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® (abobotulinumtoxinA) 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 about Dysport® throughout this brochure and accompanying Full Prescribing Information, including **Boxed Warning**, and Medication Guide.
What are the causes of 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 also been approved in the United States for over 6 years for the treatment of another neurological condition called cervical dystonia.

What are the potential benefits of treatment with Dysport®?

In a clinical study, Dysport® significantly reduced stiffness in the elbow, wrist, and finger muscles at Week 4. 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 about Dysport® throughout this brochure and accompanying Full Prescribing Information, including Boxed Warning, and Medication Guide.

What You Should Know: 
About receiving treatment

How is Dysport® treatment given?

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

How long before my symptoms come back?

In Dysport® clinical studies of adults with upper limb spasticity, most people needed treatment again between 3 and 4 months. Some had a longer response and were treated again at 5 months. Dysport® injections should be given at least 3 months apart, as needed, when your symptoms return.

*Based on the return of symptoms.
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.

Please see additional Important Safety Information about Dysport® throughout this brochure and accompanying Full Prescribing Information, including Boxed Warning, and Medication Guide.
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.

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 $3,750 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* for the Dysport® Copay Assistance Program, you will receive copay assistance covering a portion of your out-of-pocket costs for up to 4 treatments per year—a maximum of up to $3,750 in total savings per year
- Use your Dysport® Copay Assistance Program at your doctor’s office or at your specialty pharmacy to cover your out-of-pocket costs† for Dysport®
- After each injection, send the IPSEN CARES™ team your Explanation of Benefits (EOB) or pharmacy receipt and you will be reimbursed for your out-of-pocket costs

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

Eligible* patients may save up to $3,750 annually in out-of-pocket expenses for Dysport®.

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.

*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 must be used within 60 days and cannot be used anywhere other than your doctor’s office or at a specialty pharmacy.

Please see additional Important Safety Information about Dysport® throughout this brochure and accompanying Full Prescribing Information, including Boxed Warning, and Medication Guide.
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

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.

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.

Please see additional Important Safety Information about Dysport® throughout this brochure and accompanying Full Prescribing Information, including Boxed Warning, and Medication Guide.
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 at Week 4
  - 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 $3,750 in out-of-pocket expenses for Dysport® every year

- To learn more about the Dysport® Copay Assistance Program:
  - Visit Dysport.com/copay-assistance-program
  - 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® (abobotulinumtoxinA) 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 about Dysport® throughout this brochure and accompanying Full Prescribing Information, including Boxed Warning, and Medication Guide.
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

WARNING: DISTANT SPREAD OF TOXIN EFFECT
See full prescribing information for complete boxed warning
The effects of DYSPORT® and all botulinum toxin products may spread from the area of injection to other areas of the body, resulting in the symptoms of botulinum toxin effects. These symptoms may 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 occur in adults, particularly in those patients who have underlying conditions that would predispose them to these symptoms.

RECENT MAJOR CHANGES
7/2016
Dosage and Administration, Instructions for Safe Use (2.1)
12/2016
Dosage and Administration, Dosing in Cervical Dysotnia (2.2)
7/2016
Dosage and Administration, Pediatric Lower Limb Spasticity (2.5)

INDICATIONS AND USAGE
DYSPORT® is an acetylcholine release inhibitor and a neuromuscular blocking agent indicated for:

• The treatment of adults with cervical dystonia (1.1)
• The temporary improvement in the appearance of moderate to severe glabellar lines associated with procerus and corrugator muscle activity in adult patients < 65 years of age (1.2)
• The treatment of upper limb spasticity in adults (1.3)
• The treatment of lower limb spasticity in pediatric patients 2 years of age and older (1.4)

DOSE AND ADMINISTRATION
Instructions for Safe Use (2.1)

• Once reconstituted, store in original container in a refrigerator at 2°C to 8°C (36°F to 46°F) and use within 24 hours (2.1)
• Do not freeze after reconstitution (2.1)
• 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.

