

## New Zealand Datasheet

### Name of Medicine

Dysport<sup>®</sup>

Clostridium botulinum type A toxin-haemagglutinin complex

### Presentation

	Per Vial
Active Constituent	
<i>Clostridium botulinum</i> type A toxin-haemagglutinin complex	500U*
Other Constituents	
Albumin solution 20%	125 mcg
Lactose	2.5 mg

One unit (U) is defined as the median lethal intraperitoneal dose in mice.

Dysport is a white lyophilised powder for reconstitution contained in Type 1 glass vials 3ml of capacity, with 13mm chlorobutyl freeze-drying closures oversealed by 13mm aluminium overseals with centre hole, crimped over.

### Uses

#### Actions

ATC code: M03AX01

*Clostridium botulinum* type A toxin-haemagglutinin complex blocks peripheral cholinergic transmission at the neuromuscular junction by a presynaptic action at a site proximal to the release of acetylcholine. The toxin acts within the nerve ending to antagonise those events that are triggered by Ca<sup>2+</sup> which culminate in transmitter release. It does not affect postganglionic cholinergic transmission or postganglionic sympathetic transmission.

The action of toxin involves an initial binding step whereby the toxin attaches rapidly and avidly to the presynaptic nerve membrane. Secondly, there is an internalisation step in which toxin crosses the presynaptic membrane, without causing onset of paralysis. Finally the toxin inhibits the release of acetylcholine by disrupting the Ca<sup>2+</sup> mediated acetylcholine release mechanism, thereby diminishing the endplate potential and causing paralysis.

Recovery of impulse transmission occurs gradually as new nerve terminals sprout and contact is made with the post synaptic motor endplate, a process which takes 6-8 weeks in the experimental animal.

#### Pharmacokinetics

Pharmacokinetic studies with botulinum toxin pose problems in animals because of the high potency, the minute doses involved, the large molecular weight of the compound and the difficulty of labelling toxin to produce sufficiently high specific activity. Studies using I<sup>125</sup> labelled toxin have shown that the receptor binding is specific and saturable,

and the high density of toxin receptors is a contributory factor to the high potency. Dose and time responses in monkeys showed that at low doses there was a delay of 2-3 days with peak effect seen 5-6 days after injection. The duration of action, measured by changes of ocular alignment and muscle paralysis varied between 2 weeks and 8 months. This pattern is also seen in man, and is attributed to the process of binding, internalisation and changes at the neuromuscular junction.

## **Indications**

Dysport is indicated for the treatment of:

Glabellar lines

Spasticity of the arm in patients following a stroke

Dynamic equinus foot deformity due to spasticity in paediatric cerebral palsy patients, two years of age or older, only in hospital specialist centres with appropriately trained personnel.

Spasmodic torticollis in adults

Blepharospasm in adults

Hemifacial spasm in adults

Dysport is also indicated for the symptomatic treatment of axillary hyperhidrosis (excessive sweating).

## **Dosage and Administration**

The units of Dysport are specific to the preparation and are not interchangeable with other preparations of botulinum toxin.

Dysport should only be administered by appropriately trained physicians.

The exposed central portion of the rubber stopper should be cleaned with alcohol immediately prior to piercing the septum. A sterile 23 or 25 gauge needle should be used, or a 29-30 gauge needle for glabellar lines.

### **Glabellar lines**

#### Dosage

The dosage is dependant on the severity of the lines and the specific muscle being treated.

Adults and elderly: Remove the make-up and disinfect the skin with a local antiseptic. Intramuscular injections should be performed at right angles to the skin using a sterile 29-30 gauge needle.

