Package leaflet: Information for the user

VISTABEL, 4 Allergan Units/0.1ml,
Powder for solution for injection
Botulinum toxin type A

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1 What VISTABEL is and what it is used for

VISTABEL is a peripherally acting muscle relaxant.
VISTABEL acts by blocking the nervous impulses directed towards all the muscles in which it has been injected. This prevents muscles from contracting, leading to a temporary and reversible paralysis.

VISTABEL is used for the temporary improvement in the appearance of:

- vertical lines between the eyebrows seen at maximum frown and/or,
- fan-shaped lines from the corner of the eyes seen at maximum smile and/or,
- forehead lines seen at maximum raised eyebrows,

when the severity of the facial lines has an important psychological impact in adult patients.

2 What you need to know before you use VISTABEL

Do not use VISTABEL:
- If you are allergic (hypersensitive) to botulinum toxin type A or any of the other ingredients of this medicine (listed in section 6);
- If you are diagnosed with myasthenia gravis or Eaton Lambert Syndrome (chronic diseases affecting the muscles);
- If you have infection at the proposed injection sites.

Warnings and precautions:

Adverse reactions possibly related to the spread of toxin distant from the site of administration have been reported very rarely with botulinum toxin (e.g. muscle weakness, difficulty to swallow or unwanted food or liquid in the airways). Patients receiving recommended doses may experience exaggerated muscle weakness.

- Visit your doctor immediately:
  - If you find it difficult to swallow, to speak or to breathe after treatment.

- The use of VISTABEL is not recommended in patients with a history of dysphagia (difficulty to swallow) and impaired swallowing.
- The use of VISTABEL is not recommended in individuals under 18 years.
- There is limited experience of using VISTABEL in patients older than 65 years.
- Too frequent or excessive dosing may enhance the risk of antibody formation. Antibody formation may lead to treatment failure of botulinum toxin type A even for other uses. To limit this risk, the interval between two treatments must not be less than three months.
- Very rarely, an allergic reaction can occur after the injection of botulinum toxin.
- Drooping of the eyelid may occur after treatment.

- Please inform your doctor if:
  - you had problems in the past with previous botulinum toxin injections;
  - you see no significant improvement of your lines one month after your first course of treatment;
  - you suffer from certain diseases affecting your nervous system (such as amyotrophic lateral sclerosis or motor neuropathy);
  - you have inflammation at the proposed injection site(s);
  - the muscles to be injected are weak or wasted;
  - you have had an operation or injured your head, neck or chest;
  - you will have an operation soon.

Other medicines and VISTABEL:

The use of botulinum toxin is not recommended in association with aminoglycoside antibiotics, spectinomycin or other medicinal products that interfere with neuromuscular transmission.

Please tell your doctor if you have recently been injected with a medicine containing botulinum toxin (the active substance of VISTABEL), as this may increase the effect of VISTABEL too much.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

The use of VISTABEL is not recommended during pregnancy and in women of childbearing potential not using contraception.

VISTABEL is not recommended in breast-feeding women.

Contact your doctor if you are pregnant, planning pregnancy or become pregnant whilst being treated. Your doctor will discuss with you whether you should continue treatment.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines:

Attention is drawn to drivers or persons using machines to the risk of generalised and/or muscular weakness, dizziness, and visual disturbance linked with the use of this medicine, which could make the driving of vehicles or the use of machines dangerous. Do not drive or use machinery until such signs have cleared.

VISTABEL contains Sodium

This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3 How to use VISTABEL

Method and route of administration

VISTABEL should only be administered by physicians with appropriate qualifications and expertise in this treatment and use of the required equipment.

Vertical lines between the eyebrows seen at maximum frown:
VISTABEL is injected into your muscles (intramuscularly), directly into the affected area between the eyebrows.
The usual dose is 20 Units. You will be injected with the recommended volume of 0.1 millilitre (ml) (4 Units) of VISTABEL into each of 5 injection sites.

Improvement of severity of the lines located between the eyebrows seen at maximum frown generally occurs within one week after treatment, the maximum effect being observed 5 to 6 weeks after injection. The treatment effect has been demonstrated for up to 4 months after injection.

Fan-shaped lines from the corner of the eyes seen at maximum smile:
VISTABEL is injected directly into the affected area at the side of each eye.
The usual dose is 24 Units. You will be injected with the recommended volume of 0.1 millilitre (ml) (4 Units) of VISTABEL into each of 6 injection sites (3 injection sites at the side of each eye).

Improvement of severity of the fan-shaped lines from the corner of the eyes seen at maximum smile generally occurs within one week after treatment. The treatment effect has been demonstrated for an average of 4 months after injection.

