of increased muscle tone in elbow flexors, wrist flexors and finger flexors.

2.1 **Instructions for Safe Use**

2.1.1 **Slimming 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 underlying conditions 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 or lower than the maximum recommended total dose. [See Warnings and Precautions (5.2)]

2.2 **Dosing in Cervical Dystonia**

The recommended initial dose of DYSPORT® for the treatment of cervical dystonia is 500 Units given intramuscularly as a divided dose among affected muscles in patients with or without a history of prior treatment with botulinum toxin. (A description of the average DYSPORT® dose and percentage of total dose injected into specific muscles in the pivotal clinical trials can be found in Table 8 of Section 14.1, Clinical Studies – Cervical Dystonia.) Limiting the dose injected into the sternocleidomastoid muscle may reduce the occurrence of dysphagia. Clinical studies with DYSPORT® in cervical dystonia suggest that the peak effect occurs between two and four weeks after injection. Simultaneous EMG-guided application of DYSPORT® may be helpful in locating active muscles.

**Dose Modification**

Where dose modification is necessary for the treatment of cervical dystonia, uncontrolled open-label studies suggest that dose adjustment can be made in 250 Unit steps according to the individual patient’s response, with re-treatment every 12 weeks or longer, as necessary, based on return of clinical symptoms. Uncontrolled open-label studies also suggest that the total dose administered in a single treatment should be between 250 Units and 1000 Units. Re-treatment, if needed, should not occur in intervals of less than 12 weeks. Doses above 1000 Units have not been systematically evaluated.

**Special Populations**

**Adults and elderly**

The starting dose of 500 Units recommended for cervical dystonia is applicable to adults of all ages [see Use in Specific Populations (8.5)].

**Pediatric Patients**

The safety and effectiveness of DYSPORT® in the treatment in pediatric patients less than 18 years of age has not been assessed [see Warnings and Precautions (5.2)].

**Instructions for Preparation and Administration for the Treatment of Cervical Dystonia**

DYSPORT® is supplied as a single-use vial. Only use sterile preservative-free 0.9% Sodium Chloride Injection, USP for reconstitution of DYSPORT®. Each 500 Unit vial of DYSPORT® is to be reconstituted with 1 mL of preservative-free 0.9% Sodium Chloride Injection USP to yield a solution of 50 Units per 0.1 mL. Each 300 Unit vial of DYSPORT® is to be reconstituted with 0.6 mL of preservative-free 0.9% Sodium Chloride Injection USP to yield a solution equivalent to 50 Units per 0.1 mL.

Using an appropriately sized sterile syringe, needle and aseptic technique, draw up 1 mL or 0.6 mL of sterile, preservative-free 0.9% Sodium Chloride Injection USP for 500 Unit and 300 Unit vials, respectively. Insert the needle into the DYSPORT® vial. The partial vacuum will begin to pull the saline into the vial. Any remaining required saline should be expressed into the vial manually. Do not use the vial if no vacuum is observed. Swirl gently to dissolve. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Reconstituted DYSPORT® should be a clear, colorless solution, free of particulate matter, otherwise it should not be injected.

Expel any air bubbles in the syringe barrel. Remove the needle used to reconstitute the product and attach an appropriately sized new sterile needle.

Discard the vial and needle in accordance with local regulations.

**2.3 Dosing in Glabellar Lines**

The dose of DYSPORT® for the treatment of glabellar lines is a total of 50 Units given intramuscularly in five equal aliquots of 10 Units each to achieve clinical effect (see Figure 1). [See Warnings and Precautions (5.2)].

**Preparation and Administration for the Treatment of Glabellar Lines**

DYSPORT® is supplied as a single-use vial. Only use sterile preservative-free 0.9% Sodium Chloride Injection, USP for reconstitution of DYSPORT®. Each 500 Unit vial of DYSPORT® is to be reconstituted with 2.5 mL of preservative-free 0.9% Sodium Chloride Injection USP prior to injection. The concentration of the resulting solution will be 10 Units per 0.08 mL (12 Units per 0.1 mL) to be delivered in five equally divided aliquots of 0.08 mL each. DYSPORT® may also be reconstituted with 1.5 mL of preservative-free 0.9% Sodium Chloride Injection USP for a solution of 10 Units per 0.05 mL (20 Units per 0.1 mL) to be delivered in five equally divided aliquots of 0.05 mL each.

Using an appropriately sized sterile syringe, needle and aseptic technique, draw up 2.5 mL or 1.5 mL of preservative-free 0.9% Sodium Chloride Injection USP into the vial of DYSPORT®. Insert the needle into the DYSPORT® vial. The partial vacuum will begin to pull the saline into the vial. Any remaining required saline should be expressed into the vial manually. Do not use the vial if no vacuum is observed. Swirl gently to dissolve. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Reconstituted DYSPORT® should be a clear, colorless solution, free of particulate matter otherwise it should not be injected.

Draw a single patient dose of DYSPORT® into a sterile syringe. Expel any air bubbles in the syringe barrel. Remove the needle used to reconstitute the product and attach a 30 gauge needle.

Discard the vial and needle in accordance with local regulations.

**Injection Technique**

Glabellar facet lines arise from the activity of the lateral corrugator and vertical procerus muscles. These can be readily identified by palpating the tensed muscle mass while having the patient frown. The corrugator depresses the skin creating a “furrowed” vertical line surrounded by tensed muscle (i.e., “frown lines”). The location, size, and use of the muscles vary markedly among individuals. Physicians administering DYSPORT® must understand the relevant neuromuscular and/or orbital anatomy of the area involved and any alterations to the anatomy due to prior surgical procedures. Risk of ptosis can be mitigated by careful examination of the upper lid for separation or weakness of the levator palpebrae muscle (true ptosis), identification of lash ptosis, and evaluation of the range of lid excursion while manually depressing the frontalis to assess compensation. In order to reduce the complication of ptosis, the following steps should be taken:

- Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- Medial corrugator injections should be placed at least 1 centimeter above the bony supraorbital ridge.
- Ensure the injected volume/dose is accurate and where feasible kept to a minimum.
- Do not inject toxin closer than 1 centimeter above the central eyebrow.
To inject DYSPORT® advance the needle through the skin into the underlying muscle while applying finger pressure on the superior medial orbital rim. Inject patients with a total of 50 Units in five equally divided aliquots. Using a 30 gauge needle, inject 10 Units of DYSPORT® into each of five sites, two in each corrugator muscle, and one in the procerus muscle (see Figure 1).

Figure 1

2.4 Dosing in Upper Limb Spasticity

Special Populations

Adults

Dosing in initial and subsequent treatment sessions should be tailored to the individual based on the size, number and location of muscles involved, severity of spasticity, the presence of local muscle weakness, the patient’s response to previous treatment, and/or adverse event history with DYSPORT®. In the pivotal clinical trial, doses of 500 Units and 1000 Units were divided among selected muscles, Table 2 and Figure 2, at a given treatment session. No more than 1 mL should generally be administered at any single injection site.