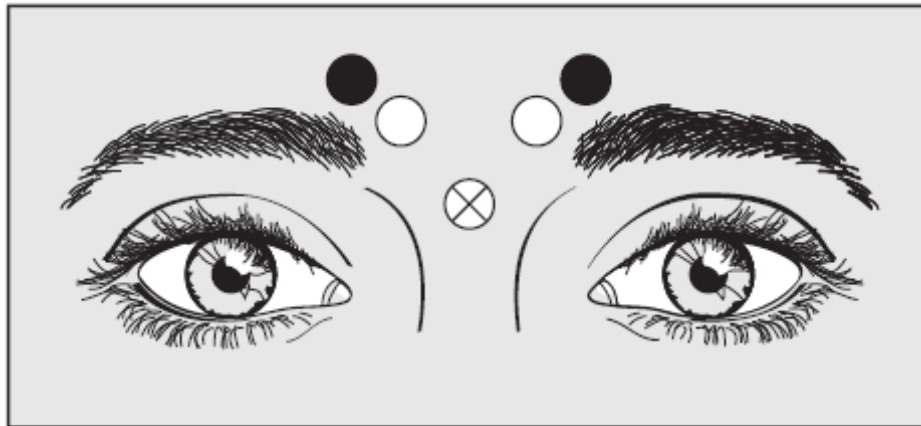
The recommended dose is 50 units (0.25 ml) of Dysport to be divided into 5 injection sites.

10 units (0.05 ml) are to be administered intramuscularly into each of these 5 sites: 2 injections into each corrugator muscle at 5 mm intervals and one into the procerus

muscle near the nasofrontal angle. The most internal point of the corrugator is located 8 mm out of the point which is in the procerus and 8 mm from the upper side of the orbit. Patients are asked to frown regularly in order to help these injection points to be located.

In order to avoid the complication of ptosis, injection near the levator palpebrae superioris must be avoided. Lateral corrugator injections should be placed at least 1 cm above the bony supraorbital ridge (Fig. 1:C: Corrugator / P: Procerus).

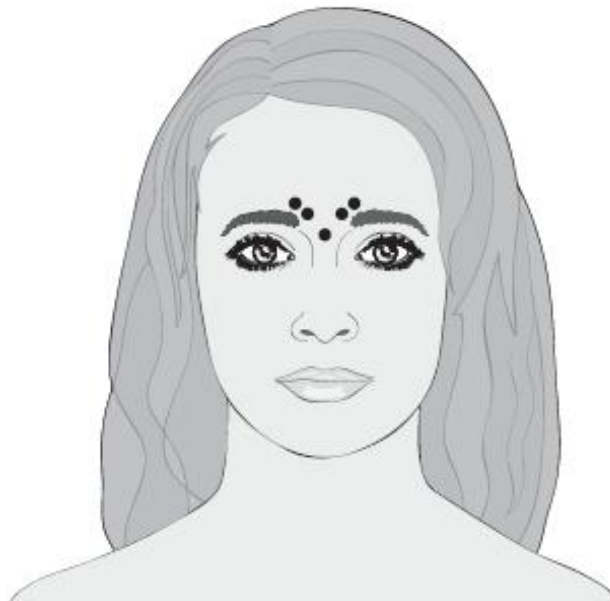
Figure 1



○ = C1

● = C2

⊗ = P



Improvement of severity of glabellar lines generally occurs within 72 hours after treatment and persists for 3 to 6 months. The interval between treatment cycles should not be less than 12 weeks.

*Children:* Use of Dysport is not recommended for the treatment of moderate to severe glabellar lines in patients under the age of 18.

Method of administration

When treating glabellar lines, Dysport is reconstituted with 2.5ml of sodium chloride injection BP (0.9%) to yield a solution containing 10 units of Dysport per 0.05 ml. Dysport is administered by intramuscular or subcutaneous injection.

**Adult spasticity of the arm post-stroke:**

Dosage

The recommended dose is 1000 units, distributed amongst the following five muscles: flexor digitorum profundus (FDP), flexor digitorum superficialis (FDS), flexor carpi ulnaris (FCU), flexor carpi radialis (FCR) and biceps brachii (BB). The maximum dose administered must not exceed 1000 units.