Cervical Dysotnia (2.2)

• 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

Glabellar Lines (2.3)

• 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

Upper Limb Spasticity (2.4)

• Select dose based on muscles affected, severity of muscle spasticity, prior response and adverse reaction history following treatment with botulinum toxins
• Re-treatment, based on return of clinical symptoms, should not occur in intervals of less than 12 weeks

Pediatric Lower Limb Spasticity (2.5)

• Select dose based on the affected muscle, severity of spasticity, and treatment history with botulinum toxins

FULL PRESCRIBING INFORMATION: CONTENTS*
WARNING: DISTANT SPREAD OF TOXIN EFFECT
1 INDICATIONS AND USAGE
1.1 Cervical Dysotnia
1.2 Glabellar Lines
1.3 Upper Limb Spasticity
1.4 Lower Limb Spasticity in Pediatric Patients

2 DOSE AND ADMINISTRATION
2.1 Instructions for Safe Use
2.2 Dosing in Cervical Dysotnia
2.3 Dosing in Glabellar Lines
2.4 Dosing in Upper Limb Spasticity in Adult Patients
2.5 Dosing in Lower Limb Spasticity in Pediatric Patients

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS
5.1 Lack of Interchangeability Between Botulinum Toxin Products
5.2 Spread of Toxin Effect
5.3 Dysphagia and Breathing Difficulties
5.4 Facial Anatomy in the Treatment of Glabellar Lines
5.5 Pre-existing Neuromuscular Disorders
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6 ADVERSE REACTIONS
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8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
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10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
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13 NONCLINICAL TOXICOLOGY
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14 CLINICAL STUDIES
14.1 Cervical Dysotnia
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14.3 Upper Limb Spasticity
14.4 Pediatric Patients with Lower Limb Spasticity

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

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

Revised: 12/2016
DYSPORT® in cervical dystonia suggest that the peak effect occurs between two and four weeks after injection. The sternocleidomastoid muscle may reduce the occurrence of dysphagia. Clinical studies with DYSPORT® demonstrated continued efficacy with up to four repeated administrations. It should be 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.

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.

DOSAGE AND ADMINISTRATION

1. INDIcATIONS AND USAGE

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.

1.4 Lower Limb Spasticity in Pediatric Patients

DYSPORT® is indicated for the treatment of lower limb spasticity in pediatric patients 2 years of age and older.

2. DOSAGE AND ADMINISTRATION

2.1 Instructions for Safe Use

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)]. Reconstituted DYSPORT® is intended for intramuscular injection only.

Reconstitution instructions are specific for each of the 300 Unit vial and the 500 Unit vial. These volumes yield concentrations specific for the use for each indication (Table 1).

Table 1: Dilution Instructions for DYSPORT® Vials (500 Units and 300 Units)

<table>
<thead>
<tr>
<th>Diluent* per 500 Unit Vial</th>
<th>Resulting Dose Units per 0.1 mL</th>
<th>Diluent* per 300 Unit Vial</th>
<th>Resulting Dose Units per 0.1 mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 mL</td>
<td>50 Units</td>
<td>0.6 mL</td>
<td>50 Units</td>
</tr>
<tr>
<td>2.5 mL</td>
<td>25 Units</td>
<td>--</td>
<td>20 Units</td>
</tr>
<tr>
<td>5 mL</td>
<td>--</td>
<td>1.5 mL</td>
<td>12 Units</td>
</tr>
<tr>
<td>10 mL</td>
<td>10 Units</td>
<td>2.5 mL</td>
<td>3 mL</td>
</tr>
</tbody>
</table>

*Preservative-free 0.9% Sodium Chloride Injection, USP Only

Note: These dilutions are calculated for an injection volume of 0.1 mL. A decrease or increase in the DYSPORT® dose is also possible by administering a smaller or larger injection volume (i.e. 0.05 mL (50% decrease in dose), 0.08 mL (20% decrease in dose) or 0.15 mL (50% increase in dose)).

** When using 5 mL of diluent for a 500 Unit vial of DYSPORT®, complete the following steps (see also 2.4 Dosing in Upper Limb Spasticity).

1. Reconstitute a 500 Unit vial of DYSPORT® with 2.5 mL of Preservative-free 0.9% Sodium Chloride Injection, USP, gently mix, and set the vial aside.

2. Withdraw 2.5 mL of Preservative-free 0.9% Sodium Chloride Injection, USP, into a 5 mL syringe.

3. Take the 5 mL syringe with 2.5 mL Preservative-free 0.9% Sodium Chloride Injection, USP, and draw up the DYSPORT® solution from the reconstituted vial without inverting and mix gently. The resulting concentration will be 10 units/0.1 mL.

4. Use immediately after reconstitution in the syringe. Dispose of any unused saline.

After reconstitution, DYSPORT® should be used for only one injection session and for only one patient. Once reconstituted, DYSPORT® should be stored in the original container, in a refrigerator at 2 °C to 8 °C (36 °F to 46 °F), protected from light for up to 24 hours. It must be discarded if not used within 24 hours. Do not freeze reconstituted DYSPORT®. Discard the vial and needle in accordance with local regulations.