Table 2: DYSPORT® Dosing by Muscle for Upper Limb Spasticity

<table>
<thead>
<tr>
<th>Muscles Injected</th>
<th>Recommended Dose</th>
<th>Recommended Number of Injection(s) per Muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexor carpi radialis (FCR)</td>
<td>100 Units to 200 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Flexor carpi ulnaris (FCU)</td>
<td>100 Units to 200 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Flexor digitorum profundus (FDP)</td>
<td>100 Units to 200 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Flexor digitorum superficialis (FDS)</td>
<td>100 Units to 200 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Brachialis</td>
<td>200 Units to 400 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Brachioradialis</td>
<td>100 Units to 200 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Biceps Brachii (BB)</td>
<td>200 Units to 400 Units</td>
<td>1 to 2</td>
</tr>
<tr>
<td>Pronator Teres</td>
<td>100 Units to 200 Units</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 2: Muscles for Injection for Upper Limb Spasticity

Although actual location of the injection sites can be determined by palpation, the use of injection guiding technique e.g. electromyography, electrical stimulation is recommended to target the injection sites.

Repeat DYSPORT® treatment should be administered when the effect of a previous injection has diminished, but no sooner than 12 weeks after the previous injection. A majority of patients in clinical studies were retreated between 12-16 weeks; however some patients had a longer duration of response, i.e. 20 weeks. The degree and pattern of muscle spasticity at the time of re-injection may necessitate alterations in the dose of DYSPORT® and muscles to be injected. Clinical improvement may be expected one week after administration of DYSPORT®.

Pediatric Patients

The safety and effectiveness of DYSPORT® in the treatment of upper limb spasticity in pediatric patients less than 18 years of age has not been demonstrated. [see Warnings and Precautions (5.2)]

Instructions for Preparation and Administration for the Treatment of Upper Limb Spasticity in Adults

DYSPORT® is supplied as a single-use vial. Only use sterile preservative-free 0.9% Sodium Chloride Injection, USP for reconstitution of DYSPORT®. The recommended concentration is 100 Units/mL or 200 Units/mL with preservative-free 0.9% Sodium Chloride Injection USP (see Table 1).

Using an appropriately sized sterile syringe, needle and aseptic technique, draw up the required volume (Table 1) of preservative-free 0.9% Sodium Chloride Injection USP.

Insert the needle into the DYSPORT® vial. The partial vacuum will begin to pull the saline into the vial. Do not more than 2.5 mL of saline should be introduced into the vial (see Footnote in Table 1).

Do not use the vial if a vacuum is absent. Gently swirl to dissolve. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. Reconstituted DYSPORT® should be a clear, colorless solution, free of particulate matter; otherwise it should not be injected.

Expel any air bubbles in the syringe barrel. Remove the needle used to reconstitute the product and attach an appropriately sized new sterile needle.

Discard the vial and needle in accordance with local regulations.

DOSAGE FORMS AND STRENGTHS

For injection: 300 Units or 500 Units of lyophilized powder in a single-use vial for reconstitution with preservative-free 0.9% Sodium Chloride Injection, USP.

4 CONTRAINDICATIONS

DYSPORT® is contraindicated in patients with:

- Known hypersensitivity to any botulinum toxin preparation or to any of the components in the formulation [see Adverse Reactions (6.1), Description (11)]. This product may contain trace amounts of cow’s milk protein. Patients known to be allergic to cow’s milk protein should not be treated with DYSPORT®.
- Infection at the proposed injection site(s).

5 WARNINGS AND PRECAUTIONS

5.1 Lack of Interchangeability between Botulinum Toxin Products

The potency Units of DYSPORT® 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 DYSPORT® cannot be compared to or converted into units of any other botulinum toxin products assessed with any other specific assay method [see Description (11)].

5.2 Spread of Toxin Effect

Post-marketing safety data from DYSPORT® and other approved botulinum toxins suggest that botulinum toxin effects may, in some cases, be observed beyond the site of local injection. The symptoms are consistent with the mechanism of action of botulinum toxin and may include: areflexia, generalized muscle weakness, dysarthria, blurred vision, strabismus, 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 related to spread of toxin effects. The risk of the symptoms is probably greatest in children treated for spasticity but symptoms can also occur in adults treated for spasticity and other conditions, and particularly in those patients who have underlying conditions that would predispose them to these symptoms. In unapproved uses, including spasticity in children and in approved indications, symptoms consistent with spread of toxin effect have been reported at doses comparable to or lower than the maximum recommended total dose.

5.3 Dysphagia and Breathing Difficulties

Treatment with DYSPORT® 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 distressful effects occur, additional respiratory muscles may be involved [see Warnings and Precautions (5.2)].

Deaths as a complication of severe dysphagia have been reported after treatment with botulinum toxin. Dysphagia may persist for several weeks, 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.

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 post-marketing reports of serious breathing difficulties, including respiratory failure. 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 [see Warnings and Precautions (5.2), Adverse Reactions (6.1), Clinical Pharmacology (12.2)].

5.4 Facial Anatomy in the Treatment of Glabellar Lines

Caution should be exercised when administering DYSPORT® to patients with surgical alterations to the facial anatomy, excessive weakness or atrophy in the target muscle(s), marked facial asymmetry, inflammation at the injection site(s), ptosis, excessive dermatochalasis, deep dermal scarring, thick sebaceous skin [see Dosage and Administration (2.3)] or the inability to substantially lessen glabellar lines by physically spreading them apart [see Clinical Studies (14.2)].

Do not exceed the recommended dosage and frequency of administration of DYSPORT®. In clinical trials, subjects who received a higher dose of DYSPORT® had an increased incidence of eyelid ptosis.

5.5 Pre-existing Neuromuscular Disorders

Individuals with peripheral motor neuropathic diseases, amyotrophic lateral sclerosis or neuromuscular junction 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 DYSPORT® [see Adverse Reactions (6.1)].
5.6 Human Albumin
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.

5.7 Intradermal Immune Reaction
The possibility of an immune reaction when injected intradermally is unknown. The safety of DYSPORT® for the treatment of hyperhidrosis has not been established. DYSPORT® is approved only for intramuscular injection.