The sites of injection should be guided by standard locations used for electromyography, although actual location of the injection site will be determined by palpation. All muscles except the biceps brachii will be injected at one site, whilst the biceps will be injected at two sites. The recommended distribution of dose is given below:

	BB (units)	FDP (units)	FDS (units)	FCU (units)	FCR (units)	Total Dose (units)
Dysport	300-400	150	150-250	150	150	1,000

The starting dose should be lowered if there is evidence to suggest that this dose may result in excessive weakness of the target muscles, such as for patients whose target muscles are small, where the BB muscle is not to be injected or patients who require concomitant injections into other muscle groups. Clinical improvement may be expected within two weeks after injection. Injections may be repeated approximately every 16 weeks, or as required to maintain response, but not more frequently than every 12 weeks.

*Children:* The safety and effectiveness of Dysport in the treatment of post-stroke leg spasticity in children have not been demonstrated.

Method of administration

When treating post-stroke arm spasticity, Dysport is reconstituted with 1.0ml of sodium chloride injection B.P. (0.9%) to yield a solution containing 500 units per ml of Dysport. Dysport is administered by intramuscular injection into the five muscles detailed above when treating arm spasticity.

**Paediatric cerebral palsy spasticity**

The initial recommended dose is 20 units/kg body weight given as a divided dose between both calf muscles. If only one calf is affected, a dose of 10 units/kg bodyweight should be used. Consideration should be given to lowering this starting dose if there is evidence to suggest that this dose may result in excessive weakness of the target muscles, such as for patients whose target muscles are small or patients who require concomitant injections to other muscle groups. Following evaluation of response to the

starting dose subsequent treatment may be titrated within the range 10 units/kg and 30 units/kg divided between both legs. The maximum dose administered must not exceed 1000 units/patient.

Administration should primarily be targeted to the gastrocnemius, although injections of the soleus and injection of the tibialis posterior should also be considered. The use of electromyography (EMG) is not routine clinical practice but may assist in identifying the most active muscles.

Clinical improvement may be expected within two weeks after injection. Injections may be repeated approximately every 16 weeks or as required to maintain response, but not more frequently than every 12 weeks.

#### Method of administration

When treating paediatric cerebral palsy spasticity, Dysport is reconstituted with 1.0ml of sodium chloride injection B.P. (0.9%) to yield a solution containing 500 units per ml of Dysport. Dysport is administered by intramuscular injection into the calf muscles when treating paediatric cerebral palsy spasticity.

### **Spasmodic torticollis**

#### Dosage

*Adults and elderly:* The doses recommended for torticollis are applicable to adults of all ages providing the adults are of normal weight with no evidence of low neck muscle mass. A reduced dose may be appropriate if the patient is markedly underweight or in the elderly, where reduced muscle mass may exist.

The initial recommended dose for the treatment of spasmodic torticollis is 500 units per patient given as a divided dose and administered to the two or three most active neck muscles.

For rotational torticollis distribute the 500 units by administering 350 units into the splenius capitis muscle, ipsilateral to the direction of the chin/head rotation and 150 units into the sternomastoid muscle, contralateral to the rotation.

For laterocollis, distribute the 500 units by administering 350 units into the ipsilateral splenius capitis muscle and 150 units into the ipsilateral sternomastoid muscle. In cases associated with shoulder elevation the ipsilateral trapezoid or levator scapulae muscles may also require treatment, according to visible hypertrophy of the muscle or electromyographic (EMG) findings. Where injections of three muscles are required, distribute the 500 units as follows, 300 units splenius capitis, 100 units sternomastoid and 100 units to the third muscle.

For retrocollis distribute the 500 units by administering 250 units into each of the splenius capitis muscles. This may be followed by bilateral trapezius injections (up to 250 units per muscle) after 6 weeks, if there is insufficient response. Bilateral splenii injections may increase the risk of neck muscle weakness.

All other forms of torticollis are highly dependent on specialist knowledge and EMG to identify and treat the most active muscles. EMG should be used diagnostically for all complex forms of torticollis, for reassessment after unsuccessful injections in non

complex cases, and for guiding injections into deep muscles or in overweight patients with poorly palpable neck muscles.

