1039472

SUMMARY OF PRODUCT CHARACTERISTICS

Dysport®

500 units, powder for solution for injection

Clostridium botulinum type A toxin-haemagglutinin complex

1 NAME OF THE MEDICINAL PRODUCT

Dysport 500 units powder for solution for injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Clostridium botulinum type A toxin-haemagglutinin complex 500 units*

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

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dysport is indicated for focal spasticity, including the treatment of:

- arm symptoms associated with focal spasticity in conjunction with physiotherapy;

and

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

Dysport is also indicated for the following treatments:

- Spasmodic torticollis in adults
- Blepharospasm in adults
- Hemifacial spasm in adults
- The temporary improvement in the appearance of moderate to severe glabellar lines (vertical lines between the eyebrows) seen at frown, in adult patients under 65 years, when the severity of these lines has an important psychological impact on the patient.

4.2 Posology and method of administration

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

Training: Dysport should only be administered by appropriately trained physicians.

Ipsen can facilitate training in administration of Dysport injections.

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.

Arm spasticity

Posology

The recommended dose is 1000 units in total, distributed amongst the following five muscles:

Biceps brachii (BB)	Flexor digitorum profundus (FDP)	Flexor digitorum superficialis (FDS)	Flexor carpi ulnaris (FCU)	Flexor carpi radialis (FCR)	Total Dose
300-400 units (0.6-0.8mL)	150 units (0.3mL)	150-250 units (0.3-0.5mL)	150 units (0.3mL)	150 units (0.3mL)	1,000 units (2.0mL)

The sites of injection should be guided by standard locations used for electromyography (EMG), although actual location of the injection site will be determined by palpation. All muscles except the biceps brachii (BB) should be injected at one site, whilst the biceps should be injected at two sites. The maximum dose administered must not exceed 1000 units.

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 for 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 a response, but not more frequently than every 12 weeks.

Children: The safety and effectiveness of Dysport in the treatment of arm spasticity in children have not been demonstrated.

Method of administration

When treating 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

Posology

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 body weight 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 30units /kg or 1000 units/patient, whichever is the lower.

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 spasticity.

Spasmodic torticollis

Posology

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. 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 may be repeated approximately every 16 weeks or as required to maintain a response, but not more frequently than every 12 weeks.

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 1.0mL of sodium chloride injection B.P. (0.9%) to yield a solution containing 500 units per mL of Dysport.

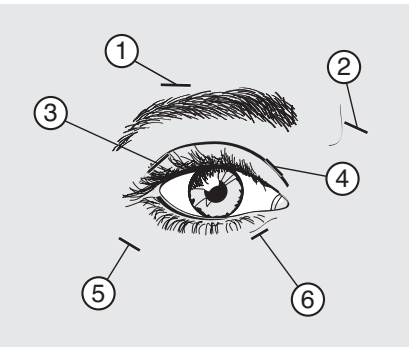
Dysport is administered by intramuscular injection as above when treating spasmodic torticollis.

Blepharospasm and hemifacial spasm

Posology

In a dose ranging clinical trial on the use of Dysport for the treatment of benign essential blepharospasm, a dose of 40 units per eye was significantly effective. Doses of 80 units and 120 units per eye resulted in a longer duration of effect. However, the incidence of local adverse events, specifically ptosis, was dose related. In the treatment of blepharospasm and hemifacial spasm, the maximum dose used must not exceed a total dose of 120 units per eye.

An injection of 10 units (0.05mL) medially and 10 units (0.05mL) laterally should be made 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 (0.05mL) medially and 20 units (0.1mL) laterally, 80 units: 20 units (0.1mL) medially and 20 units (0.1mL) laterally or up to 120 units: 20 units (0.1mL) medially and 40 units (0.2mL) laterally above and below each eye in the manner previously described. Additional sites in the frontalis muscle above the 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.

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 B.P. (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.