6 ADVERSE REACTIONS
The following serious adverse reactions are discussed below and elsewhere in labeling:

• Distant Spread of Toxin Effect [see Boxed Warning]
• Lack of Interchangeability between Botulinum Toxin Products [see Warnings and Precautions (5.1)]
• Spread of Effects from Toxin [see Warnings and Precautions (5.2)]
• Dysphagia and Breathing Difficulties [see Warnings and Precautions (5.3)]
• Facial Anatomy in the Treatment of Glabellar Lines [see Warnings and Precautions (5.4)]
• Pre-existing Neuromuscular Disorders [see Warnings and Precautions (5.5)]
• Human Albumin [see Warnings and Precautions (5.6)]

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Cervical Dystonia
The data described below reflect exposure to DYSPORT® in 357 cervical dystonia patients in 6 studies. Of these, two studies were randomized, double-blind, single treatment, placebo-controlled studies with subsequent optional open-label treatment in which dose optimization (250 to 1000 Units per treatment) over the course of 5 treatment cycles was allowed. The population was almost entirely Caucasian (99%) with a median age of 51 years (range 18–82 years). Most patients (87%) were less than 65 years of age; 58.4% were women.

Common Adverse Reactions
The most commonly reported adverse reactions (occurring in more than 5% of patients who received 500 Units of DYSPORT® in the placebo controlled clinical trials) in cervical dystonia patients were: muscular weakness, dysphagia, dry mouth, injection site discomfort, fatigue, headache, neck pain, musculoskeletal pain, dysphonia, injection site pain, and eye disorders (consisting of blurred vision, diplopia, and reduced visual acuity and accommodation). Other than injection site reactions, most adverse reactions became noticeable about one week after treatment and lasted several weeks. The rates of adverse reactions were higher in the combined controlled and open-label experience than in the placebo-controlled trials.

During the clinical studies, two patients (<1%) experienced adverse reactions leading to withdrawal. One patient experienced disturbance in attention, eyelid disorder, feeling abnormal and headache, and one patient experienced dysphagia.

Table 3 compares the incidence of the most frequent adverse reactions from a single treatment cycle of 500 Units of DYSPORT® compared to placebo [see Clinical Studies (14.1)].

Table 3: Most Common Adverse Reactions (>5%) and Greater than Placebo in the Pooling, Double-blind Phase of Clinical Trials in Patients with Cervical Dystonia

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DYSPORT® 500 Units (N=173)</th>
<th>Placebo (N=182)</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Any Adverse Reaction</td>
<td>61%</td>
<td>51%</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>30%</td>
<td>23%</td>
</tr>
<tr>
<td>Injection site discomfort</td>
<td>13%</td>
<td>8%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>12%</td>
<td>10%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>30%</td>
<td>18%</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>16%</td>
<td>4%</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>7%</td>
<td>3%</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>28%</td>
<td>15%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>15%</td>
<td>4%</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>13%</td>
<td>7%</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>16%</td>
<td>13%</td>
</tr>
<tr>
<td>Headache</td>
<td>11%</td>
<td>9%</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td>13%</td>
<td>9%</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>12%</td>
<td>8%</td>
</tr>
<tr>
<td>Dysphonia</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Eye Disorders*</td>
<td>7%</td>
<td>2%</td>
</tr>
</tbody>
</table>

*The following preferred terms were reported: vision blurred, diplopia, visual acuity reduced, eye pain, eyelid disorder, accommodation disorder, dry eye, eye pruritus.

Dose-response relationships for common adverse reactions in a randomized multiple fixed-dose study in which the total dose was divided between two muscles (the sternocleidomastoid and splenius capitis) are shown in Table 4.

Table 4: Common Adverse Reactions by Dose in Fixed-dose study in Patients with Cervical Dystonia

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo</th>
<th>DYSPORT® Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>500 Units</td>
<td>500 Units</td>
</tr>
<tr>
<td>Placebo</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Any Adverse Event</td>
<td>30%</td>
<td>37%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>5%</td>
<td>21%</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>10%</td>
<td>21%</td>
</tr>
<tr>
<td>Muscular Weakness</td>
<td>0%</td>
<td>11%</td>
</tr>
<tr>
<td>Injection Site Discomfort</td>
<td>10%</td>
<td>5%</td>
</tr>
<tr>
<td>Dysphonia</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Facial Paralysis</td>
<td>0%</td>
<td>5%</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

a. The following preferred terms were reported: vision blurred, diplopia, visual acuity reduced, eye pain, eyelid disorder, accommodation disorder, dry eye, eye pruritus.

Injection Site Reactions
Injection site discomfort and injection site pain were common adverse reactions following DYSPORT® administration.

Less Common Adverse Reactions
The following adverse reactions were reported less frequently (<5%).

Breathing Difficulty
Breathing difficulties were reported by approximately 3% of patients following DYSPORT® administration and in 1% of placebo patients in clinical trials during the double-blind phase. These consisted mainly of dyspnea. The median time to onset from last dose of DYSPORT® was approximately one week, and the median duration was approximately three weeks.

Other adverse reactions with incidences of less than 5% in the DYSPORT® 500 Units group in the double-blind phase of clinical trials included dizziness in 3.5% of DYSPORT®-treated patients and 1% of placebo-treated patients, and muscle atrophy in 1% of DYSPORT®-treated patients and in none of the placebo-treated patients.

Laboratory Findings
Patients treated with DYSPORT® exhibited a small increase from baseline (0.23 mol/L) in mean blood glucose relative to placebo-treated patients. This was not clinically significant among patients in the development program but could be a factor in patients whose diabetes is difficult to control.

Electrocardiographic Findings
ECG measurements were only recorded in a limited number of patients in an open-label study without a placebo or active control. This study showed a statistically significant reduction in heart rate compared to baseline, averaging about three beats per minute after injection.

Glabellar Lines
In placebo-controlled clinical trials of DYSPORT®, the most common adverse reaction(2%) following injection of DYSPORT® were nasopharyngitis, headache, injection site pain, injection site reaction, upper respiratory tract infection, eyelid edema, eyelid ptosis, sinusitis, and nausea.

Table 5 reflects exposure to DYSPORT® in 398 patients 19 to 75 years of age who were evaluated in the randomized, placebo-controlled clinical studies that assessed the use of DYSPORT® for the temporary improvement in the appearance of glabellar lines [see Clinical Studies (14.1)]. Adverse reactions of any cause occurred in 48% of the DYSPORT®-treated patients and 33% of the placebo-treated patients.

Table 5: Most Common Adverse Reactions with > 1% Incidence in Pooling, Placebo-Controlled Trials for Glabellar Lines

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>DYSPORT® n=398 (%)*</th>
<th>Placebo n=496 (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Adverse Reaction</td>
<td>48</td>
<td>33</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>Eyelid Edema</td>
<td>2</td>
</tr>
<tr>
<td>Eyelid Ptosis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Injection Site Pain</td>
<td>3</td>
</tr>
<tr>
<td>Injection Site Reaction</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td>Nasopharyngitis</td>
<td>10</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Investigations</td>
<td>Blood Present in Urine</td>
<td>2</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Headache</td>
<td>9</td>
</tr>
</tbody>
</table>

* Patients who received treatment with placebo and DYSPORT® are counted in both treatment columns.