On subsequent administration, the doses may be adjusted according to the clinical response and side effects observed. Doses within the range of 250-1000 units are recommended, although the higher doses may be accompanied by an increase in side effects, particularly dysphagia. The maximum dose administered must not exceed 1000 units. The relief of symptoms of torticollis may be expected within a week after the injection. Injections should be repeated approximately every twelve weeks or as required to prevent recurrence of symptoms.

*Children:* The safety and effectiveness of Dysport in the treatment of spasmodic torticollis in children have not been demonstrated.

#### Method of administration

When treating spasmodic torticollis Dysport is reconstituted with 1ml of sodium chloride injection B.P. (0.9%) to yield a solution containing 500 units per ml of Dysport. Dysport is administered by intramuscular injection as above when treating spasmodic torticollis.

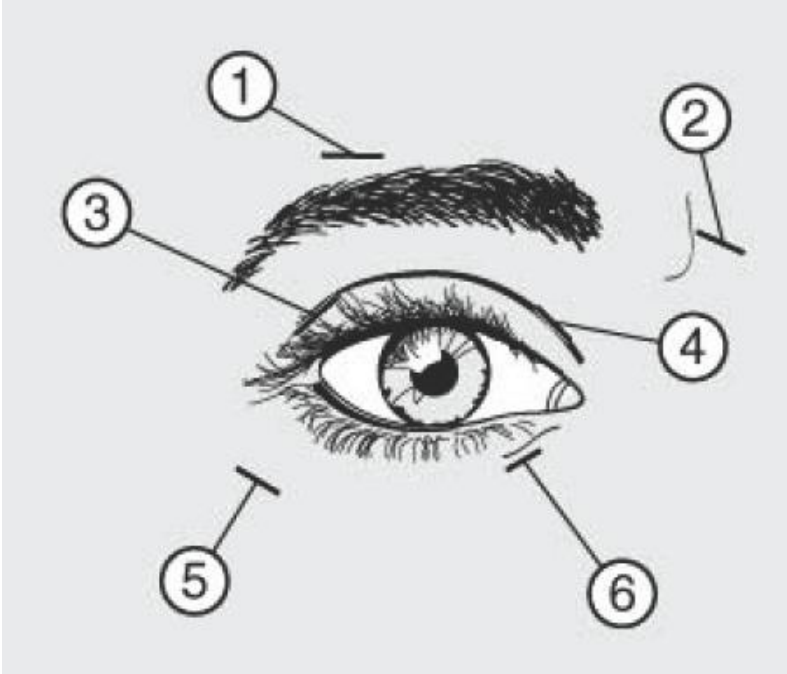
#### **Blepharospasm and hemifacial spasm**

##### Dosage

*Adults and elderly:* In a dose ranging clinical trial of the use of Dysport for the treatment of benign essential blepharospasm a dose of 40 units per eye was significantly effective. A dose of 80 units per eye resulted in a longer duration of effect. Thus, if a dose of 40 units per eye is chosen for the initial treatment, the patient may benefit from a dose of 80 units per eye for subsequent treatments if a longer duration of action is required.

Injection of 10 units (0.05ml) should be made medially and of 10 units (0.05 ml) should be made laterally into the junction between the preseptal and orbital parts of both the upper (3 and 4) and lower orbicularis oculi muscles (5 and 6) of each eye.

In order to reduce the risk of ptosis, injections near the levator palpebrae superioris should be avoided.



For injections into the upper lid the needle should be directed away from its centre to avoid the levator muscle. A diagram to aid placement of these injections is provided. The relief of symptoms may be expected to begin within two to four days with maximal effect within two weeks.

