SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Relfydess 100 units/mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Botulinum toxin type A 100 units/mL manufactured from *Clostridium botulinum*, free from complex proteins.
The potency units are specific to Relfydess and are not interchangeable with other preparations of botulinum toxin.
Each vial contains 150 units in 1.5 mL of solution.

Excipient with known effect
One mL of solution contains 1.1 mg polysorbate 80.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection).
Clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Relfydess is indicated for the temporary improvement in the appearance of:

- Moderate to severe glabellar lines at maximum frown
- Moderate to severe lateral canthal lines seen at maximum smile

alone or in combination, 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 treatment interval should be no more frequently than every twelve weeks.

The efficacy and safety of the repeated administration of this product has not been studied for more than 52 weeks.

Consideration of the cumulative dose is necessary if other botulinum toxin products are being or have been used to treat other indications for those products.

Posology

The potency units are specific to Relfydess and are not interchangeable with other preparations of botulinum toxin.

Relfydess is ready-to-use with a concentration of 10 units per 0.1 mL and no reconstitution is required.

Table 1: Dosing Instructions for Relfydess

Treatment(s)	**Total Recommended Dose**	**Dose per injection**
Glabellar Lines (GL)	50 units (0.5 mL)	5 injections of 10 units (0.1 mL): 2 injections on each side at the *corrugator* muscle and 1 injection at the *procerus* muscle near the nasofrontal angle (see **Figure 1**)
Lateral Canthal Lines (LCL)	60 units (0.6 mL)	6 injections of 10 units (0.1 mL): 3 injections on each side at the *orbicularis oculi* muscle (see **Figure 2**)
Combined treatment of Glabellar Lines and Lateral Canthal Lines	110 units (1.1 mL)	11 injections total of 10 units (0.1 mL) for combined GL and LCL

General information
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, inappropriate injection technique, and formation of toxin-neutralising antibodies.
- Re-evaluation of the relevance of treatment with botulinum toxin A.

Paediatric population
The safety and efficacy of Relfydess in children aged up to 18 years have not been established.
The use of Relfydess is not recommended in patients under 18 years.

Elderly population
There is limited phase 3 clinical data with Relfydess in patients 65 years and older.

Method of administration

Relfydess should only be administered by health care professionals with appropriate qualifications and expertise in this treatment and having the required equipment, in accordance with national guidelines and legislation.

Intramuscular use.

Dosing and treatment intervals depend on assessment of the individual patient's response, but dosing should not exceed maximum doses allowed and the treatment interval should be at least 12 weeks.

Each vial should be used for a single patient during a single treatment session only. Any residual product after the treatment should be discarded.

Use aseptic technique and standard practice to prevent cross-infections. For instructions for handling and disposal of the vials, see section 6.6.

The median time to onset is 2 to 3 days, with some patients reporting an effect within 1 day. Treatment effect has been demonstrated for 6 months, with up to 75% of patients not returning to baseline.

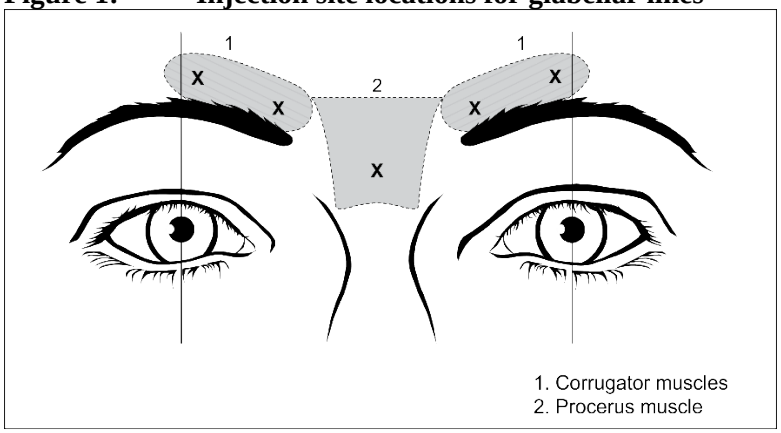
Glabellar lines
The recommended dose for the treatment of glabellar lines in adults is a total of 50 units/0.5 mL administered by intramuscular injection divided equally (10 units/0.1 mL per injection) into each of

the 5 intramuscular injection sites (see **Figure 1**): 2 injections on each side at the *corrugator* muscle and 1 injection at the *procerus* muscle near the nasofrontal angle. The anatomical landmarks can be more readily identified if palpated and observed at patient maximum frown. Before and during the injection, place the thumb or index finger firmly below the orbital rim in order to prevent extravasation below the orbital rim. The needle bevel should be pointed upward and medially during the injection.