In the overall safety database, where some patients received up to twelve treatments with DYSPORT® adverse reactions were reported for 57% (1425/2491) of patients. The most frequently reported of these adverse reactions were headache, nasopharyngitis, injection site pain, sinusitis, URI, injection site bruising, and injection site reaction (numbness, discomfort, erythema, tenderness, tingling, itching, stinging, warmth, irritation, tightness, swelling).
Adverse reactions that occurred after repeated injections in 2–3% of the population included bruising, influenza, pharyngolaryngeal pain, cough, contact dermatitis, injection site swelling, and injection site discomfort. The incidence of eyelid ptosis did not increase in the long-term safety studies with multiple repeat treatments at intervals ≥ three months. The majority of the reports of eyelid ptosis were mild to moderate in severity and resolved over several weeks. [see Dosage and Administration (2.3)].

Upper Limb Spasticity Table 6 lists the most frequently reported adverse reactions (≥2%) in any DYSPORT® dose group and more frequent than placebo in double blind studies evaluating the treatment of upper limb spasticity in adults with DYSPORT®.

Table 6: Most Common Adverse Reactions Observed in at Least 2% of Patients Treated in Pooled, Double-Blind Trials of Patients with Upper Limb Spasticity Reported More Frequently than with Placebo

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>DYSPORT® 500 Units (N=197) %</th>
<th>DYSPORT® 1000 Units (N=194) %</th>
<th>Placebo (N=279) %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections and infestations</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Infection</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>2</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Back pain</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Nervous system disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Convulsion</td>
<td>2</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Syncope</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>0</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Partial seizures</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td><strong>General disorders and administration site conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Asthenia</td>
<td>2</td>
<td>1</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>Injury, poisoning and procedural complications</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Injury</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Contusion</td>
<td>1</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Constipation</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Investigation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood triglycerides increased</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Vascular disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td><strong>Psychiatric disorders</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Injection Site Reactions Injection site reactions (e.g. pain, bruising, haemorrhage, injection site erythema/haematoma etc.) have occurred following administration of DYSPORT®.

Less Common Adverse Reactions In a pooled analysis of clinical studies, adverse reactions with an incidence of less than 2% reported in DYSPORT® treatment groups included dysphagia 0.5%, gait disturbance 0.5%, hypertonia 0.5%, and sensation of heaviness 0.3%.

6.2 Postmarketing Experience Because adverse reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The following adverse reactions have been identified during post-approval use of DYSPORT®: vertigo, photophobia, influenza-like illness, amyotrophy, burning sensation, facial paresis, hypoaesthesia, erythema, and excessive granulation tissue.

6.3 Immunogenicity As with all therapeutic proteins, there is a potential for immunogenicity. The incidence of antibody formation is highly dependent on the sensitivity and specificity of the assay. In addition, the observed incidence of antibody positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies across products in this class may be misleading.

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>DYSPORT® 500 Units (N=197) %</th>
<th>DYSPORT® 1000 Units (N=194) %</th>
<th>Placebo (N=279) %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cervical Dystonia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>About 3% of subjects developed antibodies (binding or neutralizing) over time with DYSPORT® treatment.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| **Glabellar Lines** Testing for antibodies to DYSPORT® was performed for 1554 subjects who had up to nine cycles of treatment. Two subjects (0.13%) tested positive for binding antibodies at baseline. Three additional subjects tested positive for binding antibodies after receiving DYSPORT® treatment. None of the subjects tested positive for neutralizing antibodies. From 230 subjects treated with DYSPORT® and tested for the presence of binding antibodies, 5 subjects were positive at baseline and 17 developed antibodies after treatment. Among those 17 subjects, 10 subjects developed neutralizing antibodies. An additional 51 subjects from a separate repeat dose study were tested for the presence of neutralizing antibodies only. None of the subjects tested positive. In total, from the 281 subjects treated in the long-term studies and tested for the presence of neutralizing antibodies, 3.6% developed neutralizing antibodies after treatment. In the presence of binding and neutralizing antibodies to DYSPORT®, some patients continue to experience clinical benefit.

7. DRUG INTERACTIONS

No formal drug interaction studies have been conducted with DYSPORT®. Patients treated concomitantly with botulinum toxins and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents) should be observed closely because the effect of the botulinum toxin may be potentiated. Use of anticholinergic drugs after administration of DYSPORT® may potentiate systemic anticholinergic effects such as blurred vision. The effect of administering different botulinum neurotoxin products at the same time or within several months of each other is unknown. Excessive weakness may be exacerbated by another administration of 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 DYSPORT®.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Pregnancy Category C DYSPORT® produced embryo-fetal toxicity when given to pregnant rats at doses similar to or greater than the maximum recommended human dose (MRHD) of 1000 Units on a body weight (Units/kg) basis. In an embryo-fetal development study in which pregnant rats received intramuscular injections daily (2, 6, 9, or 22 Units/kg on gestation days 6 through 17) or intermittently (44 Units/kg on gestation days 6 and 12 only) during organogenesis, increased early embryonic death was observed with both dosing schedules. The no-effect dose for embryo-fetal developmental toxicity was 2.2 Units/kg (one-tenth the MRHD on a body weight basis). Maternal toxicity was seen at 22 and 44 Units/kg. In a pre- and post-natal development study in which female rats received 6 weekly intramuscular injections (4, 11, 1, 22, 2, or 44 Units/kg) beginning on day 6 of gestation and continuing through parturition to weaning, an increase in stillbirths was observed at the highest dose, which was maternally toxic. The no-effect dose for pre- and post-natal developmental toxicity was 22.2 Units/kg (approximately equal to the MRHD on a body weight basis). There are no adequate and well-controlled studies in pregnant women. DYSPORT® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers It is not known whether DYSPORT® is excreted in human milk.

8.4 Pediatric Use Cervical Dystonia Safety and effectiveness in pediatric patients have not been established [see Warnings and Precautions (5.2)].

Glabellar Lines DYSPORT® is not recommended for use in pediatric patients less than 18 years of age.

Upper Limb Spasticity Safety and effectiveness in pediatric patients have not been established [see Warnings and Precautions (5.2)].

8.5 Geriatric Use Cervical Dystonia There were insufficient numbers of patients aged 65 and over in the clinical studies to determine whether they respond differently than younger patients. In general, elderly patients should be observed to evaluate their tolerability of DYSPORT®, due to the greater frequency of concomitant disease and other drug therapy [see Dosage and Administration (2.1)].

Glabellar Lines Of the total number of subjects in the placebo-controlled clinical studies of DYSPORT®, 8 (1%) were 65 and over. Efficacy was not observed in subjects 65 years and over [see Clinical Studies (14.2)]. For the entire safety database of geriatric subjects, although there was no increase in the incidence of eyelid ptosis, glabellar subjects did have an increase in the number of ocular adverse reactions compared to younger subjects (11% vs. 5%) [see Dosage and Administration (2.2)].