Injections should be repeated approximately every twelve weeks or as required to prevent recurrence of symptoms but not more frequently than every twelve weeks. On such subsequent administrations, if the response from the initial treatment is considered insufficient, the dose per eye may need to be increased to 60 units: 10 units (0.05 ml) medially and 20 units (0.1 ml) laterally, 80 units: 20 units (0.1 ml) medially and 20 units (0.1 ml) laterally or up to 120 units: 20 units (0.1 ml) medially and 40 units (0.2 ml) laterally above and below each eye in the manner previously described. Additional sites in frontalis muscle above brow (1 and 2) may also be injected if spasms here interfere with vision.

In cases of unilateral blepharospasm the injections should be confined to the affected eye. Patients with hemifacial spasm should be treated as for unilateral blepharospasm. The doses recommended are applicable to adults of all ages including the elderly.

In the treatment of blepharospasm and hemifacial spasm, the maximum dose should not exceed the total dose of 120 units per eye.

*Children:* The safety and effectiveness of Dysport in the treatment of blepharospasm and hemifacial spasm in children have not been demonstrated.

#### Method of administration

When treating blepharospasm and hemifacial spasm Dysport is reconstituted with 2.5ml of sodium chloride injection BP (0.9%) to yield a solution containing 200 units per ml of Dysport. Dysport is administered by subcutaneous injection medially and laterally into

the junction between the preseptal and orbital parts of both the upper and lower orbicularis oculi muscles of the eyes.

### **Axillary hyperhidrosis (excessive sweating).**

#### Dosage

The recommended initial dosage is 100 units per axilla. If the desired effect is not attained, up to 200 units per axilla can be administered for subsequent injections.

The area to be injected should be determined beforehand using the iodine-starch test. Both axillae should be cleaned and disinfected. Intradermal injections at ten sites, each site receiving 10 units, 100 units per axilla, are then administered.

The maximum effect should be seen by week two after injection. In the majority of cases, the recommended dose will provide adequate suppression of sweat secretion for approximately 48 weeks. The time point for further applications should be determined on an individual basis, when the patient's sweat secretion has returned to an unacceptable level, but not more often than every 12 weeks. There is some evidence for a cumulative effect of repeated doses so the time of each treatment for a given patient should be assessed individually. The maximum dose administered must not exceed 200 units per axilla.

*Children:* The safety and effectiveness of Dysport in the treatment of axillary hyperhidrosis in children has not been demonstrated.

#### Method of administration

When treating axillary hyperhidrosis, Dysport is reconstituted with 2.5ml of sodium chloride solution (0.9%) to yield a solution containing 200 units per ml of Dysport. Dysport is administered by intradermal injection at ten sites per axilla when treating axillary hyperhidrosis.

### **Contraindications**

Dysport is contraindicated in individuals with known hypersensitivity to any component of Dysport and in pregnancy.

### **Warnings and Precautions**

Adverse effects resulting from the distribution of the effects of the toxin to sites remote from the site of administration have been reported (see Adverse Effects). Patients treated with therapeutic doses may present with excessive muscle weakness. The risk of occurrence of such undesirable effects may be reduced by using the lowest effective dose and by not exceeding the recommended dose.

Careful consideration should be given before the reinjection of patients who have experienced a previous allergic reaction. The risk of a further allergic reaction must be considered in relation to the benefit of treatment.

For the treatment of spasmodic torticollis and paediatric cerebral palsy spasticity Dysport should only be injected by specialists experienced in the diagnosis and

management of these conditions and who have received training on the administration of Dysport.

Dysport should only be used with caution and under close supervision in patients with subclinical or clinical evidence of marked defective neuro-muscular transmission. Such patients may have an increased sensitivity to agents such as Dysport, which may result in excessive muscle weakness.

Dysport should be administered with caution to patients with existing problems in swallowing or breathing as these problems can worsen following the distribution of the effect of toxin into the relevant muscles. Aspiration has occurred in rare cases and is a risk when treating patients who have a chronic respiratory disorder.

Very rare cases of death, occasionally in a context of dysphagia, pneumopathy and/or in patients with significant asthenia have been reported after treatment with botulinum toxin A or B.

