Help your patients experience lasting relief between injections*

Dysport® (abobotulinumtoxinA)

*In clinical trials, the primary endpoint for cervical dystonia was based on the total TWSTRS change at Week 4. A majority of adults with cervical dystonia did not need retreatment until Weeks 14-18. However, some patients had a longer duration of response.[1,2]

For adult patients with cervical dystonia

TWSTRS=Toronto Western Spasmodic Torticollis Rating Scale.

INDICATIONS

DYSPORT (abobotulinumtoxinA) for injection is indicated for the treatment of:

- spasticity in patients 2 years of age and older
- cervical dystonia in adults

IMPORTANT SAFETY INFORMATION

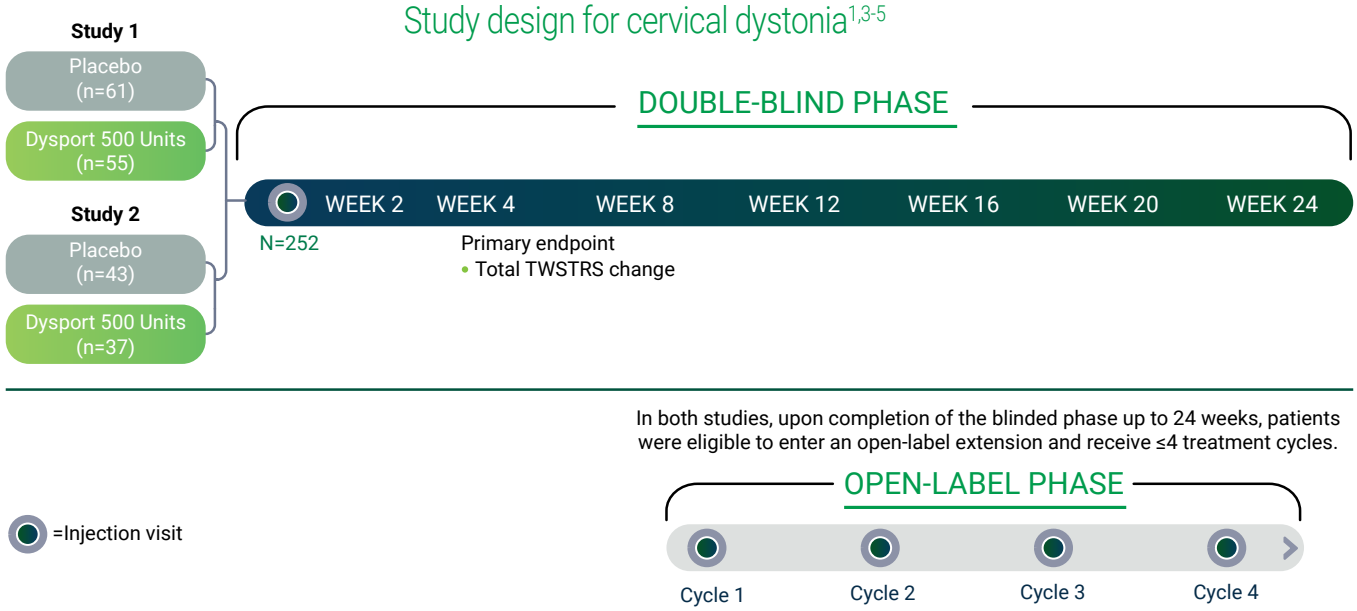
WARNING: DISTANT SPREAD OF TOXIN EFFECT

Postmarketing reports indicate that the effects of DYSPORT and all botulinum toxin products may spread from the area of injection to produce symptoms consistent with botulinum toxin effects. These may include asthenia, generalized muscle weakness, diplopia, 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. 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 and in approved indications, cases of spread of effect have been reported at doses comparable to or lower than the maximum recommended total dose.

Robust study designs support efficacy data

- Two randomized, double-blind, **placebo-controlled, single-dose, parallel-group studies** of **252 patients with CD**[1]
- The **primary efficacy endpoint** for both studies was **total TWSTRS change from baseline at Week 4**[1]
- Patients remained **blinded up to 24 weeks in the double-blind phase. This was followed by long-term open-label extensions when retreatment was needed**[1]

Study design for cervical dystonia[1,3-5]



CD=cervical dystonia; TWSTRS=Toronto Western Spasmodic Torticollis Rating Scale.