In order to reduce the risk of eyelid ptosis, the following steps should be taken:

- Avoid injections near the *levator palpebrae superioris* muscle, particularly in patients with larger brow-depressor complexes.
- Lateral *corrugator* injections should be placed at least 1 centimetre above the bony supraorbital ridge.
- Ensure the injected dose (volume) is accurate.
- Avoid injecting closer than 1 centimetre above the central eyebrow.

Figure 1: Injection site locations for glabellar lines



Lateral canthal lines

The recommended dose for the treatment of lateral canthal lines in adults is a total of 60 units/0.6 mL administered by intramuscular injection divided equally into 10 units/0.1 mL into each of the 6 intramuscular injection sites (see **Figure 2**: Option 1 and Option 2): 3 injections (30 units/0.3 mL) on each side at the *orbicularis oculi* muscle. Injections should be given with the needle bevel-up and oriented away from the eye in the lateral *orbicularis oculi* muscle. When lines in the lateral canthal region appear both above and below the lateral *canthus*, inject per Option 1. In case lines in the lateral canthal region are mainly below the lateral *canthus*, inject per Option 2.

Figure 2: Injection site locations for lateral canthal lines

Option 1: Above and below lateral *canthus* **Option 2: Below lateral *canthus***

Lateral canthal line anatomical landmarks can be more readily identified if observed and palpated at maximal smile. Care must be taken to avoid injecting the *zygomaticus major*/*minor* muscles to avoid lateral mouth drop and asymmetrical smile.

Glabellar lines/lateral canthal lines combined treatment
For combination treatment of glabellar lines and lateral canthal lines, the respective individual dosing and administration should be followed for a total dose of 110 units/1.1 mL of Relfydess.

The recommended dose for the treatment of glabellar lines is 50 units/0.5 mL (10 units/0.1 mL per injection) into each of 5 intramuscular injection sites and for lateral canthal lines is 60 units/0.6 mL (10 units/0.1 mL in each of 6 intramuscular injection sites).

4.3 Contraindications

Known hypersensitivity to any botulinum toxin products or to any of the excipients listed in section 6.1.
Presence of infection at the proposed injection sites.
Presence of myasthenia gravis, Eaton Lambert Syndrome or amyotrophic lateral sclerosis.

4.4 Special warnings and precautions for use

General
Relfydess should not be injected into a blood vessel.

As with all intramuscular injections, use of Relfydess is not recommended in patients who have a prolonged bleeding time.

Patients treated with the recommended dose may experience exaggerated muscle weakness.

Each vial of Relfydess must be used for a single patient treatment during a single session.

Any excess of unused product must be disposed of as detailed in section 6.6. Specific precautions must be taken for the inactivation and disposal of any unused solution (see section 6.6).

Hypersensitivity reactions
Serious and/or immediate hypersensitivity reactions have been reported for botulinum toxin products and anaphylactic reactions can occur very rarely (see section 4.8). These reactions include anaphylaxis, serum sickness, urticaria, soft tissue oedema, and dyspnoea. Equipment and medications (including adrenaline) needed to treat anaphylaxis should therefore be readily available. If such a reaction occurs, further injection of Relfydess should be discontinued, and appropriate medical therapy immediately instituted.

Spread of Toxin effect
Post-marketing safety data from other approved botulinum toxin products suggest that botulinum toxin effects (such as diplopia, blurred vision and ptosis) may be observed beyond the site of local injection (see section 4.8). Cases of iatrogenic botulism have been reported following injection of botulinum toxin products. In addition, adverse reactions possibly related to the spread of toxin effect distant from the site of injection have been reported very rarely with botulinum toxin and may include asthenia, generalised muscle weakness, dysphagia, dysphonia, dysarthria, urinary incontinence, and breathing difficulties. These symptoms are consistent with the mechanism of action of botulinum toxins and 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. Patients with pre-existing swallowing or breathing difficulties may be more susceptible to these complications. More specifically, following treatment with botulinum toxin, very rare cases of death have been reported in the context of patients who have dysphagia, pneumopathy, or significant asthenia. Therefore, Relfydess is not recommended in such patients.