Patients with disorders resulting in defective neuro-muscular transmission, difficulty in swallowing or breathing are more at risk of experiencing these effects. In these patients, treatment must be administered under the control of a specialist and only if the benefit of treatment outweighs the risk.

Patients and their care-givers must be warned of the necessity of immediate medical treatment in case of problems with swallowing, speech or respiratory disorders.

For the treatment of cerebral palsy in children, Dysport should only be used in children over 2 years of age.

The recommended dosage and frequency of administration for Dysport must not be exceeded.

Antibody formation to botulinum toxin has been noted rarely in patients receiving Dysport. Clinically, neutralizing antibodies might be detected by substantial deterioration in response to therapy and/or a need for consistent use of increased doses.

As with any intramuscular injection, Dysport should be used only where strictly necessary in patients with prolonged bleeding times, or infection or inflammation at the proposed injection site.

It is essential to study the patient's facial anatomy prior to administering Dysport for correction of glabellar and lateral canthal lines. Facial asymmetry, ptosis, excessive dermatochalasis, scarring, and any alterations to this anatomy as a result of previous surgical interventions should be taken into consideration.

Dysport should only be used to treat a single patient, during a single session. Any unused product remaining should be disposed of in accordance with Pharmaceutical Precautions: Instructions for Use. Specific precautions must be taken for the preparation and administration of the product; the inactivation and disposal of any unused reconstituted solution (see Pharmaceutical Precautions: Instructions for Use).

This product contains a small amount of human albumin. The risk of transmission of viral infection cannot be excluded with absolute certainty following the use of human blood or blood products.

### **Use in Pregnancy and Lactation**

There are limited data from the use of *Clostridium botulinum* toxin type A – haemagglutinin complex in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/fetal development, parturition or postnatal development other than at high doses causing maternal toxicity (see Further Information: Preclinical Safety).

Dysport should be used during pregnancy only if the benefit justifies any potential risk to the fetus. Caution should be exercised when prescribing to pregnant women.

It is not known whether *Clostridium botulinum* toxin type A – haemagglutinin complex is excreted in human milk. The excretion of *Clostridium botulinum* toxin type A – haemagglutinin complex in milk has not been studied in animals. The use of *Clostridium botulinum* toxin type A – haemagglutinin complex during lactation cannot be recommended.

### **Effects on the Ability to Drive and Use Machines**

There is a potential risk of muscle weakness or visual disturbances which, if experienced, may temporarily impair the ability to drive or operate machinery.

### **Adverse Effects**

*Very common* >1/10, *Common* >1/100, <1/10; *Uncommon* >1/1000, <1/100;  
*Rare* >1/10 000, <1/1000, *Very rare* <1/10 000

In patients who were treated with Dysport during a series of clinical trials for blepharospasm, hemifacial spasm, torticollis, spasticity associated with either cerebral palsy or stroke, axillary hyperhidrosis, glabellar lines or lateral canthal lines approximately 25% experienced an adverse event.

The following adverse reaction were seen in patients treated across variety of indications including blepharospasm, hemifacial spasm, torticollis, spasticity associated with either cerebral palsy or stroke and axillary hyperhidrosis:

#### Nervous system disorders

Rare: Neuralgic amyotrophy

#### Skin and subcutaneous tissue disorders

Uncommon: Itching

Rare: Skin rashes

General disorders and administration site conditions

Common: Generalised weakness, fatigue, flu-like syndrome and pain / bruising at injection site

In addition, the following adverse reactions specific to individual indication were reported:

**Adult spasticity of the arm post-stroke**

The following adverse events, usually mild to moderate intensity, were observed in patients treated with Dysport for adult spasticity of the arm post-stroke.

Gastrointestinal disorders

Common: Dysphagia

Musculoskeletal and connective tissue disorders

Common: Arm muscle weakness

Injury, poisoning and procedural complications

Common: Accidental injury / falls

Dysphagia was reported when doses in excess of 2700 units were used either as a single or divided dose.