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 10 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

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 25 Units per 0.1 mL or reconstituted with 2 mL of preservative-free 0.9% Sodium Chloride Injection USP to yield a solution of 25 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 2 mL or 1 mL of sterile, preservative-free 0.9% Sodium Chloride Injection USP for the 500 Unit vial or 0.6 mL of sterile, preservative-free 0.9% Sodium Chloride Injection USP for the 300 Unit vial. 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).

Special Populations

Adults

A total dose of 50 Units of DYSPORT®, in five equal aliquots, should be administered to achieve clinical effect.

The clinical effect of DYSPORT® may last up to four months. Repeat dose clinical studies demonstrated continued efficacy with up to four repeated administrations. It should be administered no more frequently than every three months. When used for re-treatment, DYSPORT® should be reconstituted and injected using the same techniques as the initial treatment.

Pediatric Patients

DYSPORT® for glabellar lines is not recommended for use in pediatric patients less than 18 years of age [see Warnings and Precautions (5.2)].

Instructions for 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 300 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 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 lines facial areas 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 neurovascular 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 superiors, particularly in patients with larger brow depressor complexes.

• Medial corrugator injections should be placed at least 1 centimeter above the bony superorbital rim.
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).

2.4 Dosing in Upper Limb Spasticity in Adult Patients

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 botulinum toxins. 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 in Adult Patients

<table>
<thead>
<tr>
<th>Muscles Injected</th>
<th>Recommended Dose DYSPORT®</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>

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®.

2.5 Dosing in Lower Limb Spasticity in Pediatric Patients

Pediatric Lower Limb Spasticity Patients 2 years of age and older

DYSPORT® dosing for pediatric lower limb spasticity is based on Units per kilogram of body weight. Table 3 describes the recommended Units/kg dose of DYSPORT® per muscle of the Gastrocnemius-Soleus Complex (GSC). The recommended total DYSPORT® dose per treatment session is 10 to 15 Units/kg for unilateral lower limb injections or 20 to 30 Units/kg for bilateral lower limb injections. However, the total dose of DYSPORT® administered per treatment session must not exceed 15 Units/kg for unilateral lower limb injections or 30 Units/kg for bilateral lower limb injections or 1000 units, whichever is lower. The total dose administered should be divided between the affected spastic muscles of the lower limb(s). When possible, the dose should be distributed across more than 1 injection site in any single muscle (see Table 3). No more than 0.5 mL of DYSPORT® should be administered in any single injection site.

Dosing in initial and sequential treatment sessions should be tailored to the individual patient 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 botulinum toxins.

Table 3: DYSPORT® Dosing by Muscle for Lower Limb Spasticity in Pediatric Patients

<table>
<thead>
<tr>
<th>Muscle Injected</th>
<th>Recommended DYSPORT® Dose Range per muscle per leg (Units/kg Body Weight)</th>
<th>Recommended number of injections per muscle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrocnemius</td>
<td>6 to 9 Units/kg</td>
<td>Up to 4</td>
</tr>
<tr>
<td>Soleus</td>
<td>4 to 6 Units/kg</td>
<td>Up to 2</td>
</tr>
<tr>
<td>Total</td>
<td>10 to 15 Units/kg divided across both muscles</td>
<td>Up to 6</td>
</tr>
</tbody>
</table>

Note: a – the listed individual doses to be injected in the muscles can be used within the range mentioned without exceeding 15 Units/kg total dose for unilateral injection or 30 Units/kg for bilateral injections or 1000 Units whichever is lower.

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

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 the clinical studies were retreated between 16-22 weeks, however; some had a longer duration of response. The degree and pattern of muscle spasticity and overall clinical benefit at the time of re-injection may necessitate alterations in the dose of DYSPORT® and muscles to be injected.

Treatment of Lower Limb Spasticity in Pediatric Patients less than 2 years of age
The safety and effectiveness of DYSPORT® in the treatment of lower limb spasticity in pediatric patients of less than 2 years of age has not been evaluated.

Treatment of Spasticity in Upper Limb Muscles or Proximal Muscles of the Lower Limb in Pediatric Patients 0 to 17 years of age
The safety and effectiveness of DYSPORT® injected into upper limb muscles or proximal muscles of the lower limb for the treatment of spasticity in pediatric patients has not been established.

Treatment of Lower Limb Spasticity in Adult Patients
The safety and effectiveness of DYSPORT® in the treatment of lower limb spasticity in adult patients has not been demonstrated.