Upper Limb Spasticity Of the total number of subjects in placebo controlled clinical studies of DYSPORT®, 28.0 percent were 65 and over, while 6.2 percent were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
8.6 Ethnic Groups

Exploratory analyses in trials for glabellar lines in African-American subjects with Fitzpatrick skin types IV, V, or VI and in Hispanic subjects suggested that response rates at Day 30 were comparable to and no worse than the overall population.

10 OVERDOSAGE

Excessive doses of DYSPORT® may be expected to produce neuromuscular weakness with a variety of symptoms. Respiratory support may be required where excessive doses cause paralyzation of respiratory muscles. In the event of overdose, the patient should be medically monitored for symptoms of excessive muscle weakness or muscle paralysis [see Warnings and Precautions (8.2)]. Symptomatic treatment may be necessary.

Symptoms of overdose are likely not to be present immediately following injection. Should accidental injection or oral ingestion occur, the person should be medically supervised for several weeks for signs and symptoms of excessive muscle weakness or paralysis.

There is no significant information regarding overdose from clinical studies.

In the event of overdose, antitoxin raised against botulinum toxin is available from the Centers for Disease Control and Prevention (CDC) in Atlanta, GA. However, the antitoxin will not reverse any botulinum toxin-induced effects already apparent by the time of antitoxin administration. In the event of suspected or actual cases of botulinum toxin poisoning, please contact your local or state Health Department to process a request for antitoxin through the CDC. If you do not receive a response within 30 minutes, please contact the CDC directly at 770-488-7100. More information can be obtained at http://www.cdc.gov/nccdphp/dnpa/drugs/driver-service.html.

11 DESCRIPTION

Botulinum toxin type A, the active ingredient in DYSPORT® (abobotulinumtoxinA), is a purified neurotoxin type A complex produced by fermentation of the bacterium Clostridium botulinum type A, Hall Strain. It is purified from the culture supernatant by a series of precipitation, dialysis, and chromatography steps. The neurotoxin complex is composed of the neurotoxin, hemagglutinin proteins and non-toxin non-hemagglutinin protein.

DYSPORT® is supplied in a single-use, sterile vial for reconstitution intended for intramuscular injection. Each vial contains 300 Units or 500 Units of lyophilized abobotulinumtoxinA, human serum albumin (125 mcg) and lactose (2.5 mg). DYSPORT® may contain trace amounts of cow’s milk proteins [see Contraindications (4)].

One unit of DYSPORT® corresponds to the calculated median lethal intraperitoneal dose (LD50) in mice. The method for performing the assay is specific to Ipsen’s product DYSPORT®. Due to differences in specific details such as vehicle, dilution scheme and laboratory protocols for various mouse LD50 assays, Units of biological activity of DYSPORT® are not interchangeable with Units of any other botulinum toxin or any toxin assessed with any other specific assay method [see Dosage Forms and Strengths (3)].

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

DYSPORT® inhibits release of the neurotransmitter, acetylcholine, from peripheral cholinergic nerve endings. Toxin activity occurs in the following sequence: Toxin heavy chain mediated binding to specific surface receptors on nerve endings, internalization of the toxin by receptor mediated endocytosis, pH-induced translocation of the toxin light chain to the cell cytosol and cleavage of SNAP25 leading to intracellular blockage of neurotransmitter exocytosis into the neuromuscular junction. This accounts for the therapeutic utility of the toxin in diseases characterized by excessive effenter activity in motor nerves.

Recovery of transmission occurs gradually as the neuromuscular junction recovers from SNAP25 cleavage and as new nerve endings are formed.

12.2 Pharmacodynamics

The primary pharmacodynamic effect of DYSPORT® is due to chemical denervation of the treated muscle resulting in a measurable decrease of the compound muscle action potential, causing a localized reduction of muscle activity.

12.3 Pharmacokinetics

Using currently available analytical technology, it is not possible to detect DYSPORT® in the peripheral blood following intramuscular injection at the recommended doses.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Studies to evaluate the carcinogenic potential of DYSPORT® have not been conducted.

Mutagenesis

Genotoxicity studies have not been conducted for DYSPORT®.

Impairment of Fertility

In a fertility and early embryonic development study in rats in which either males (2.9, 7.2, 14.5 or 29 Units/kg) or females (7.4, 19.7, 39.4 or 78.8 Units/kg) received weekly intramuscular injections prior to and after mating, dose-related increases in pre-implantation loss and reduced numbers of corpora lutea were noted in treated females. Failure to mate was observed in males that received the high dose. The no-effect dose for effects on fertility was 7.4 Units/kg in females and 14.5 Units/kg in males (approximately one-half and equal to, respectively, the maximum recommended human dose of 1000 Units on a body weight basis).

14 CLINICAL STUDIES

14.1 Cervical Dystonia

The efficacy of DYSPORT® was evaluated in two randomized, double-blind, placebo controlled, single dose, parallel group studies in treatment-naïve cervical dystonia patients. The principal analyses from these trials provide the primary demonstration of efficacy involving 252 patients (121 on DYSPORT®; 131 on placebo) with 36% male and 64% female. Ninety-nine percent of the patients were Caucasian.

In both placebo controlled studies (Study 1 and Study 2), a dose of 500 Units DYSPORT® was given by intramuscular injection divided among two to four affected muscles. These studies were followed by long-term open label extensions that allowed titration in 250 Unit steps to doses in a range of 250 to 1000 Units, after the initial dose of 500 Units. In the extension studies, re-treatment was determined by clinical need after a minimum of 12 weeks. The median time to re-treatment was 14 weeks and 18 weeks for the 75th percentile.

The primary assessment of efficacy was based on the total Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) change from baseline at Week 4 for both studies. The scale evaluates the severity of dystonia, patient perceived disability from dystonia, and pain. The adjusted mean change from baseline in the TWSTRS total score was statistically significantly greater for the DYSPORT® group than the placebo group at Weeks 4 in both studies (see Table 7).