**Paediatric leg spasticity due to cerebral palsy**

The following adverse events, usually mild to moderate intensity, were observed in patients treated with Dysport for paediatric leg spasticity due to cerebral palsy.

Gastrointestinal disorders

Common: Diarrhoea

Musculoskeletal and connective tissue disorders

Common: Leg muscle weakness

Renal and urinary disorders

Common: Urinary incontinence

General disorders and administration site conditions

Common: Abnormal gait

Injury, poisoning and procedural complications

Common: Accidental injury due to falling

Accidental injury due to falling and abnormal gait may have been due to the over-weakening of the target muscle and/or the local spread of Dysport to other muscles involved in ambulation and balance.

**Spasmodic torticollis**

The following adverse events, usually mild to moderate intensity, were observed in patients treated with Dysport for spasmodic torticollis.

Nervous system disorders

Common: Dysphonia

Uncommon: Headache

Eye disorders

Uncommon: Diplopia, Blurred vision

Respiratory, thoracic and mediastinal disorders

Rare: Respiratory disorders

Gastrointestinal disorders

Very common: Dysphagia

Uncommon: Dry mouth

Musculoskeletal and connective tissue disorders

Common: Neck muscle weakness

Dysphagia appeared to be dose-related and occurred most frequently following injection into the sternomastoid muscle. A soft diet may be required until symptoms resolve.

**Blepharospasm and hemifacial spasm**

The following adverse events, usually mild to moderate intensity, were observed in patients treated with Dysport for Blepharospasm and hemifacial spasm.

Nervous system disorders

Common: Facial muscle weakness

Uncommon: Facial nerve paresis

Eye disorders

Very common: Ptosis

Common: Diplopia, Dry eyes, Tearing

Rare: Ophthalmoplegia

Skin and subcutaneous tissue disorders

Common: Eyelid oedema

Rare: Entropion

Side effects may occur due to deep or misplaced injections of Dysport temporarily paralysing other nearby muscle groups.

**Axillary hyperhidrosis**

The following adverse events, usually mild to moderate intensity, were observed in patients treated with Dysport for hyperhidrosis:

*Skin and subcutaneous tissue disorders*

Common: Compensatory sweating

**Treatment of moderate to severe glabellar lines**

The following adverse events, usually mild to moderate intensity, were observed in patients treated with Dysport for correction of moderate to severe glabellar lines.

*Eye disorders*

Common: Asthenopia, ptosis, eyelid oedema, lacrimation increase, dry eye, muscle twitching

Uncommon: Visual disturbances, vision blurred, diplopia, eye movement disorder

*General disorders and administration site conditions*

Very common: Injection site reactions (including pain, bruising, pruritis, paraesthesia, erythema, rash, also frequently seen in placebo group)

*Immune system disorders*

Rare: Hypersensitivity

*Musculoskeletal and connective tissue system disorders*

Common: Weakness of adjacent muscle to the area of injection. This may commonly lead to eyelid ptosis, asthenopia or uncommonly to paresis of facial muscles or visual disturbances.

*Nervous system disorders*

Very common: Headache

Common: Facial paresis

*Skin and subcutaneous tissue disorders*

Uncommon: Skin rash, pruritus

Rare: Urticaria

**Post-marketing experience**

The profile of adverse reactions reported to the Company during post-marketing use reflects the pharmacology of the product and those seen during clinical trials. There have been occasional reports of hypersensitivity. There have been no cases of severe anaphylaxis or anaphylactic shock.

Adverse effects resulting from distribution of the effects of the toxin to sites remote from the site of injection have been very rarely reported (excessive muscle weakness, dysphagia, aspiration pneumonia that may be fatal) (see Warnings and Precautions).

**Interactions**

The effects of botulinum toxin may be enhanced by drugs interfering directly or indirectly with the neuromuscular function and such drugs should be used with caution in patients treated with botulinum toxin.