Patients or caregivers should be advised to seek immediate medical care if they experience any signs or symptoms consistent with the spread of botulinum toxin effect or if swallowing, speech or respiratory disorders arise (see section 4.9).

Pre-existing neuromuscular disorders
Relfydess should be used with caution in patients with a risk of, or clinical evidence of, marked defective neuro-muscular transmission. These patients may have an increased sensitivity to agents such as botulinum toxin, and excessive muscle weakness (including systemic effects of severe dysphagia and respiratory compromise) may follow treatment. In some of these cases, dysphagia has lasted several months and required placement of a gastric feeding tube.

Pre-existing conditions at the injection site
Caution should be taken when Relfydess is used in the presence of inflammation at the proposed injection site(s) or when excessive weakness or atrophy is present in the targeted muscle(s).
Caution should be used when Relfydess treatment is used in patients who have marked facial asymmetry, ptosis, excessive skin laxity (such as dermatochalasis, see section 5.1), deep dermal scarring, or thick sebaceous skin.

Ophthalmic adverse reactions
Dry eye, reduced tear production, reduced blinking, and corneal disorders may occur with the use of botulinum toxins. If symptoms of dry eye (e.g., eye irritation, photophobia, or visual changes) persist, consider referring the patient to an ophthalmologist. Increased lacrimation may occur with the use of botulinum toxins.

Muscle atrophy
Muscle atrophy is expected after repeated botulinum treatment secondary to the flaccid paralysis of the treated muscles.

Antibody formation
Injections at more frequent intervals or at higher doses may increase the risk of neutralising antibody formation to botulinum toxin. Clinically, the formation of neutralising antibodies may reduce the effectiveness of subsequent treatment.

Traceability
In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Potassium and Sodium content
This medicine contains potassium, less than 1 mmol (39 mg) per 150 units vial, i.e. essentially ‘potassium-free’.
This medicine contains less than 1 mmol sodium (23 mg) per 150 units vial, i.e. essentially ‘sodium-free’.

Polysorbate 80 content
This medicine contains 1.6 mg of polysorbate 80 per 150 units vial which is equivalent to 1.1 mg/mL. Polysorbates may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interaction studies have been conducted.

Concomitant treatment with Relfydess and aminoglycosides or other agents interfering with neuromuscular transmission (e.g. curare-like agents or other botulinum toxin products in other locations) should only be used with caution since the effect of botulinum toxin may be potentiated.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of botulinum toxin type A in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity other than at high doses causing maternal toxicity (see section 5.3). The potential risk for humans is unknown.
Relfydess should not be used during pregnancy and in women of childbearing potential not using contraception.

Breastfeeding
It is unknown if Relfydess is excreted in human milk. The excretion of Relfydess in milk has not been studied in animals. Relfydess should not be used during breast-feeding.

Fertility
There are no clinical data examining the effect of Relfydess on fertility. There is no evidence of direct effect of botulinum toxin A on fertility in animal studies (see section 5.3).

4.7 Effects on ability to drive and use machines

Other botulinum toxin products have been reported to have a minor or moderate influence on the ability to drive and/or use machines. There is a potential risk of localised muscle weakness or visual disturbances linked with the use of Relfydess which may temporarily impair the ability to drive or operate machinery.

4.8 Undesirable effects

Summary of safety profile
The majority of adverse reactions reported after one treatment with Relfydess in subjects receiving ≥ 50 units in all placebo-controlled studies in the development program were of mild to moderate intensity. The most frequently reported adverse reactions were injection site reactions and headache occurring in approximately 7% and 5% of subjects, respectively.
In general, treatment/injection technique-related reactions occurred within the first month following injection and were transient.

When glabellar lines and lateral canthal lines were treated in combination, the nature and frequency of adverse reactions were comparable to what was observed when patients were treated for the individual indications.

Tabulated list of adverse reactions
The frequency of undesirable reactions is classified as follows:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Table 2: Moderate to severe glabellar lines
The following adverse reactions were observed in patients that were administered Relfydess for the temporary improvement in the appearance of moderate to severe glabellar lines.