Table 7: TWSTRS Total Score Efficacy Outcome from the Phase 3 Cervical Dystonia Studies Intent to Treat Population

<table>
<thead>
<tr>
<th>Study</th>
<th>DYSPORT® 500 Units</th>
<th>Placebo</th>
<th>DYSPORT® 500 Units</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=55</td>
<td>43.8 (8.0)</td>
<td>45.8 (8.9)</td>
<td>45.1 (8.7)</td>
<td>46.2 (9.4)</td>
</tr>
<tr>
<td>N=61</td>
<td>30.0 (12.7)</td>
<td>40.2 (11.8)</td>
<td>35.2 (13.8)</td>
<td>42.4 (12.2)</td>
</tr>
<tr>
<td>N=37</td>
<td>-15.6 (2.0)</td>
<td>-6.7 (2.0)</td>
<td>-8.6 (2.0)</td>
<td>-3.7 (1.8)</td>
</tr>
</tbody>
</table>

Change from Baseline:

Week 1: -8.9% (95% confidence interval: [-12.9 to -4.7])
Week 2: -8.4% (95% confidence interval: [-10.6 to -6.0])

Timepoint: Mean (SD)

Week 1: 29.3 (11.0) 39.6 (13.5)
Week 2: -14.7 (2.0) -5.9 (2.0)

14.2 Glabellar Lines

Three double-blind, randomized, placebo-controlled, clinical studies evaluated the efficacy of DYSPORT® for use in the temporary improvement of the appearance of moderate to severe glabellar lines. These three studies enrolled healthy adults (ages 19-75) with glabellar lines of at least moderate severity at maximum frown. Subjects were excluded if they had marked ptosis, deep dermal scarring, or a substantial inability to lessen glabellar lines, even by physically spreading them apart. The subjects in these studies received either DYSPORT® or placebo. The total dose was delivered in equally divided aliquots to specified injection sites (see Figure 7).

Investigators and subjects assessed efficacy at maximum frown by using a 4-point scale (none, mild, moderate, severe). Overall treatment success was defined as post-treatment glabellar line severity of none or mild with at least 2 grade improvement from Baseline for the combined investigator and subject assessments (composite assessment) on Day 30 (see Table 9). Additional endpoints for each of the studies were post-treatment glabellar line severity of none or mild with at least a 1 grade improvement from Baseline for the separate investigator and subject assessments on Day 30.

After completion of the randomized studies, subjects were offered participation in a two-year, open-label re-treatment study to assess the safety of multiple treatments.
Treatment with DYSPORT® reduced the severity of glabellar lines for up to four months.

**Study GL-1**

Study GL-1 was a single dose, double-blind, multi-center, randomized, placebo-controlled study in which 158 previously untreated subjects received either placebo or 50 Units of DYSPORT®, administered in five aliquots of 10 Units (see Figure 1). Subjects were followed for 180 days. The mean age was 43 years; most of the subjects were women (85%), and predominantly Caucasian (49%) or Hispanic (47%). At Day 30, 55% of DYSPORT®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (Table 9).

In study GL-1, the reduction of glabellar line severity at maximum frown was greater at Day 30 in the DYSPORT® group compared to the placebo group as assessed by both Investigators and subjects (Table 10).

**Table 10: GL-1: Investigator’s and Subject’s Assessment of Glabellar Line Severity at Maximum Frown Using a 4-point Scale (% and Number of Subjects with Severity of None or Mild)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Investigator’s Assessment</th>
<th>Subject’s Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DYSPORT®</td>
<td>Placebo</td>
</tr>
<tr>
<td>GL-1</td>
<td>N=105</td>
<td>N=53</td>
</tr>
<tr>
<td>14</td>
<td>90%</td>
<td>17%</td>
</tr>
<tr>
<td>30</td>
<td>88%</td>
<td>4%</td>
</tr>
<tr>
<td>60</td>
<td>64%</td>
<td>2%</td>
</tr>
<tr>
<td>90</td>
<td>43%</td>
<td>6%</td>
</tr>
<tr>
<td>120</td>
<td>25%</td>
<td>4%</td>
</tr>
<tr>
<td>150</td>
<td>9%</td>
<td>2%</td>
</tr>
<tr>
<td>180</td>
<td>6%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Study GL-2**

Study GL-2 was a repeat dose, double-blind, multi-center, placebo-controlled, randomized study. The study was initiated with two or three open-label treatment cycles of 50 Units of DYSPORT® administered in five aliquots of 10 Units DYSPORT® (see Figure 1). After the open-label treatments, subjects were randomized to receive either placebo or 50 Units of DYSPORT®. Subjects could have received up to four treatments through the course of the study. Efficacy was assessed in the final randomized treatment cycle. The study enrolled 311 subjects into the first treatment cycle and 142 subjects were randomized into the final treatment cycle. Overall, the mean age was 47 years; most of the subjects were women (86%) and predominantly Caucasian (80%). At Day 30, 52% of DYSPORT®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (see Table 9). The proportion of responders in the final treatment cycle was comparable to the proportion of responders in all prior treatment cycles.

After the final repeat treatment with DYSPORT®, the reduction of glabellar line severity at maximum frown was greater at Day 30 in the DYSPORT® group compared to the placebo group as assessed by both Investigators and subjects (Table 12).

**Table 11: GL-2: Investigator’s and Subject’s Assessments of Glabellar Line Severity at Maximum Frown Using a 4-point Scale (% and Number of Subjects with Severity of None or Mild)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Investigator’s Assessment</th>
<th>Subject’s Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DYSPORT®</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>N=71</td>
<td>N=71</td>
</tr>
<tr>
<td>30</td>
<td>85%</td>
<td>4%</td>
</tr>
</tbody>
</table>
| 60    | 60% | 3 | 56 | 1%

**Study GL-3**

Study GL-3 was a single dose, double-blind, multi-center, randomized, placebo-controlled study in which 300 previously untreated subjects received either placebo or 50 Units of DYSPORT®, administered in five aliquots of 10 Units (see Figure 1). Subjects were followed for 150 days. The mean age was 44 years; most of the subjects were women (87%), and predominantly Caucasian (75%) or Hispanic (18%).

At Day 30, 60% of DYSPORT®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (see Table 9). In study GL-3, the reduction of glabellar line severity at maximum frown was greater at Day 30 in the DYSPORT® group compared to the placebo group as assessed by both Investigators and subjects (see Table 12).

**Table 12: GL-3: Investigator’s and Subject’s Assessment of Glabellar Line Severity at Maximum Frown Using a 4-point Scale (% and Number of Subjects with Severity of None or Mild)**

<table>
<thead>
<tr>
<th>Day</th>
<th>DYSPORT® N=200</th>
<th>Placebo N=100</th>
<th>DYSPORT® N=200</th>
<th>Placebo N=100</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>83%</td>
<td>166</td>
<td>5%</td>
<td>165</td>
</tr>
<tr>
<td>30</td>
<td>86%</td>
<td>171</td>
<td>0</td>
<td>163</td>
</tr>
<tr>
<td>60</td>
<td>73%</td>
<td>150</td>
<td>1%</td>
<td>120</td>
</tr>
<tr>
<td>90</td>
<td>51%</td>
<td>102</td>
<td>1%</td>
<td>91</td>
</tr>
<tr>
<td>120</td>
<td>29%</td>
<td>58</td>
<td>1%</td>
<td>61</td>
</tr>
<tr>
<td>150</td>
<td>18%</td>
<td>32</td>
<td>1%</td>
<td>31</td>
</tr>
</tbody>
</table>

**Geriatric Subjects**

In GL1, GL2, and GL3, there were 8 subjects aged 65 and older who were randomized to DYSPORT® 50 Units in 5 equal aliquots of 10 Units (4) or placebo (4). None of the geriatric DYSPORT® subjects were a treatment success at maximum frown at Day 30.