Forehead lines seen at maximum raised eyebrows:
VISTABEL is injected directly into the muscle of the affected area on the forehead.
The usual dose is 20 Units. You will be injected with the recommended volume of 0.1 millilitre (ml) (4 Units) of VISTABEL into each of 5 injection sites.

The total dose for treatment of forehead lines (20 Units) in conjunction with glabellar lines (20 Units) is 40 Units.

Improvement of severity of forehead lines seen at maximum raised eyebrows generally occurs within one week after treatment. The treatment effect has been demonstrated for approximately 4 months after injection.

General Information:

If you are treated for fan-shaped lines from the corner of the eyes seen at maximum smile at the same time as vertical lines between the eyebrows seen at maximum frown, you will receive a total dose of 44 Units.

If you are treated for all 3 facial lines at the same time (fan-shaped lines from the corner of the eyes seen at maximum smile, vertical lines between the eyebrows seen at maximum frown, and forehead lines seen at maximum raised eyebrows) you will receive a total dose of 64 Units.

The interval between two treatments must not be less than three months.
The efficacy and safety of repeated injections of VISTABEL beyond 12 months has not been evaluated.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4 Possible side effects

Like all medicines, VISTABEL can have side effects, although not everybody gets them.
In general, adverse reactions occur within the first few days following injection and are temporary. Most adverse events reported were of mild to moderate severity.
Approximately 1 out of 4 patients may experience side effects following VISTABEL injection for the vertical lines between the eyebrows seen at maximum frown. Approximately 8% of patients may experience side effects following VISTABEL injection for the fan-shaped lines from the corner of the eyes seen at maximum smile when treated alone or at the same time as vertical lines between the eyebrows seen at maximum frown. Approximately 20% of patients may experience side effects following VISTABEL injection for forehead lines seen at maximum raised eyebrows when treated in conjuction with vertical lines between the eyebrows seen at maximum frown. Approximately 14% of patients may experience side effects when treatment of forehead lines in conjuction with vertical lines is combined with treatment for fan-shaped lines from the corner of the eyes seen at maximum smile.

These adverse reactions may be related to treatment, injection technique or both. Drooping of the eyelid, which may be technique-related, is consistent with the local muscle relaxant action of VISTABEL.

Adverse reactions possibly related to the spread of toxin distant from the site of administration have been reported very rarely with botulinum toxin (e.g. muscle weakness, difficulty to swallow, constipation or pneumonia due to unwanted food or liquid in the airways, which can be fatal). Injection of VISTABEL is not recommended in patients with a history of dysphagia (difficulty to swallow) and impaired swallowing.

IF YOU HAVE ANY DIFFICULTY IN <u>BREATHING</u>, <u>SWALLOWING</u> OR <u>SPEAKING</u> AFTER RECEIVING VISTABEL, CONTACT YOUR DOCTOR IMMEDIATELY.

If you experience <u>hives</u>, <u>swelling</u> including swelling of the face or throat, <u>wheezing</u>, feeling <u>faint</u> and shortness of <u>breath</u>, contact your doctor immediately.

Diffusion of botulinum toxin into nearby muscles is possible when high doses are injected, particularly in the neck area.

As expected for any injection procedure, pain/burning/stinging, swelling and/or bruising may be associated with the injection.
Speak to your doctor if you are worried about this.

The chance of having a side effect is described by the following categories:

Common	may affect up to 1 in 10 people
Uncommon	may affect up to 1 in 100 people

Injections for the temporary improvement in the vertical lines between the eyebrows

Common	Headaches, numbness, drooping eyelid, nausea (feeling sick), skin redness, skin tightness, localised muscle weakness, face pain, injection site swelling, bruising under the skin, injection site pain, injection site irritation.
Uncommon	Infection, anxiety, dizziness, inflammation of the eyelid, eye pain, visual disturbance, blurred vision, dry mouth, swelling (face, eyelid, around the eyes), sensitivity to light, itching, dry skin, muscle twitching, flu syndrome, lack of strength, fever, Mephisto sign (raising of the outer eyebrows).

Injections for the temporary improvement in the fan-shaped lines from the corner of the eyes, when treated with or without vertical lines between the eyebrows seen at frown

Common	Injection site haematoma*.
Uncommon	Eyelid swelling, injection site bleeding*, injection site pain*, injection site tingling or numbness.

*Some of these side effects may also be related to the injection procedure.

Injections for the temporary improvement in the forehead lines and vertical lines between the eyebrows seen at frown when treated with or without the fan-shaped lines from the corner of the eyes

Common	Headaches, drooping eyelid[1], skin tightness, drooping eyebrow[2], injection site bruising*, injection site haematoma*, Mephisto sign (raising of the outer eyebrows).
Uncommon	injection site pain*.