Glabellar Lines

Posology and method of administration

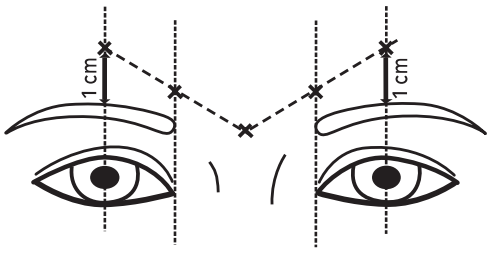
Once reconstituted, Dysport should only be used to treat a single patient, during a single session.

Prior to injection, the product should be reconstituted, instructions for which are given in Section 6.6.

Remove any 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 (0.25mL of reconstituted solution) of Dysport to be divided into 5 injection sites, 10 units (0.05mL of reconstituted solution) are to be administered intramuscularly into each of the 5 sites: 2 injections into each corrugator muscle and one into the procerus muscle near the nasofrontal angle as shown below:



The anatomical landmarks can be more readily identified if observed and palpated at maximal frown. Before injection, place the thumb or index finger firmly below the orbital rim in order to prevent extravasation below the orbital rim. The needle should be pointed upward and medially during the injection. In order to reduce the risk of ptosis, avoid injections near the levator palpebrae superioris muscle, particularly in patients with larger brow-depressor complexes (depressor supercilii). Injections in the corrugator muscle must be made into the central part of that muscle, at least 1cm above the orbital rim.

The treatment interval depends on the individual patient's response after assessment. In clinical studies, an optimal effect was demonstrated for up to 4 months after injection. Some patients were still responders at 5 months. Treatment interval should not be more frequent than every three months.

In the event of treatment failure or diminished effect following repeat injections, alternative treatment methods should be employed. In case of treatment failure after the first treatment session, the following approaches may be considered:

- Analysis of the causes of failure, e.g. incorrect muscles injected, injection technique, and formation of toxin-neutralising antibodies;
- Re-evaluation of the relevance of treatment with Dysport

Children

The safety and effectiveness of Dysport in treating glabellar lines in individuals under 18 years of age have not been demonstrated.

4.3 Contraindications

Dysport is contraindicated in individuals with known hypersensitivity to any components of Dysport.

4.4 Special warnings and precautions for use

Side effects related to spread of toxin distant from the site of administration have been reported (see section 4.8) which, in some cases, were associated with dysphagia, pneumonia and/or significant debility resulting, very rarely, in death. 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 possible dose and by not exceeding the maximum recommended dose.

Dysport should only be used with caution and under close medical supervision in patients with subclinical or clinical evidence of marked defective neuromuscular transmission (e.g. myasthenia gravis). Such patients may have an increased sensitivity to agents such as Dysport, which may result in excessive muscle weakness with therapeutic doses. Patients with underlying neurological disorders are at increased risk of this side effect.

Very rare cases of death, occasionally in the context of dysphagia, pneumopathy and/or in patients with significant asthenia have been reported following treatment with botulinum toxin A or B. Patients with disorders resulting in defective neuromuscular 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.

Dysport should be administered with caution to patients with pre-existing swallowing or breathing problems as these 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.

The recommended posology and frequency of administration for Dysport must not be exceeded (see section 4.2).

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

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

Dysport should not be used to treat spasticity in patients who have developed a fixed contracture.

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

Dysport should only be used to treat a single patient, during a single session. Specific precautions must be taken during the preparation and administration of the product (see section 4.2) and for the inactivation and disposal of any unused reconstituted solution (see section 6.6).

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.

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

When treating glabellar lines, it is essential to study the patient's facial anatomy prior to administration. Facial asymmetry, ptosis, excessive dermatochalasis, scarring and any alterations to this anatomy, as a result of previous surgical interventions should be taken into consideration. Caution should be taken when the targeted muscle shows excessive weakness or atrophy.

Careful consideration should be given before the injection of patients who have experienced a previous allergic reaction to a product containing botulinum toxin type A. The risk of a further allergic reaction must considered in relation to the benefit of treatment.