**14.3 Upper Limb Spasticity**

The efficacy and safety of DYSPORT® for the treatment of upper limb spasticity was evaluated in a randomized, multi-center, double-blind, placebo-controlled study that included 238 patients (159 DYSPORT® and 79 placebo) with upper limb spasticity (Modified Ashworth Scale (MAS) score ≥2 in the primary targeted muscle group for toxin naive patients or MAS score ≥3 in the primary targeted muscle group for toxin naïve patients at least 4 months after the last botulinum toxin injection, of any serotype) who were at least 6 months post-stroke or post-traumatic brain injury. DYSPORT® 500 Units (N=80), DYSPORT® 1000 Units (N=79), or placebo (N=79) was injected intramuscularly into the affected upper limb muscles. After injection of the primary targeted muscle groups (PTMG), the remainder of the dose was injected into at least two additional upper limb muscles determined by the patient’s individual presentation. Table 13 provides the mean and range of DYSPORT® doses injected and the number of injections into specific muscles of the upper limb.

**Table 13: DYSPORT® Dose Injected and Number of Injections per Muscle**

<table>
<thead>
<tr>
<th>Muscle</th>
<th>DYSPORT® Treatment Group</th>
<th>Number of Patients</th>
<th>Mean DYSPORT® Units Injected (Min, Max)</th>
<th>Number Of Injection Sites Median, (D1 : D3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexor digitorum profundus (FDP)*</td>
<td>500 U</td>
<td>54</td>
<td>93.5 Units (50 to 100)</td>
<td>1, [1 : 2]</td>
</tr>
<tr>
<td>Flexor digitorum superficialis (FDS)*</td>
<td>1000 U</td>
<td>65</td>
<td>195.5 Units (100 to 300)</td>
<td>2, [1 : 2]</td>
</tr>
<tr>
<td>Flexor carpi radialis (FCR)*</td>
<td>500 U</td>
<td>63</td>
<td>95.4 Units (50 to 100)</td>
<td>2, [1 : 2]</td>
</tr>
<tr>
<td>Flexor carpi ulnaris (FCU)*</td>
<td>1000 U</td>
<td>73</td>
<td>196.8 Units (100 to 300)</td>
<td>2, [1 : 2]</td>
</tr>
<tr>
<td>Brachialis*</td>
<td>500 U</td>
<td>57</td>
<td>92.2 Units (25 to 100)</td>
<td>1, [1 : 2]</td>
</tr>
<tr>
<td>Brachioradialis*</td>
<td>1000 U</td>
<td>57</td>
<td>178.1 Units (80 to 300)</td>
<td>3, [1 : 2]</td>
</tr>
<tr>
<td>Biceps Brachii (BB)</td>
<td>500 U</td>
<td>42</td>
<td>88.3 Units (50 to 200)</td>
<td>2, [1 : 2]</td>
</tr>
<tr>
<td>Pronator Teres</td>
<td>1000 U</td>
<td>28</td>
<td>106.4 Units (50 to 200)</td>
<td>3, [1 : 2]</td>
</tr>
</tbody>
</table>

*PTMG

The co-primary efficacy variables were muscle tone assessed by the MAS at the primary targeted muscle group at week 4 and the Physician Global Assessment (PGA) at week 4.
Table 14 Primary Endpoints (PTMG MAS and PGA) and MAS by Muscle Group at Week 4

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=79)</th>
<th>DYSPORT® (500 units) (N=80)</th>
<th>DYSPORT® (1000 units) (N=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS Mean Change from Baseline in PTMG Muscle Tone on the MAS</td>
<td>-0.3</td>
<td>-1.2*</td>
<td>-1.4*</td>
</tr>
<tr>
<td>LS Mean PGA of Response to Treatment</td>
<td>0.7</td>
<td>1.4*</td>
<td>1.8*</td>
</tr>
<tr>
<td>LS Mean Change from Baseline in Wrist Flexor Muscle Tone on the MAS</td>
<td>-0.3 (n=54)</td>
<td>-1.4 (n=57)</td>
<td>-1.6 (n=58)</td>
</tr>
<tr>
<td>LS Mean Change from Baseline in Finger Flexor Muscle Tone on the MAS</td>
<td>-0.3 (n=70)</td>
<td>-0.9 (n=66)</td>
<td>-1.2 (n=73)</td>
</tr>
<tr>
<td>LS Mean Change from Baseline in Elbow Flexor Muscle Tone on the MAS</td>
<td>-0.3 (n=56)</td>
<td>-1.0 (n=61)</td>
<td>-1.2 (n=48)</td>
</tr>
</tbody>
</table>

LS= Least Square; p<0.05

16 HOW SUPPLIED/STORAGE AND HANDLING

DYSPORT® for Injection is supplied in a sterile, single-use, glass vial. DYSPORT® must be stored under refrigeration at 2° to 8°C. Protect from light. Do not use after the expiration date on the vial. All vials, including expired vials, or equipment used with DYSPORT® should be disposed of carefully as is done with all medical waste.

DYSPORT® contains a unique hologram on the carton. If you do not see the hologram, do not use the product. Instead contact 877-397-7671.

Cervical Dystonia and Adult Upper Limb Spasticity

500 Unit Vial
- Each vial contains 500 Units of freeze-dried abobotulinumtoxinA.
- Box containing 1 vial—NDC 15054-0500-1
- Box containing 2 vials—NDC 15054-0500-2

300 Unit Vial
- Each vial contains 300 Units of freeze-dried abobotulinumtoxinA.
- Box containing 1 vial—NDC 15054-0503-6

Glabellar Lines
- Each vial contains 300 Units of freeze-dried abobotulinumtoxinA.
- Box containing 1 vial—NDC 0299-5962-30

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labelling (Medication Guide). Advise patients to inform their doctor or pharmacist if they develop any unusual symptoms (including difficulty with swallowing, speaking or breathing). Inform patients that if loss of strength, muscle weakness, blurred vision or drooping eyelids occur, they should avoid driving a car or engaging in other potentially hazardous activities.

Manufactured by:
Ipsen Biopharm Ltd.
Wrexham, LL13 9UF, UK
U.S. License No. 1787

Distributed by:
Ipsen Biopharmaceuticals, Inc.
Basking Ridge, NJ 07920
and
Galdemra Laboratories, L.P.
Fort Worth, TX 76177 USA

MEDICATION GUIDE
DYSPORT® (Dis-port) (abobotulinumtoxinA) for Injection

What is the most important information I should know about DYSPORT®?