Instructing for Preparatory Intramuscular Administration for the Treatment of Lower Limb Spasticity in Pediatric Patients 2 years and older
DYSPORT® is supplied as single-use 300Unit or 500Unit vials. 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. Each 300 Unit vial of DYSPORT® is to be reconstituted with 1.5 mL of preservative-free 0.9% Sodium Chloride Injection, USP prior to injection. The concentration of the resulting solution will be 20 Units per 0.1 mL. Further dilution with preservative-free 0.9% Sodium Chloride Injection, USP, may be required to achieve the final volume for injection. No more than 0.5 mL of DYSPORT® should be administered in any single injection site.

To calculate the total units of DYSPORT® required for treatment of one leg, select the dose of DYSPORT® in Units/kg/leg and the body weight (kg) of the patient (see Table 3). Using an appropriately sized sterile syringe (e.g., 3 mL syringe), needle and aseptic technique, draw up 2.5 mL of preservative-free 0.9% Sodium Chloride Injection, USP. Insert the needle into the DYSPORT® 500 Unit 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 the required patient dose of DYSPORT® into a sterile syringe and dilute with additional preservative-free 0.9% Sodium Chloride Injection, USP, if required, to achieve the final volume for injection. Expel any air bubbles in the syringe barrel. Remove the needle used to reconstitute the product and attach an appropriately sized new sterile needle.

Use immediately after reconstitution in the syringe.

Discard the vial and needle in accordance with local regulations.

3  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 asthenia, generalized muscle weakness, diplopia, blurred vision, 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 related to spread of toxin effects. 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 upper limb spasticity in children and approved indications, symptoms consistent with spread of toxin effect have been reported at doses comparable to or lower than the maximum recommended total dose [see Use in Specific Populations (8.4)].

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 swallowing or breathing. When distant 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 become dependent upon these accessory muscles. There have been post-marketing reports of severe 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)].

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 DYSHORT® [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 Graft-versus-Host disease (GVHD) is also considered extremely remote. No cases of transmission of viral diseases or GVHD 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)]

• Intradermal Immune Reaction [see Warnings and Precautions (5.7)]

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 446 cervical dystonia patients in 7 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 (90%) 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 5% or more 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, 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 4 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)].
**DYSPORT® (abobotulinumtoxinA)**

### Injection Site Reactions

Electrocardiographic Findings in the development program but could be a factor in patients whose diabetes is difficult to control. Blood glucose relative to placebo-treated patients. This was not clinically significant among patients.

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.

Other adverse reactions with incidences of less than 5% in the DYSPORT® groups are shown in Table 5.

### Laboratory Findings

- **Blood triglycerides**: Increased 2
- **Blood urea nitrogen**: Increased 2
- **Blood glucose**: Increased 2

### Nervous System Disorders

- **Headache**: Headache, facial paresthesia, eye pain, facial paresthesia, accommodation disorder, dry eye, eye pruritus.

- **Eye Disorders**: 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

**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® groups are shown in Table 5.

### Laboratory Findings

Patients treated with DYSPORT® exhibited a small increase from baseline (0.23 mmol/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, observed thirty minutes after injection.

### Glabellar Lines

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

Table 6 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)]. Adverse reactions of any cause occurred in 48% of the DYSPORT®-treated patients and 33% of the placebo-treated patients.

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**Table 4: Most Common Adverse Reactions (≥5%) and Greater than Placebo in the Pooled, Double-blind, Placebo-Controlled Phase of Clinical Trials in Patients with Cervical Dystonia**

<table>
<thead>
<tr>
<th>Adverse Reactions</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>Dysphagia</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>7</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 5: Common Adverse Reactions by Dose in Fixed-dose Study in Patients with Cervical Dystonia**

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>DYSPORT® Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo 250 Units</td>
</tr>
<tr>
<td>Any Adverse Event</td>
<td>30%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>5%</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>10%</td>
</tr>
<tr>
<td>Muscular Weakness</td>
<td>0%</td>
</tr>
<tr>
<td>Injection Site Discomfort</td>
<td>10%</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>0%</td>
</tr>
<tr>
<td>Facial Paresis</td>
<td>0%</td>
</tr>
<tr>
<td>Eye Disorders</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Table 6: Most Common Adverse Reactions with > 1% Incidence in Pooled, Placebo-Controlled Trials for Glabellar Lines**