4.5 Interaction with other medicinal products and other forms of interaction

The effects of botulinum toxin may be potentiated by drugs interfering either directly or indirectly with the neuromuscular function (e.g. aminoglycosides, curare-like non-depolarising blockers) and such drugs should be used with caution in patients treated with botulinum toxin.

4.6 Pregnancy and lactation

Pregnancy:

There are limited data from the use of *Clostridium botulinum* type A toxin-haemagglutinin complex in pregnant women. Studies in animals have shown reproductive toxicity at doses causing maternal toxicity (see section 5.3).

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

Lactation:

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

4.7 Effects on 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.

4.8 Undesirable 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.

Side effects related to spread of toxin distant from the site of administration have been reported (exaggerated muscle weakness, dysphagia, aspiration/ aspiration pneumonia, with fatal outcome in some very rare cases). (see section 4.4).

General

In the clinical trial programme, approximately 28% of the patients treated with Dysport experienced an adverse event.

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

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, pain / bruising at injection site.

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

Arm spasticity

Gastrointestinal disorders

Common: Dysphagia

Musculoskeletal and connective tissue disorders

Common: Arm muscle weakness

Injury, poisoning and procedural complications

Common: Accidental injury/falls

Paediatric cerebral palsy spasticity

Gastrointestinal disorders

Common: Diarrhoea

Musculoskeletal and connective tissue disorders

Common: Leg muscle weakness, muscle pain

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

Nervous system disorders

Common: Headache, dizziness, facial pareis

Eye disorders

Common: Blurred vision, visual acuity reduced

Uncommon: Diplopia, ptosis

Respiratory, thoracic and mediastinal disorders

Common: Dysphonia, dyspnoea

Rare: Aspiration

Gastrointestinal disorders

Very Common: Dysphagia, dry mouth

Musculoskeletal and connective tissue disorders

Very Common: Muscle weakness

Common: Neck pain, musculoskeletal pain, myalgia, pain in extremity, musculoskeletal stiffness

Uncommon: Muscle atrophy, jaw disorder

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.

These side effects may be expected to resolve within two to four weeks.

Blepharospasm and hemifacial spasm

Nervous system disorders

Common: Facial muscle weakness

Uncommon: Facial paralysis

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.

Glabellar Lines

Nervous system disorders	Very Common Headache Common Facial paresis (predominantly describes brow paresis) Uncommon Dizziness
Eye disorders	Common Asthenopia, Ptosis, Eyelid oedema, Lacrimation increase, Dry eye, Muscle twitching (twitching of muscles around the eyes) Uncommon Visual disturbances, Vision blurred, Diplopia Rare Eye movement disorder
Skin and subcutaneous tissue disorders	Uncommon Pruritus, Rash Rare Urticaria
General disorders and administration site conditions	Very Common Injection site reactions (e.g. erythema, oedema, irritation, rash, pruritus, paraesthesia, pain, discomfort, stinging and bruising)
Immune system disorders	Uncommon Hypersensitivity

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. In addition, hypersensitivity reactions have been reported.

4.9 Overdose

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 dysphagia 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 signs and /or 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/or symptoms of excessive muscle weakness or muscle paralysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Other muscle relaxants, peripherally acting agents.

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^{2+} 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^{2+} 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.

Alternative Dysport doses were investigated for the treatment of blepharospasm over 1 treatment cycle in a clinical study.

Efficacy was measured by the medians of differences in the Percentage of Normal Activity (PNA) values (derived from the Blepharospasm Disability Scale) between each treatment group and placebo. A dose-dependent improvement in blepharospasm was evident with increasing Dysport dose, with all treatment groups being superior to placebo.