DYSPORT® may cause serious side effects that can be life threatening including:

- **Problems breathing or swallowing**
- **Spread of toxin effects**

These problems can happen within hours, or days to weeks after an injection of DYSPORT®. Call your doctor or get medical help right away if you have any of these problems after treatment with DYSPORT®:

1. **Problems swallowing, speaking, or breathing.** These problems can happen within hours, or days to weeks after an injection of DYSPORT® usually because the muscles that you use to breathe and swallow can become weak after the injection. Death can happen as a complication if you have severe problems with swallowing or breathing after treatment with DYSPORT®.
   - People with certain breathing problems may need to use muscles in their neck to help them breathe. These patients may be at greater risk for serious breathing problems with DYSPORT®.
   - Swallowing problems may last for several weeks. People who cannot swallow well may need a feeding tube to receive food and water. If swallowing problems are severe, food or liquids may go into your lungs. People who already have swallowing or breathing problems before receiving DYSPORT® have the highest risk of getting these problems.

2. **Spread of toxin effects.** In some cases, the effect of botulinum toxin may affect areas of the body away from the injection site and cause symptoms of a serious condition called botulism. The symptoms of botulism include:
   - loss of strength and muscle weakness all over the body
   - blurred vision and drooping eyelids
   - trouble saying words clearly (dysarthria)
   - trouble breathing
   - double vision
   - hoarseness or change or loss of voice (dysphonia)
   - loss of bladder control
   - trouble swallowing

These symptoms can happen within hours, or days to weeks after you receive an injection of DYSPORT®. These problems could make it unsafe for you to drive a car or do other dangerous activities. See “What should I avoid while receiving DYSPORT®?”

What is DYSORT®?

DYSPORT® is a prescription medicine that is injected into muscles and used:

- to treat cervical dystonia (CD) in adults
- to improve the look of moderate to severe frown lines between the eyebrows (glabellar lines) in adults younger than 65 years of age for a short period of time (temporary)
- to treat increased muscle stiffness in, elbow, wrist, and finger muscles in adults with upper limb spasticity.
CD is caused by muscle spasms in the neck. These spasms cause abnormal position of the head and often neck pain. After DYSPORT® is injected into muscles; those muscles are weakened for up to 12 to 16 weeks or longer. This may help lessen your symptoms.

Frown lines (wrinkles) happen because the muscles that control facial expression are used often (muscle tightening over and over). After DYSPORT® is injected into the muscles that control facial expression, the medicine stops the tightening of these muscles for up to 4 months.

- It is not known whether DYSPORT® is safe or effective in children under 18 years of age.
- It is not known whether DYSPORT® is safe or effective for the treatment of other types of muscle spasms.
- It is not known whether DYSPORT® is safe or effective for the treatment of other wrinkles.

Who should not take DYSPORT®?

Do not take DYSPORT® if you:
- are allergic to DYSPORT® or any of the ingredients in DYSPORT®.
- are allergic to cow’s milk protein
- had an allergic reaction to any other botulinum toxin product such as Myobloc® (rimabotulinumtoxinB), Botox® (onabotulinumtoxinA), or Xeomin® (incobotulinumtoxinA).
- have a skin infection at the planned injection site

What should I tell my doctor before taking DYSPORT®?

Tell your doctor about all your medical conditions, including if you:
- have a disease that affects your muscles and nerves (such as amyotrophic lateral sclerosis [ALS or Lou Gehrig’s disease], myasthenia gravis or Lambert-Eaton syndrome). See “What is the most important information I should know about DYSPORT®?”
- have allergies to any botulinum toxin product
- had any side effect from any botulinum toxin product in the past
- have or have had a breathing problem, such as asthma or emphysema
- have or have had swallowing problems
- have or have had bleeding problems
- have diabetes
- have or have had a slow heart beat or other problem with your heart rate or rhythm
- have plans to have surgery
- had surgery on your face
- have weakness of your forehead muscles (such as trouble raising your eyebrows)
- have drooping eyelids
- have any other change in the way your face normally looks
- are pregnant or plan to become pregnant. It is not known if DYSPORT® can harm your unborn baby
- are breast-feeding or planning to breast-feed. It is not known if DYSPORT® passes into breast milk

Tell your doctor about all the medicines you take, including prescription and nonprescription medicines, vitamins and herbal products. Using DYSPORT® with certain other medicines may cause serious side effects. Do not start any new medicines until you have told your doctor that you have received DYSPORT® in the past.

Especially tell your doctor if you:
- have received any other botulinum toxin product in the last four months
- have received injections of botulinum toxin, such as Myobloc® (rimabotulinumtoxinB), Botox® (onabotulinumtoxinA) or Xeomin® (incobotulinumtoxinA) in the past; be sure your doctor knows exactly which product you received
- have recently received an antibiotic by injection
- take muscle relaxants
- take an allergy or cold medicine
- take a sleep medicine

Ask your doctor if you are not sure if your medicine is one that is listed above.

Know the medicines you take. Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

How should I take DYSPORT®?

DYSPORT® is an injection that your doctor will give you
- DYSPORT® is injected into the affected muscles
- Your doctor may give you another dose of DYSPORT® after 12 weeks or longer, if it is needed
- If you are being treated for CD or upper limb spasticity, your doctor may change your dose of DYSPORT®, until you and your doctor find the best dose for you
- The dose of DYSPORT® is not the same as the dose of any other botulinum toxin product

What should I avoid while taking DYSPORT®?

DYSPORT® may cause loss of strength or general muscle weakness, blurred vision, or drooping eyelids within hours to weeks of taking DYSPORT®. If this happens, do not drive a car, operate machinery, or do other dangerous activities. See “What is the most important information I should know about DYSPORT®?”

What are the possible side effects of DYSPORT®?

DYSPORT® can cause serious side effects. See “What is the most important information I should know about DYSPORT®?”

The most common side effects of DYSPORT® in people with cervical dystonia include:
- muscle weakness
- dry mouth
- feeling of tiredness
- neck pain or muscle pain
- problems speaking
- eye problems
- difficulty swallowing
- injection site pain
- headache

The most common side effects of DYSPORT® in people with glabellar lines include:
- stuffy or runny nose and sore throat
- injection site pain
- upper respiratory infection
- headache
- injection site reaction
- swelling of eyelids
- drooping eyelids
- sinus infection
- nausea
The most common side effects of DYSPORT® in people with upper limb spasticity include:

- urinary tract infection
- muscle weakness
- musculoskeletal pain
- fall
- depression
- stuffy or runny nose and sore throat
- dizziness

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of DYSPORT®. For more information, ask your doctor pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about DYSPORT®:
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide.
This Medication Guide summarizes the most important information about DYSPORT®. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about DYSPORT® that is written for healthcare professionals.
For more information about DYSPORT® call 877-397-7671 or go to www.dysport.com or www.DysportUSA.com.

What are the ingredients in DYSPORT®?
Active ingredient: (botulinum toxin Type A)
Inactive ingredients: human albumin and lactose. DYSPORT® may contain cow’s milk protein.

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This Medication Guide has been approved by the U.S. Food and Drug Administration

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