## **Overdosage**

Excessive doses may produce distant and profound neuromuscular paralysis. Overdose could lead to an increased-risk of the neurotoxin entering the bloodstream and may cause complications associated with the effects of oral botulinum poisoning. (e.g. deglutition and dysphonia). Respiratory support may be required where excessive doses cause paralysis of respiratory muscles. There is no specific antidote, antitoxin should not be expected to be beneficial and general supportive care is advised.

In the event of overdose the patient should be medically monitored for symptoms of excessive muscle weakness or muscle paralysis. Symptomatic treatment should be instigated if necessary.

Symptoms of overdose may not 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 muscle paralysis.

## **Pharmaceutical Precautions**

### **Special Precautions for Storage**

Unopened vials must be maintained at temperatures between 2°C and 8°C. Dysport must be stored in a refrigerator at the hospital where the injections are to be carried out and should not be given to the patient to store.

Reconstituted Dysport may be stored in a refrigerator (2-8°C) for up to 8 hours prior to use. Dysport should not be frozen.

### **Shelf life**

The shelf life of the packaged product is 24 months when stored at 2-8°C. Maximum storage time of reconstituted product is 8 hours at 2-8°C.

The product does not contain an anti-microbial agent. The reconstituted product should therefore be used as soon as possible.

### **Incompatibilities**

Dysport should not be mixed with other medicinal products except those mentioned in the Dosage and Administration section.

### **Instructions for use/handling**

Botulinum toxin is very susceptible to heat and certain chemical products. Any spills of the freeze-dried product must be wiped up:

- Either using absorbent material impregnated with a solution of sodium hypochlorite (bleach) in case of freeze-dried product.
- Or with dry, absorbent material in case of reconstituted product.

Gloves should be worn when cleaning product spills.

The contaminated surfaces should be cleaned using absorbent material impregnated with a solution of sodium hypochlorite (bleach), then dried.

If a vial is broken, proceed as indicated above. Carefully collect the pieces of broken glass and wipe up the product, avoiding any cuts to the skin.

If the product enters into contact with the skin, wash with a solution of sodium hypochlorite (bleach) then rinse abundantly with water.

If product enters into contact with the eyes, rinse abundantly with water or with a dedicated eye-rinsing solution.

In the event of injury to the handler (cut or self-injection), proceed as indicated above and take the appropriate medical measures depending on the dose injected.

#### Recommendations for the disposal of contaminated materials

The needles, syringes and vials - which should not be emptied - must be placed in suitable containers intended for incineration after use.

Contaminated materials (absorbent cloth, gloves, ampoule debris) should be placed in an unpiercable bag for disposal by incineration.

### **Package Quantities**

Dysport is available in packs of 2 x 2.5 ml vials each containing 500 units Clostridium botulinum type A toxin-haemagglutinin complex.

### **Medicine Classification**

Prescription Medicine.

### **Further Information**

#### **List of Excipients**

Albumin and lactose.

#### **Preclinical Safety Data**

Reproductive toxicity studies in pregnant rats and rabbits given *Clostridium botulinum* toxin type A - haemagglutinin complex by daily intramuscular injection, at doses of 79 units/kg and 42 units/kg in rats and rabbits respectively, did not result in embryo/fetal toxicity. Severe maternal toxicity associated with implantation losses were observed at higher doses in both species. *Clostridium botulinum* toxin type A -haemagglutinin complex demonstrated no teratogenic activity in either rats or rabbits and no effects were observed in the pre- and post-natal study on the F1 generation in rats. Fertility of the males and females was decreased due to reduced mating secondary to muscle paralysis at high doses.

In a chronic toxicity study performed in rats up to 12 units/animal, there was no indication of systemic toxicity. Effects in reproduction and chronic toxicity non-clinical studies were limited to changes on injected muscles related to the mechanism of action of *Clostridium botulinum* toxin type A - haemagglutinin complex.

There was no ocular irritation following administration of *Clostridium botulinum* toxin type A - haemagglutinin complex onto the eye of rabbits.

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**Date of Preparation**

3 November 2009

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