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Uncommon	Hypersensitivity
Nervous system disorders	Common	Headache
Eye disorders	Common	Eyelid ptosis
	Uncommon	Visual impairment, dry eye, asthenopia
Skin and subcutaneous tissue disorders	Uncommon	Brow ptosis, urticaria
Musculoskeletal and connective tissue disorders	Uncommon	Muscular weakness, muscle spasm
General disorders and administration site conditions	Common	Injection site reactions (e.g. bruising, swelling, pruritus, pain, discomfort, haematoma, hypersensitivity and warmth)

Table 3: Moderate to severe lateral canthal lines
The following adverse reactions were observed in patients that were administered Relfydess for the temporary improvement in the appearance of moderate to severe lateral canthal lines.

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Uncommon	Hypersensitivity
Nervous system disorders	Common	Headache
Eye disorders	Uncommon	Dry eye, asthenopia, swelling of eyelid
Musculoskeletal and connective tissue disorders	Uncommon	Muscular weakness
General disorders and administration site conditions	Common	Injection site reactions (e.g. erythema, pain, and bruising)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Excessive doses may produce distant and profound neuromuscular paralysis with a variety of symptoms. Respiratory support may be required where excessive doses cause paralysis of respiratory muscles. In the event of overdose or spread of toxin, the patient should be medically monitored for several weeks for any signs and/or symptoms of excessive muscle weakness or muscle paralysis. Symptomatic treatment may be necessary.

Symptoms of overdose may not be present immediately post-injection.

Admission to hospital should be considered for patients with symptoms of botulinum toxin overdose (e.g. a combination of muscle weakness, ptosis, diplopia, swallowing and speech disorders, or paresis of the respiratory muscles).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other muscle relaxants, peripherally acting agents
ATC code: M03AX01

Mechanism of action

The primary pharmacodynamic effect of botulinum toxin type A is chemical denervation of the treated muscle, resulting in a measurable decrease of the compound muscle action potential. This causes a localized reduction of muscle activity.

When injected intramuscularly, the toxin induces paralysis of the affected muscle which temporarily reduces muscle activity. The effect lasts for sustained periods until the neuromuscular junction has recovered and muscle activity returns.

Clinical efficacy and safety

The data described below reflect results in the Phase III placebo-controlled studies READY-1, READY-2 and READY-3. A total of 1,012 patients were treated in 3 pivotal trials including 806 patients treated with Relfydess and 206 patients treated with placebo. There were also an additional 902 Relfydess-treated patients in an open-label long term safety study (READY-4). Across all Phase III studies, 1708 subjects were treated with Relfydess.

Onset of action were reported within 1 day (up to 39% and 34% in glabellar and lateral canthal lines, respectively), with a median time to onset of 2 to 3 days. Treatment effect has been demonstrated for 6 months, with up to 75% of patients not returning to baseline.

Patients receiving ≥ 50 units Relfydess (1699 in total) were tested for antidrug antibody (ADA) formation at baseline, and following each treatment. Clinical data suggests the potential for low titer ADA in some individuals following treatment; overall, 1.1% of subjects tested positive for ADA. Low immunogenicity can be concluded for Relfydess.

Glabellar lines (READY-1 and READY-3)

In two pivotal Phase III multi-center, double-blind, placebo-controlled studies 451 patients were treated in GLs at the recommended dose of 50 units. READY-1 assessed Relfydess treatment of GL only; READY-3 assessed combination treatment of GL and LCL.

Primary efficacy was the proportion of responders, defined as achievement of a score of 0 or 1 in glabellar line severity on the GL-ILA 4-Point Photographic Scale at maximum frown at the Month 1 visit. The majority of subjects in both the Relfydess or placebo group had severe glabellar lines at baseline as determined by the investigator (74.5% and 75.8% respectively). Patients with excessive skin laxity in the treatment area or periorbital area were excluded from the studies. The proportion of responders was statistically significantly greater ($p < 0.001$) in the Relfydess group compared to the placebo group at 1 month (Table 4).

Table 4: Investigator Assessment of Glabellar Line Treatment Success[a] (% and Number of Subjects) at Month 1[b] in Double-blind, Placebo-Controlled Clinical Studies, mITT Population[c]

Study	Relfydess 50 units GL	Relfydess 50 units GL and 60 units LCL	Placebo
READY-1, GL only	96.3% N = 199	-	4.5% N = 67
READY-3 LCL & GL treatment	94.3% N = 106	96.3% N = 108	1.8% N = 55

[a] achieved a score of 0 (none) or 1 (mild) in GL severity on GL-ILA

[b] Day 30 primary efficacy endpoint; $p < 0.001$

[c] The modified intention-to-treat (mITT) population included all subjects who were randomized and dispensed the study product and were analyzed according to the randomization scheme. Subjects with a photographic and categorical scale Month 1 assessment via a remote visit were excluded from the mITT population

For subjects in READY-1, response (achieving 0 or 1 on the GL-ILA at maximum frown) was statistically significantly greater in Relfydess compared with placebo from Day 7 through 6 months ($p < 0.001$), as displayed in Table 5.