<table>
<thead>
<tr>
<th>Adverse Reactions</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></td>
<td></td>
</tr>
<tr>
<td>Eyelid Edema</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Eyelid Ptsis</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Injection Site Pain</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>10</td>
<td>4</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></td>
<td></td>
</tr>
<tr>
<td>Blood Present in Urine</td>
<td>2</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>9</td>
<td>5</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, UIR, 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 bronchitis, 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 re-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 in Adults**

Table 7 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 7: Most Common Adverse Reactions Observed in at Least 2% of Patients Treated in Pooled, Double-blind Trials of Adult Patients with Upper Limb Spasticity Reported More Frequently than with Placebo**

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

* Patients who received treatment with placebo and DYSPORT® are counted in both treatment columns.
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%. Injection site reactions (e.g. pain, bruising, haemorrhage, injection site erythema/haematoma etc.) have occurred following administration of DYSPORT.

Lower Limb Spasticity in Pediatric Patients

Table 8 reflects exposure to DYSPORT in 180 children, 2 to 17 years of age, who were evaluated in the randomized, placebo-controlled clinical study that assessed the use of DYSPORT for the treatment of unilateral or bilateral lower limb spasticity in pediatric cerebral palsy patients [see Clinical Studies (14.4)]. The most commonly observed adverse reactions (>10% of patients) are: upper respiratory tract infection, nasopharyngitis, influenza, pharyngitis, cough and pyrexia.

Table 8: Adverse Reactions Observed in >4% of Patients Treated in the Double-Blind Trial of Pediatric Patients with Lower Limb Spasticity and Reported More Frequently than with Placebo

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Placebo (N=78)</th>
<th>Unilateral (N=48)</th>
<th>Bilateral (N=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>5</td>
<td>9</td>
<td>12</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>13</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Influenza</td>
<td>8</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>8</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>3</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>4</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Varicella</td>
<td>1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Ear infection</td>
<td>3</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Respiratory tract infection viral</td>
<td>0</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Gastroenteritis viral</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>5</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>6</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Oropharyngeal pain</td>
<td>2</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>5</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>5</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Convulsion/Epilepsy</td>
<td>0</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

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, focial paresis, hypoesthesia, 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.

Cervical Dystonia

About 3% of subjects developed antibodies (binding or neutralizing) over time with DYSPORT treatment.

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.

Upper Limb Spasticity

From 238 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.

Lower Limb Spasticity in Pediatric Patients

From 226 subjects treated with DYSPORT and tested for the presence of binding antibodies, 5 subjects previously receiving botulinum toxins were positive at baseline and 9 patients developed binding antibodies after injections. Among those 9 subjects, 3 subjects developed neutralizing antibodies, while one subject developed neutralizing antibodies from the 5 subjects testing positive for binding antibodies at baseline who previously received botulinum toxin injections.

From a separate repeat-dose study, 203 subjects were tested for the presence of neutralizing antibodies. None of the subjects were positive for neutralizing antibodies at baseline and 5 subjects developed neutralizing antibodies after treatments. In total, from the 429 patients tested for the presence of neutralizing antibodies, 2.1% developed neutralizing antibodies after treatment. In the presence of binding and neutralizing antibodies to DYSPORT, some patients continued 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

Risk Summary

There are no adequate and well-controlled clinical studies with DYSPORT in pregnant women. DYSPORT should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

DYSPORT produced embryo-fetal toxicity in relation to maternal toxicity when given to pregnant rats and rabbits at doses lower than or similar to the maximum recommended human dose (MRHD) of 1000 Units on a body weight (Units/kg) basis (see Data). In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated populations is unknown.

Data

In a study in which pregnant rats received daily intramuscular injections of DYSPORT (2.2, 6.6, 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 schedules at the highest tested doses (22 and 44 Units/kg), which were associated with maternal toxicity.

The no-effect dose for embryo-fetal developmental toxicity was 2.2 Units/kg (less than the maximum recommended human dose [MRHD] on a body weight basis).

In a study in which pregnant rabbits received daily intramuscular injections of DYSPORT (0.3, 3.3, or 6.7 Units/kg) on gestation days 6 through 19 or intermittently (13.3 Units/kg on gestation days 6 and 13 only) during organogenesis, no embryofetal data were available at the highest dose administered daily (6.7 Units/kg) because of premature death in all does at that dose. At the lower daily doses or with intermittent dosing, no adverse developmental effects were observed. All doses for which data were available are less than the MRHD on a body weight basis.

In a study in which pregnant rabbits received 6 weekly intramuscular injections of DYSPORT (4.4, 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 tested, which was maternally toxic. The no-effect dose for pre- and post-natal developmental toxicity was 22.2 Units/kg (similar to the MRHD).