Demographics are consistent across groups

Demographics and baseline characteristics

	Study 1[3,4]		Study 2[5]	
	Placebo (n=61)	Dysport 500 Units (n=55)	Placebo (n=43)	Dysport 500 Units (n=37)
Age, years, mean (SD)	53.9 (12.5)	51.9 (13.4)	53.6 (12.1)	53.4 (11.6)
Sex, %				
Male	38	33	37	38
Female	62	67	63	62
Caucasian, %	100	100	93	81
Weight, kg, mean (SD)	77.4 (15.0)	73.4 (13.8)	74.5 (17.7)	76.1 (13.9)
Height, cm, mean (SD)	170 (8.5)	167 (10.3)	169.2 (10.2)	167.5 (10.7)
BoNT status: naïve/non-naïve, %	16/84	18/82	28/72	24/76
Time since onset of signs/symptoms, months, mean (SD)	141.6 (105.6)	144 (105.6)	140.3 (115.4)	145.7 (114.4)

BoNT=botulinum neurotoxin; SD=standard deviation.

IMPORTANT SAFETY INFORMATION (continued)

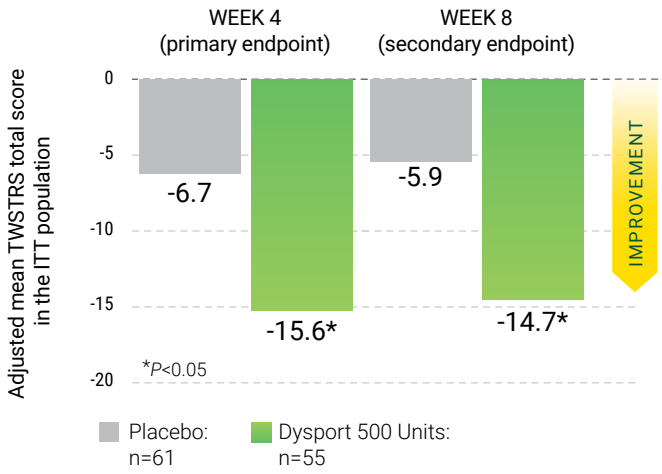
Contraindications

DYSPORT is contraindicated in patients with known hypersensitivity to any botulinum toxin products, cow's milk protein, or to any of the components in the formulation, or infection at the proposed injection site(s). Serious hypersensitivity reactions including anaphylaxis, serum sickness, urticaria, soft tissue edema, and dyspnea have been reported. If such a serious reaction occurs, discontinue DYSPORT and institute appropriate medical therapy immediately.

Head posture in CD

Study 1

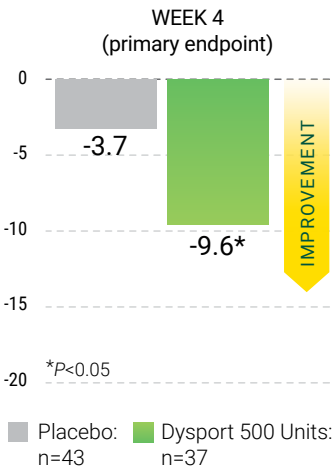
Dysport significantly improved head posture at Week 4 and Week 8[1]



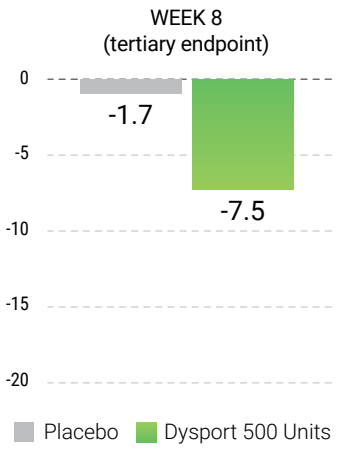
- The primary assessment of efficacy was based on the total TWSTRS change from baseline at Week 4[1]
- Total score at baseline (mean [SD]): placebo, 45.8 (8.9); Dysport 500 Units, 43.8 (8.0)[1]

Study 2

Dysport significantly improved head posture at Week 4[1]



- The primary assessment of efficacy was based on the total TWSTRS change from baseline at Week 4
- Total score at baseline (mean [SD]): placebo, 46.2 (9.4); Dysport 500 Units, 45.1 (8.7)[1]



Study Limitations: Week 8 results may represent chance findings, as multiplicity adjustments were not applied; therefore, the results should be interpreted cautiously.