1.The median time to onset of drooping eyelid was 9 days following treatment
2. The median time to onset of drooping eyebrow was 5 days following treatment
*Some of these side effects may also be related to the injection procedure.

The following list describes **additional side effects** reported for VISTABEL since it has been marketed for the treatment of glabellar lines, crow's feet lines and other clinical indications:

- severe allergic reaction (swelling under the skin, difficulty breathing)
- hives
- loss of appetite
- nerve damage
- difficulty moving the arm and shoulder
- voice and speech problems
- weakness of the face muscles
- decreased skin sensation
- muscle weakness
- chronic disease affecting the muscles (myasthenia gravis)
- numbness
- pain or weakness starting from the spine
- fainting
- droop of the muscles on one side of the face
- increase in eye pressure

- drooping eyelid
- difficulty in completely closing the eye
- strabismus (squint)
- blurred vision, difficulties in seeing clearly
- decreased hearing
- noises in the ear
- feeling of dizziness or “spinning” (vertigo)
- aspiration pneumonia (lung inflammation caused by accidentally breathing in food, drink, saliva or vomit)
- shortness of breath
- breathing problems, respiratory depression and/or respiratory failure
- abdominal pain
- diarrhoea
- dry mouth
- difficulty swallowing
- nausea
- vomiting
- hair loss
- drooping eyebrow
- psoriasis-like skin patches (red, thick, dry and scaly)
- different types of red blotchy skin rashes
- excessive sweating
- loss of eyebrow
- itching
- rash
- muscle wasting
- muscle pain
- loss of nerve supply to/ shrinkage of injected muscle
- malaise
- feeling generally unwell
- fever
- dry eye
- localised muscle twitching/involuntary muscle contractions
- Swelling of the eyelid

Reporting of side effects
If you get any side effects, talk to your doctoror pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Ireland
HPRA Pharmacovigilance
Website: www.hpra.ie

Malta
ADR Reporting
Website: www.medicinesauthority.gov.mt

By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store VISTABEL

Keep out of the sight and reach of children.

Do not use VISTABEL after the expiry date which is stated on the vial and the carton after Exp:. The expiry date refers to the last day of that month.
Store in a refrigerator (2°C - 8°C).
After reconstitution, an immediate use of the solution for injection is recommended; however it can be stored for up to 24 hours in a refrigerator (2°C - 8°C).

6 Contents of the pack and other information

What VISTABEL contains

- The active substance is: botulinum toxin type A[1] (0.1 ml of reconstituted solution for injection contains 4 Allergan units).

[1]of *Clostridium botulinum*

- The other ingredients are human albumin and sodium chloride.

What VISTABEL looks like and contents of the pack

VISTABEL is presented as a thin white powder for solution for injection that may be difficult to see on the bottom of a transparent glass vial. Prior to injection, the product must be dissolved in sterile unpreserved normal saline solution (0.9% sodium chloride solution for injection). Each vial contains either 50 or 100 Allergan Units of botulinum toxin type A.
Each pack contains 1 or 2 vials.
NOT ALL PACK SIZES MAY BE MARKETED

Marketing Authorisation Holder

AbbVie Limited
Citywest Business Campus
Dublin 24
Ireland

Manufacturer

Allergan Pharmaceuticals Ireland
Castlebar Road
Westport
County Mayo
Ireland

This medicine is authorised in the Member States of the European Economic Area under the following names:

Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden	VISTABEL
Germany	VISTABEL 4 Allergan-Einheiten/0,1 ml Pulver zur Herstellung einer Injektionslösung

Italy	VISTABEX

This leaflet was approved in 03/2023

THE FOLLOWING INFORMATION IS INTENDED FOR MEDICAL OR HEALTHCARE PROFESSIONALS ONLY

Botulinum toxin units are not interchangeable from one product to another. Doses recommended in Allergan Units are different from other botulinum toxin preparations.

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

- moderate to severe vertical lines between the eyebrows seen at maximum frown (glabellar lines) and/or,
- moderate to severe lateral canthal lines (crow's feet lines) seen at maximum smile and/or,
- moderate to severe forehead lines seen at maximum eyebrow elevation,

when the severity of the facial lines has an important psychological impact in adult patients.

Reconstitution should be performed in accordance with good practices rules, particularly for the respect of asepsis. VISTABEL has to be reconstituted with sterile unpreserved normal saline solution (0.9% sodium chloride solution for injection). When using a 50 Unit vial, 1.25 ml of sterile unpreserved normal saline solution (0.9% sodium chloride solution for injection) has to be drawn up into a syringe in order to obtain a reconstituted solution for injection at a concentration of 4 Units/0.1 ml. When using a 100 Unit vial, 2.5 ml of sterile unpreserved normal saline solution (0.9% sodium chloride solution for injection) has to be drawn up into a syringe in order to obtain a reconstituted solution for injection at a concentration of 4 Units/0.1 ml.