8.2 Lactation

Risk Summary

There are no data on the presence of DYSPORT in human or animal milk, the effects on the breastfed child, or the effects on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for DYSPORT and any potential adverse effects on the breastfed infant from DYSPORT or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Infertility

In rats, DYSPORT produced adverse effects on mating behavior and fertility [see Nonclinical Toxicology (13.1)].

8.4 Pediatric Use

Cervical Dystonia

Safety and effectiveness in pediatric patients have not been established [see Warnings and Precautions (5.2)].
DYSPORT® (abobotulinumtoxinA)

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)].

Lower Limb Spasticity in Pediatric Patients

The safety and effectiveness of DYSPORT® injected into proximal muscles of the lower limb for the treatment of spasticity in pediatric patients has not been established [see Warnings and Precautions (5.2) and Adverse Reactions (6.1)].

Safety and effectiveness in pediatric patients with lower limb spasticity below 2 years of age have not been evaluated [see Warnings and Precautions (5.2)].

Juvenile Animal Data

In a study in which juvenile rats received a single intramuscular injection of DYSPORT® (1, 3, or 10 Units/animal) on postnatal day 21, decreased growth and bone length (contracted and contralateral limbs), delayed sexual maturation, and decreased fertility were observed at the highest dose tested, which was associated with excessive toxicity during the first week after dosing. In a study in which juvenile rats received weekly intramuscular injections of DYSPORT® (0.1, 0.3, or 1.0 Units/animal) from postnatal day 21 to 13 weeks of age, decreases in bone mineral content in the injected limb, associated with atrophy of injected and adjacent muscles, were observed at the highest dose tested. No adverse effects were observed on neurobehavioral development. However, dose levels were not adjusted for growth of the pups. On a body weight basis, the doses at the end of the dosing period were approximately 15% of those at initiation of dosing. Therefore, the effects of DYSPORT® throughout postnatal development were not adequately evaluated.

8.5 Geriatric Use

Cervical Dystonia

There were insufficient numbers of patients aged 65 years 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 years and over. Efficacy was not observed in subjects aged 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, geriatric subjects did have an increase in the number of ocular adverse reactions compared to younger subjects (11% vs. 3%) [see Dosage and Administration (2.2)].

Upper Limb Spasticity

Of the total number of subjects in placebo-controlled clinical studies of DYSPORT®, 28.0% were aged 65 years and over, while 8.2% were aged 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. 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, and VI 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 paralysis 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 (5.2)]. 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 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/ncidod/ssp/drugs/drug-service.html.

11 DESCRIPTION

Botulinum toxin type A, the active ingredient in DYSPORT® (abobotulinumtoxinA), is a purified neurotoxin type 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.

DYSPORT® Placebo DYSPORT® Placebo

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>DYSPORT® 500 Units</td>
<td>Placebo</td>
</tr>
<tr>
<td>N=55</td>
<td>N=61</td>
</tr>
<tr>
<td>DYSPORT® 500 Units</td>
<td>Placebo</td>
</tr>
<tr>
<td>N=57</td>
<td>N=43</td>
</tr>
<tr>
<td><strong>Baseline (week 0)</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>43.8 (8.0)</td>
</tr>
<tr>
<td>Week 4</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>30.0 (12.7)</td>
</tr>
<tr>
<td>Change from Baseline</td>
<td>-15.6 (2.0)</td>
</tr>
<tr>
<td>Treatment difference</td>
<td>-6.9*</td>
</tr>
<tr>
<td><strong>Week 8</strong></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>29.3 (11.0)</td>
</tr>
<tr>
<td>Change from Baseline</td>
<td>-14.7 (2.0)</td>
</tr>
<tr>
<td>Treatment difference</td>
<td>-6.8*</td>
</tr>
</tbody>
</table>

* Significant at p-value < 0.05

Table 9: TWSTRS Total Score Efficacy Outcome from the Phase 3 Cervical Dystonia Studies Intent to Treat Population
Analysis by gender, weight, geographic region, underlying pain, cervical dystonia severity at baseline and history of treatment with botulinum toxin did not show any meaningful differences between groups.

Table 10 indicates the average DYSport® dose, and percentage of total dose, injected into specific muscles in the pivotal clinical trials.