- Change in TWSTRS total score at Week 8[3]

CD=cervical dystonia; ITT=intent-to-treat; SD=standard deviation; TWSTRS=Toronto Western Spasmodic Torticollis Rating Scale.

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

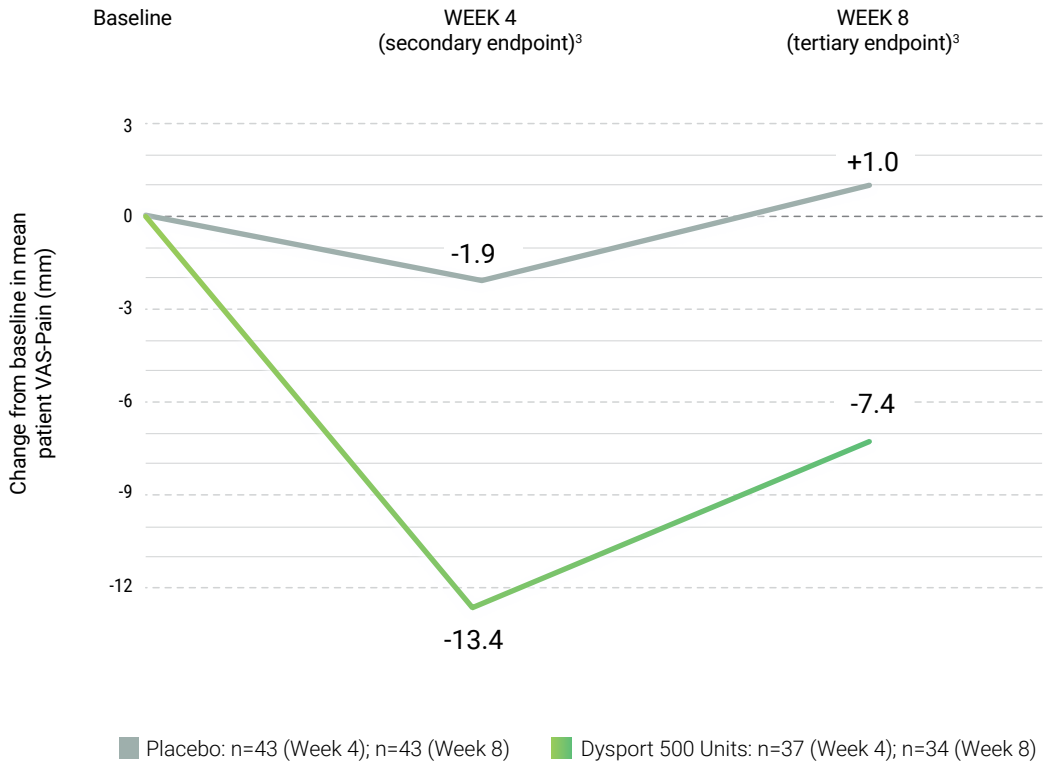
Lack of Interchangeability Between Botulinum Toxin Products

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.

Dysphagia and Breathing Difficulties

Treatment with DYSPORT and other botulinum toxin products can result in swallowing or breathing difficulties. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. In most cases, this is a consequence of weakening of muscles in the area of injection that are involved in breathing or swallowing. When distant effects occur, additional respiratory muscles may be involved. Deaths as a complication of severe dysphagia have been reported after treatment with botulinum toxin. Dysphagia may persist for several 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 accessory muscles of ventilation, which may result in a critical loss of breathing capacity in patients with respiratory disorders who may have become dependent upon these muscles. 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.

VAS at Week 4 and Week 8[5]



Study limitations: Data may represent chance findings, as multiplicity adjustments were not applied; therefore, the results should be interpreted cautiously.

- Baseline VAS score (patient self-rated) was 48.6 in the Dysport group and 52.9 in the placebo group[3]
- Evaluated on a 100-point VAS pain scale (0 mm [no symptoms] to 100 mm [worst possible symptoms]) following treatment[3]