Visit	Dysport 40 Units (N=30)	Dysport 80 Units (N=31)	Dysport 120 Units (N=31)
Week 4: Difference between the median of the changes in PNA values from baseline in the active group and the median of the changes in PNA values from baseline in the placebo group	31.2 %	41.3 %	48.5 %
Week 8: Difference between the median of the changes in PNA values from baseline in the active group the median of the changes in PNA values from baseline in placebo group	36.0 %	48.3 %	55.0 %
Week 12: Difference between the median of the changes in PNA values from baseline in the active group and the median of the changes in PNA values from baseline in placebo group	36.0 %	36.3 %	50.0 %
Week 16: Difference between the median of the changes in PNA values from baseline in the active group and the median of the changes in PNA values from baseline in placebo group	10.5 %[a]	24.2 %	31.3 %

[a] p value > 0.001

For the 40 units, 80 units and 120 units Dysport treatment groups, the medians of the changes from baseline in PNA values were statistically significantly higher compared to those in placebo group at weeks 4, 8, and 12.

A statistically significant difference compared to placebo group was also observed for the 80 units and 120 units Dysport treatment groups at week 16, indicating a greater duration of response at the 80 units and 120 units doses.

The incidence of related Treatment Emergent Adverse Events (TEAEs), specifically ptosis, was higher in the Dysport treatment groups than in the placebo treatment group and was dose-dependent with greater incidence seen at higher Dysport doses. See table below.

	Statistic	Placebo (N=26)	Dysport 40 Units (N=31)	Dysport 80 Units (N=31)	Dysport 120 Units (N=31)
Patients with related TEAEs	n (%)	3 (12)	19 (61)	23 (74)	26 (84)
Patients with related eye TEAEs	n (%)	3 (12)	16 (52)	23 (74)	26 (84)

5.2 Pharmacokinetic properties

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^{125} 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.

5.3 Preclinical safety data

Reproductive toxicity studies in pregnant rats and rabbits given *Clostridium botulinum* type A toxin-haemagglutinin complex by daily intramuscular injection, at doses of 6.6 units/kg (79 units/kg total cumulative dose) and 3.0 units/kg (42 units/kg total cumulative dose) in rats and rabbits respectively, did not result in embryo/foetal toxicity. Implantation losses at maternally toxic doses were observed at higher doses in both species. *Clostridium botulinum* type A toxin-haemagglutinin complex demonstrated no teratogenic activity in either rats or rabbits and no effects were observed in the pre- and postnatal study on the F1 generation in rats. Fertility of male and female rats was decreased due to reduced mating secondary to muscle paralysis at doses of 29.4 units/kg weekly in males and increased implantation loss at 20 units/kg weekly in females.

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Human albumin solution,

Lactose.

6.2 Incompatibilities

None known.

6.3 Shelf life

The shelf life of the packaged product is 24 months at 2-8ºC.

The product may be stored for up to 8 hours at 2-8ºC following reconstitution.

Since the product does not contain an antimicrobial agent, from a microbiological point of view, it is recommended that the product should be used immediately following reconstitution.

6.4 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 (2-8ºC) for up to 8 hours prior to use. Dysport should not be frozen.

6.5 Nature and contents of container

Nature of container/closure:

Type 1 glass vials 3mL capacity. 13mm bromobutyl freeze-drying closures oversealed by 13mm aluminium overseals with centre hole, crimped over.

Contents of container:

A white lyophilised powder for reconstitution.

6.6 Special precautions for disposal

Immediately after treatment of the patient, any residual Dysport which may be present in either vial or syringe should be inactivated with dilute hypochlorite solution (1% available chlorine). Thereafter, all items should be disposed of in accordance with standard hospital practice.

Spillage of Dysport should be wiped up with an absorbent cloth soaked in dilute hypochlorite solution.

7 MARKETING AUTHORISATION HOLDER

Ipsen Limited
190 Bath Road,
Slough
Berkshire, SL1 3XE
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 34926/0009

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 04 May 2006

Date of Latest Renewal: 04 May 2011

10 DATE OF REVISION OF THE TEXT

12 June 2012

IPSEN