**Table 10: DYSport® 500 Units starting dose (units and % of the total dose) by Unilateral Muscle Injected During Double-blind Pivotal Phase 3 Studies 2 and 1 Combined**

<table>
<thead>
<tr>
<th>Number of patients injected per muscle</th>
<th>DYSport® Dose Injected</th>
<th>Percentage of the total DYSport® Dose Injected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (DYSport® Units) (min, max)</td>
<td>75th percentile (DYSport® Units)</td>
</tr>
<tr>
<td>Sternocecostomoid</td>
<td>90</td>
<td>125 Units (50,350)</td>
</tr>
<tr>
<td>Splenius capitis</td>
<td>85</td>
<td>200 Units (75,450)</td>
</tr>
<tr>
<td>Trapezius</td>
<td>50</td>
<td>102.6 Units (50,300)</td>
</tr>
<tr>
<td>Levator scapulae</td>
<td>35</td>
<td>105.3 Units (50,300)</td>
</tr>
<tr>
<td>Scalene (medius and anterior)</td>
<td>26</td>
<td>115.5 Units (50,300)</td>
</tr>
<tr>
<td>Semispinalis capitis</td>
<td>21</td>
<td>131.6 Units (50,250)</td>
</tr>
<tr>
<td>Longissimus</td>
<td>3</td>
<td>150 Units (100,200)</td>
</tr>
</tbody>
</table>

1. Total number of patients in combined studies 2 and 1 who received initial treatment = 121.

### 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 1).

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 11). Additional endpoints for each of the studies were post-treatment glabellar line severity of none or mild with at least a grade improvement from Baseline for the separate investigator and subject assessments on Day 30.

Subjects were followed for 180 days. The study enrolled 311 subjects into the first treatment cycle and 142 subjects were randomized into the final treatment cycle.

**Table 11: Treatment Success at Day 30 (None or Mild with at least 2 Grade Improvement from Baseline at Maximum Frown for the combined Investigator and Subject Assessments (Composite))**

<table>
<thead>
<tr>
<th>Study</th>
<th>DYSport® n/N (%)</th>
<th>Placebo n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GL-1</td>
<td>58/105 (55%)</td>
<td>0/3 (%)</td>
</tr>
<tr>
<td>GL-2</td>
<td>37/71 (52%)</td>
<td>0/7 (%)</td>
</tr>
<tr>
<td>GL-3</td>
<td>120/200 (60%)</td>
<td>0/100 (0%)</td>
</tr>
</tbody>
</table>

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 (75%) or Hispanic (18%). At Day 30, 55% of DYSport®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (Table 11).

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 12).

**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 (88%) and predominantly Caucasian (88%). 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 11). 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 13).

**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, 52% of DYSport®-treated subjects achieved treatment success: a composite 2 grade improvement of glabellar line severity at maximum frown (see Table 11). 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 (Table 14).
DYSPORT® (abobotulinumtoxinA)

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 in adult patients 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 non-naive 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, the remainder of the dose was injected into at least two additional upper limb muscles determined by the patient’s individual presentation. Table 15 provides the mean and range of DYSPORT® doses injected and the number of injections into specific muscles of the upper limb.

Table 15: DYSPORT® Dose Injected and Number of Injections per Muscle in Adult Patients with Upper Limb Spasticity

<table>
<thead>
<tr>
<th>Muscle &amp; Group</th>
<th>DYSPORT® Units Injected (Min, Max)</th>
<th>Number Of Injection Sites Median, (Q1 : Q3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexor digitorum profundus (FDP)*</td>
<td>500 U 57</td>
<td>92.2 Units (25 to 100) 1, [1 ; 2]</td>
</tr>
<tr>
<td>Flexor digitorum superficialis (FDS)*</td>
<td>1000 U 57</td>
<td>178.1 Units (80 to 300) 2, [1 ; 2]</td>
</tr>
<tr>
<td>Flexor carpi radialis (FCR)*</td>
<td>500 U 57</td>
<td>92.2 Units (25 to 100) 1, [1 ; 2]</td>
</tr>
<tr>
<td>Flexor carpi ulnaris (FCU)*</td>
<td>1000 U 49</td>
<td>171.2 Units (80 to 200) 2, [1 ; 2]</td>
</tr>
<tr>
<td>Brachialis*</td>
<td>500 U 60</td>
<td>148.5 Units (50 to 200) 2, [1 ; 2]</td>
</tr>
<tr>
<td>Brachioradialis*</td>
<td>1000 U 43</td>
<td>321.4 Units (100 to 400) 2, [2 ; 2]</td>
</tr>
<tr>
<td>Biceps Brachii (BB)</td>
<td>500 U 28</td>
<td>106.4 Units (50 to 200) 2, [1 ; 2]</td>
</tr>
<tr>
<td>Pronator Teres</td>
<td>1000 U 14</td>
<td>81.8 Units (45 to 200) 1, [1 ; 1]</td>
</tr>
</tbody>
</table>

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 16).