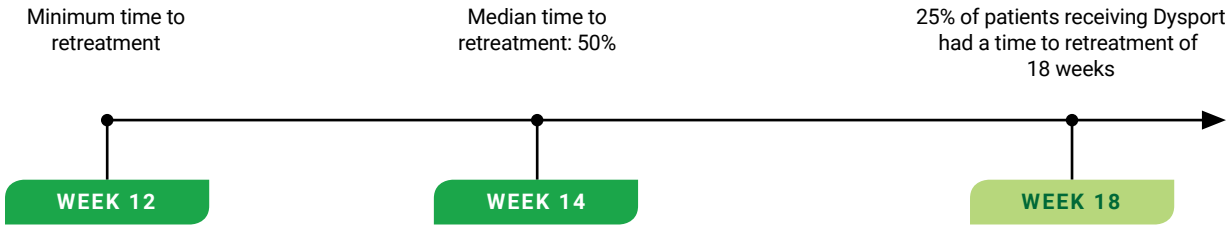
IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Pre-existing Neuromuscular Disorders

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

For most patients with CD, Dysport effects lasted beyond the minimum retreatment time of 12 weeks[1]



Retreatment was determined by clinical need after a minimum of 12 weeks. The median time to retreatment was 14 weeks and 18 weeks for the 75th percentile.

In the pivotal trials for adult CD, retreatment was determined by clinical need after a minimum of 12 weeks, as determined by change in TWSTRS total score returning to within 10% of baseline or investigator's discretion.[3-5]

Repeat Dysport retreatment should be administered no sooner than 12 weeks after the previous injection.

Provides sustained relief beyond the 12-week minimum time to retreatment

CD=cervical dystonia; TWSTRS=Toronto Western Spasmodic Torticollis Rating Scale.

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Human Albumin and Transmission of Viral Diseases

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

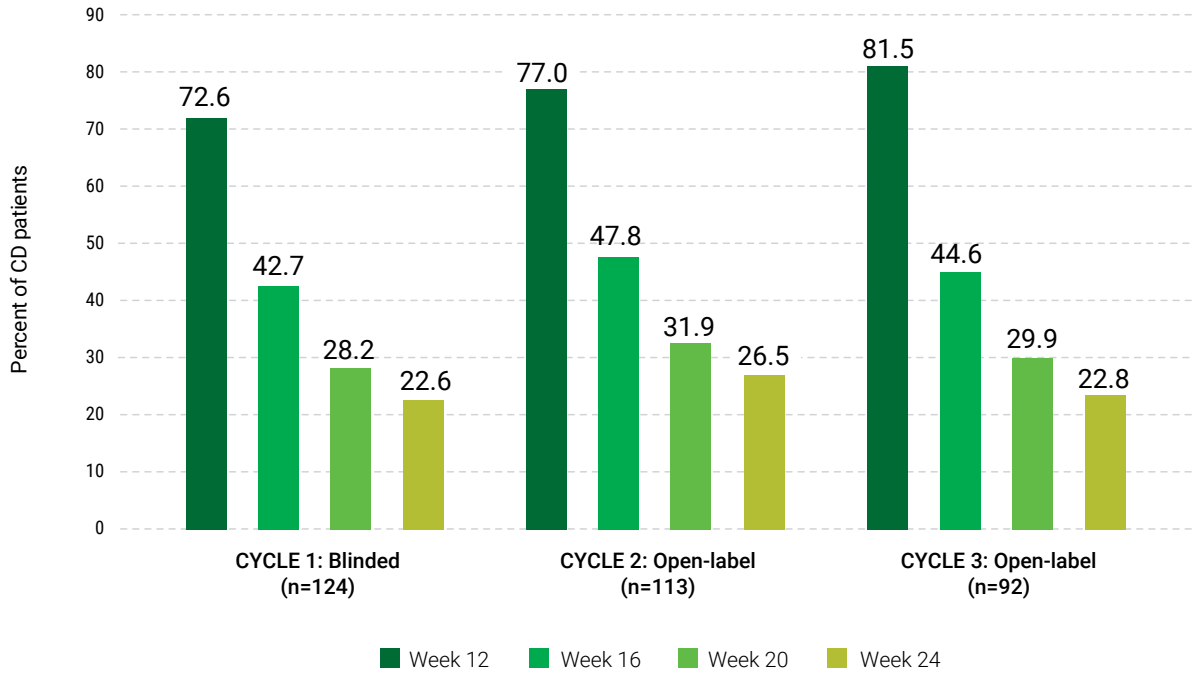
Intradermal Immune Reaction

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.

Pre-existing Conditions at the Injection Site

Caution should be exercised when DYSPORT is used where the targeted muscle shows excessive weakness or atrophy.