Vial size	Amount of diluent added (sterile unpreserved normal saline solution (0.9% sodium chloride solution for injection))	Resulting dose (Units per 0.1 ml)
50 Units	1.25 ml	4.0 Units
100 Units	2.5 ml	4.0 Units

The central part of the rubber cap has to be cleaned with alcohol.
To avoid VISTABEL denaturation, inject the diluent slowly into the vial and gently rotate the vial avoiding bubble formation. The vial has to be discarded if the vacuum does not pull the diluent into the vial. Once reconstituted, the solution for injection should be visually inspected prior to use to verify it is a clear, colourless to slightly yellow solution free of particulate matter.

It is mandatory that VISTABEL is used for one single patient treatment only during a single session.

Before injection for glabellar lines (moderate or severe vertical lines seen at maximum frown), the thumb or index finger is to be placed firmly below the orbital rim in order to prevent extravasation below the orbital rim. The needle should be oriented superiorly and medially during the injection. In order to reduce the risk of eyelid ptosis, the maximum dose of 4 Units for each injection site as well as the number of injection sites should not be exceeded. In addition, injections near the levator palpebrae superioris muscle must be avoided, 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, a distance of at least 1 cm above the arch of the eyebrows.

Injections for crow's feet lines (moderate or severe lateral canthal lines seen at maximum smile) should be given with the needle tip bevel up and oriented away from the eye. In order to reduce the risk of eyelid ptosis, the maximum dose of 4 Units for each injection site as well as the number of injection sites should not be exceeded. In addition, injections should be made temporal to the orbital rim, thereby maintaining a safe distance from the muscle controlling eyelid elevation.

The total dose for treatment of forehead lines (20 Units) in conjunction with glabellar lines (20 Units) is 40 Units/1.0mL. To identify the location of the appropriate injection sites in the frontalis muscle, the overall relationship between the size of the subject's forehead, and the distribution of frontalis muscle activity should be assessed.

Procedure to follow for safe disposal of vials, syringes and materials used:

Immediately after use, unused reconstituted VISTABEL solution for injection in the vial and/or the syringe must be inactivated, prior to disposal, with 2 ml of dilute hypochlorite solution at 0.5% or 1% available chlorine and should be disposed of in accordance with local requirements.
Used vials, syringes and materials should not be emptied and must be discarded into appropriate containers and disposed of according to local regulations.

Recommendations in the event of an accident when handling botulinum toxin.

In the event of an accident when the product is being handled, whether in the vacuum-dried state or reconstituted, the appropriate measures described below must be initiated immediately.

- Any spillage must be wiped up: either with an absorbent material soaked in a solution of sodium hypochlorite (Javel solution) in the case of the vacuum-dried product, or with a dry absorbent material in the case of the reconstituted product.

- Contaminated surfaces must be cleaned with an absorbent material soaked in a solution of sodium hypochlorite (Javel solution) and then dried.

- If a vial is broken, proceed as stated above, carefully collect up the pieces of glass and wipe up the product, avoiding cutting the skin.

- If splashed onto the skin, wash with a solution of sodium hypochlorite (Javel solution) and then rinse thoroughly with plenty of water.

- If splashed into the eyes, flush thoroughly with plenty of water or with an eye wash solution.

- If the operator injures himself (cuts, pricks himself), proceed as above and take the appropriate medical steps according to the dose injected.

Identification of the product
In order to verify receipt of actual VISTABEL product from Allergan, look for a tamper-evident seal that contains a translucent silver Allergan logo on the top and bottom flaps of the VISTABEL cartons, and a holographic film on the vial label. In order to see this film, examine the vial under a desk lamp or fluorescent light source. Rotating the vial back and forth between your fingers, look for horizontal lines of rainbow colour on the label and confirm that the name "Allergan" appears within the rainbow lines.

Do not use the product and contact your local Allergan office for additional information if:

- the horizontal lines of rainbow colour or the word “Allergan” are not present on the vial label
- the tamper-evident seal is not intact and present on both ends of the carton
- the translucent silver Allergan logo on the seal is not clearly visible or has a black circle with a diagonal line through it (i.e., prohibition sign)

Additionally, Allergan has created detachable stickers on the VISTABEL vial label, which include the lot number and expiry date of the product you have received. These stickers can be peeled off and placed in your patient’s clinical file for traceability purposes. Note that once you remove the sticker off the VISTABEL vial label, the word “USED” will show, which is to provide you with further assurance that you are using an authentic VISTABEL product manufactured by Allergan.