Table 5: READY-1 Investigator Live Assessment (ILA) of GL Severity – Responder Rates[a] (%) Post-Injection, ITT Population[b]

Timepoint Post-Injection	Relfydess (N=223)	Placebo (N=74)
	GL-ILA	GL-ILA
Day 7	93.2%	4.3%
Day 14	96.4%	6.3%
Month 1	96.4%	4.7%
Month 2	92.9%	8.9%
Month 3	73.7%	7.9%
Month 4	53.7%	6.3%
Month 5	39.7%	6.3%
Month 6	23.6%	1.5%

[a] Defined as having a GL severity grade of 2 (moderate) or 3 (severe) at baseline and of 0 (none) or 1 (mild) at a given visit as assessed by the GL-ILA severity scale

[b] The intention-to-treat (ITT) population included all subjects who were randomized and dispensed the study product and were analysed according to the randomization scheme

When used in combined treatment with LCL in READY-3, response (achieving 0 or 1 on the GL-ILA at maximum frown) was statistically significantly higher (nominal $p < 0.001$) in Relfydess-GL/Relfydess-LCL group compared with placebo GL/placebo LCL throughout the 6 months post-treatment.

Lateral canthal lines (READY-2 and READY-3)

In two pivotal Phase III multi-center, double-blind, placebo-controlled studies 471 patients were treated in LCLs at the recommended dose of 60 units. READY-2 assessed Relfydess treatment of LCL only; READY-3 assessed combination treatment of GL and LCL.

Primary efficacy was the proportion of subjects who were responders, defined as achievement of a score of 0 or 1 in lateral canthal line severity on the LCL-ILA 4-Point Photographic Scale (LCL-Investigator Live Assessment) at maximum smile, at the Month 1 visit. Patients with excessive skin laxity in the treatment area or periorbital area were excluded from the study. The proportion of responders was statistically significantly greater ($p < 0.001$) in the Relfydess group compared to the placebo group at 1 month (Table 6).

Table 6: Investigator Assessment of Lateral Canthal Line Treatment Success[a] (% and Number of Subjects) at Month 1[b] in Double-blind, Placebo-Controlled Clinical Studies, mITT Population[c]

Study	Relfydess 60 units LCL	Relfydess 60 units LCL & 50 units GL	Placebo
READY-2, LCL only	87.2% N = 204	-	11.9% N = 69
READY-3, LCL & GL treatment	78.1% N = 117	83.3% N = 108	19.3% N = 55

[a] achieved a score of 0 (none) or 1 (mild) in LCL severity on LCL-ILA

[b] Day 30 primary efficacy endpoint; $p < 0.001$

[c] The modified intention-to-treat (mITT) population included all subjects who were randomized and dispensed the study product and were analyzed according to the randomization scheme. Subjects with a photographic and categorical scale Month 1 assessment via a remote visit were excluded from the mITT population

For subjects in READY-2, response (achieving 0 or 1 on the LCL-ILA at maximum smile) was statistically significantly greater in Relfydess compared with placebo from Day 7 through 6 months ($p \leq 0.002$), as displayed in Table 7.

Table 7: READY-2 Investigator Live Assessment (ILA) of LCL Severity – Responder Rates[a] (%) Post-Injection, ITT Population[b]

Timepoint Post-injection	Relfydess (N=230)	Placebo (N=73)
	LCL-ILA	LCL-ILA
Day 7	82.5%	8.5%
Day 14	89.7%	11.4%
Month 1	87.5%	11.8%
Month 2	76.3%	14.3%
Month 3	59.8%	14.9%
Month 4	45.7%	10.9%
Month 5	32.1%	6.2%
Month 6	23.3%	7.2%

[a] Defined as having a LCL severity grade of 2 (moderate) or 3 (severe) at baseline and 0 (none) or 1 (mild) at a given visit as assessed by the LCL-ILA severity scale

[b] The intention-to-treat (ITT) population included all subjects who were randomized and dispensed the study product and were analysed according to the randomization scheme

When used in combined treatment with GL in READY-3, response (achieving 0 or 1 on the LCL-ILA at maximum smile) was statistically significantly higher (nominal $p \leq 0.007$) in Relfydess GL/Relfydess LCL group compared with placebo GL/placebo LCL at all post-treatment timepoints except month 6.