Percentage of CD patients not requiring retreatment[2]



Patients could have remained blinded up to Week 24 and then enrolled into the open-label extension when the need for re-treatment was assessed. All patients entering Cycle 1 received 500 Units of Dysport to maintain treatment blindness. Patients entering into Cycle 2 and Cycle 3 were part of the open label.[1-3]

Study limitations: Cycle 2 and Cycle 3 were part of the open-label phase; therefore, these results should be interpreted cautiously and could represent chance findings.[2,4,6]

The most frequently reported TEAEs were muscle weakness in the neck, headache, dysphagia, neck/shoulder pain, dry mouth, asthenia, injection site pain, voice alteration, jaw pain, and nervousness.[6]

TEAEs=treatment-emergent adverse events.

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions

- The most common adverse reactions (≥4%) in adults with upper limb spasticity include muscular weakness; in adults with lower limb spasticity (≥5%) include falls, muscular weakness, and pain in extremity
- The most common adverse reactions (≥10%) in pediatric patients with upper limb spasticity include upper respiratory tract infection and pharyngitis; in pediatric patients with lower limb spasticity include nasopharyngitis, cough, and pyrexia
- The most common adverse reactions (≥5%) in adults with cervical dystonia include muscular weakness, dysphagia, dry mouth, injection site discomfort, fatigue, headache, musculoskeletal pain, dysphonia, injection site pain, and eye disorders

Pooled double-blind trials: Below are the most common adverse reactions (≥5%) and greater than placebo in adult patients with cervical dystonia (CD) who received Dysport (500 Units, n=173)[1]*

Adverse Reactions	Dysport 500 Units (n=173), %	Placebo (n=182), %
Any adverse reaction	61	51
General disorders and administration site conditions		
Injection site discomfort	13	8
Fatigue	12	10
Injection site pain	5	4
Musculoskeletal and connective tissue disorders		
Muscular weakness	16	4
Musculoskeletal pain	7	3
Gastrointestinal disorders		
Dysphagia	15	4
Dry mouth	13	7
Nervous system disorders		
Headache	11	9
Respiratory, thoracic, and mediastinal disorders		
Dysphonia	6	2
Eye disorders†	7	2

To reduce the recurrence of dysphagia, limit the dose injected unilaterally into the sternocleidomastoid to 150 Units or less. Use of simultaneous electromyography-guided application of Dysport may be helpful in locating these active muscles.[1,6]

*Data from a single treatment cycle of 500 Units of Dysport.[1]
†The following preferred terms were reported: vision blurred, diplopia, visual acuity reduced, eye pain, eyelid disorder, accommodation disorder, dry eye, eye pruritus.[1]

CD=cervical dystonia.

IMPORTANT SAFETY INFORMATION (continued)

Drug Interactions

Co-administration of DYSPORT and aminoglycosides or other agents interfering with neuromuscular transmission (e.g., curare-like agents) should only be performed with caution 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 neurotoxins 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 and after administration of DYSPORT.

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Please see full Prescribing Information, including BOXED WARNING.

References:

1. Dysport® (abobotulinumtoxinA) [prescribing information]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc; September 2023.
2. Esquenazi A, Delgado MR, Hauser RA, et al. Duration of symptom relief between injections for abobotulinumtoxinA (Dysport®) in spastic paresis and cervical dystonia: comparison of evidence from clinical studies. *Front Neurol*. 2020;11:576117.
3. Data on file. Ipsen Biopharmaceuticals, Inc. Cambridge, MA.
4. Truong D, Brodsky M, Lew M, et al. Long-term efficacy and safety of botulinum toxin type A (Dysport) in cervical dystonia. *Parkinsonism Relat Disord*. 2010;16(5):316-323.
5. Truong D, Duane DD, Jankovic J, et al. Efficacy and safety of botulinum type A toxin (Dysport) in cervical dystonia: results of the first US randomized, double-blind, placebo-controlled study. *Mov Disord*. 2005;20(7):783-791.
6. Hauser RA, Truong D, Hubble J, et al. AbobotulinumtoxinA (Dysport) dosing in cervical dystonia: an exploratory analysis of two large open-label extension studies. *J Neural Transm*. 2013;120(2):299-307.

IPSEN

Dysport® (abobotulinumtoxinA) for injection, for intramuscular use 300- and 500-Unit vials.
DYSPORT is a registered trademark of Ipsen Biopharm Limited.

Dysport® (abobotulinumtoxinA)