Table 16: Primary Endpoints (PTMG MAS and PGA) and MAS by Muscle Group at Week 4 in Adult Patients with Upper Limb Spasticity

<table>
<thead>
<tr>
<th>Muscle Group</th>
<th>Placebo (N=77)</th>
<th>DYSPORT® 10 U/kg/leg (N=79)</th>
<th>DYSPORT® 15 U/kg/leg (N=79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS Mean Change from Baseline in Wrist Flexor Muscle Tone on the MAS</td>
<td>0.7</td>
<td>1.4*</td>
<td>1.8*</td>
</tr>
<tr>
<td>LS Mean Change from Baseline in Finger Flexor Muscle Tone on the MAS</td>
<td>-0.7</td>
<td>-1.6</td>
<td>-1.6</td>
</tr>
<tr>
<td>LS Mean Change from Baseline in Elbow Flexor Muscle Tone on the MAS</td>
<td>-1.0</td>
<td>-1.2</td>
<td>-1.2</td>
</tr>
</tbody>
</table>

16 HOW SUPPLIED/STORAGE AND HANDLING
DYSPORT® for Injection is supplied in a sterile, single-use, glass vial. Unopened vials of DYSPORT® must be stored under refrigeration at 2°C to 8°C (36°F to 46°F). 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, Upper Limb Spasticity in Adults, and Lower Limb Spasticity in Pediatric Patients

DYSPORT® for injection is a sterile, freeze-dried, abobotulinumtoxinA source intended for intramuscular injection in the following pediatric conditions:

- Upper Limb Spasticity
- Lower Limb Spasticity
- Cervical Dystonia

GLABLELLER COUNSELING INFORMATION
Advising the patient 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), or if any known symptom persists or worsens.

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

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Distributed by:
Ipsen Biopharmaceuticals, Inc.
Basking Ridge, NJ 07920

Galderma Laboratories, L.P.
Fort Worth, TX 76177 USA
DYSPORT® (abobotulinumtoxinA)

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 DYSPORT®?

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
• to treat increased muscle stiffness in calf muscles in children 2 years of age and older with lower limb spasticity

CD is caused by muscle spasms in the neck. These spasms cause an 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.

Upper limb spasticity is caused by muscle spasms in the elbow, wrist, and finger muscles. These spasms cause an abnormal position of these muscles. 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.

Lower limb spasticity is caused by muscle spasms in calf muscles. These spasms cause an abnormal position of these muscles. After DYSPORT® is injected into muscles, those muscles are weakened for up to 16 to 22 weeks or longer. This may help lessen your symptoms.

Who should not take DYSPORT®?

Do not take DYSPORT® if you:
• are allergic to DYSPORT® or any of the ingredients in DYSPORT®. See the end of this Medication Guide for a list of 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

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 2 years of age.

For the treatment of cervical dystonia, glabellar lines, and upper limb spasticity in adults, it is not known whether DYSPORT® is safe or effective in children under 18 years of age.

For the treatment of lower limb spasticity, 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.
Tell your doctor about all the medicines you take, including prescription and over-the-counter 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
- If you are an adult, your doctor may give you another dose of DYSPORT® after 12 weeks or longer, if it is needed
- If you are an adult being treated for CD or upper limb spasticity or you are a child (2 to 17 years of age) being treated for lower limb spasticity, your doctor may change your dose of DYSPORT®, until you and your doctor find the best dose for you. Children should not be retreated sooner than every 12 weeks.
- 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
- muscle pain
- problems speaking
- eye problems
- difficulty swallowing
- 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
- blood in urine
- headache
- injection site reaction
- swelling of eyelids
- drooping eyelids
- sinus infection
- nausea

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

The most common side effects of DYSPORT® in children (2 to 17 years of age) with lower limb spasticity include:
- upper respiratory infection
- stuffy or runny nose and sore throat
- flu
- cough
- fever

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.

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.

**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.

Distributed by: Ipsen Biopharmaceuticals, Inc. Basking Ridge, NJ 07920 and Galderma Laboratories, L.P. Fort Worth, TX 76177;
Manufactured by: Ipsen Biopharm Ltd., Wrexham, LL13 9UF, UK
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For more information about DYSPORT®, call 877-397-7671 or go to www.dysport.com or www.DysportUSA.com.

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