Subject Satisfaction and Psychological Function

Subject psychological function was observed using FACE-Q™ psychological function scale.

The FLTSQ scale (Facial Line Treatment Satisfaction Questionnaire) was used to observe subject satisfaction with GL and/or LCL appearance and also to observe subject treatment satisfaction.

FACE-Q™ psychological function scale and FLTSQ scale responses indicated Relfydess-treated subjects showed improvement in psychological function and were more satisfied with their treatment and appearance than placebo subjects at all post-treatment time points. As assessed by FACE-Q™ and FLTSQ, the positive psychological function and subject satisfaction were maintained for 6 months following treatment.

Open Label Study (READY-4)

In the phase III, multicenter, open-label study READY-4, Relfydess was administered up to 110 units per treatment and up to 4 repeat treatments in each indication (up to a total of 7 GL and/or LCL treatments over 52 weeks). The responder rates as determined by the investigator at Week 4 were maintained over repeated cycles in glabellar lines at maximum frown in the subgroup of 175 subjects receiving 4 treatment cycles (79.4% in treatment cycle 1 and 80.0% in treatment cycle 4). The corresponding responder rates in 186 subjects receiving 4 treatment cycles for lateral canthal lines at maximum smile were 64.5% in treatment cycle 1 and 60.2% in treatment cycle 4.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Relfydess in all subsets of the paediatric population for treatment of temporary improvement in the appearance of moderate to severe glabellar lines at maximum frown and lateral canthal lines seen at maximum smile (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Relfydess is not expected to be present in the peripheral blood at measurable levels following intramuscular injection at the recommended dose. Pharmacokinetic studies have therefore not been performed.

5.3 Preclinical safety data

Studies on acute toxicity, chronic toxicity and local tolerance at the injection site showed no unusual adverse local or systemic effects at clinically relevant dose levels.
Literature data indicate that botulinum toxins exhibit a short half-life in blood and limited tissue diffusion, including across the placenta. At doses below clear parental toxicity, botulinum toxin did not have adverse effects on fertility or reproductive function in rabbits. Daily intramuscular administration of botulinum toxin to pregnant rats or rabbits during the organogenesis period resulted in reduced foetal body weights and decreased skeletal ossification, especially at higher doses associated with significant maternal toxicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate dihydrate
Sodium dihydrogen phosphate dihydrate
Potassium chloride
Sodium chloride
Polysorbate 80
Tryptophan
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze. Keep vials in the outer carton in order to protect from light.
Unopened vial may be brought to room temperature at 25°C and protected from light. The stability of Relfydess (unopened vial) has been demonstrated for up to 24 hours at room temperature.

6.5 Nature and contents of container

Nature of container/closure
Type I glass vial, bromobutyl stopper and aluminium overseal with polypropylene flip-off top.

Content of container
Each vial contains 150 units of botulinum toxin type A in 1.5 mL of solution.

Pack sizes:
Pack containing 1 or 10 vials of Relfydess 100 units/mL solution for injection.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Immediately after treatment of the patient, any residual Relfydess which may be present in either vial or syringe should be inactivated with diluted sodium hypochlorite (0.1 % NaOCl) or sodium hydroxide solution (1 % NaOH).

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

RECOMMENDATIONS SHOULD ANY INCIDENT OCCUR DURING THE HANDLING OF BOTULINUM TOXIN

- Any spills of the product must be wiped up with dry, absorbent material. The material should be disposed of in accordance with local requirements.
- The contaminated surfaces should be cleaned using diluted hypochlorite or sodium hydroxide solution, then dried.
- If a vial is broken, proceed as mentioned above by carefully collecting the pieces of broken glass and wiping up the product, avoiding any cuts to the skin.
- If the product comes into contact with the skin, wash the affected area with soap and water.
- If product enters into contact with the eyes, rinse thoroughly with plenty of water or with an ophthalmic eyewash solution.
- If product enters into contact with a wound, cut or broken skin, rinse thoroughly with plenty of water and seek medical attention.

These instructions for use handling and disposal should be strictly followed.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

2026-04-02