Package leaflet: Information for the user

BOTOX®, 100 Allergan Units, Powder for Solution for Injection

Botulinum toxin type A

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See Section 6 for how to report side effects.

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 only. 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 BOTOX® is and what it is used for

BOTOX® is a muscle relaxant used to treat a number of conditions within the body. It contains the active substance Botulinum toxin type A and is injected into either the muscles, the bladder wall or deep into the skin. It works by partially blocking the nerve impulses to any muscles that have been injected and reduces excessive contractions of these muscles. In the case of chronic migraine, it is thought that BOTOX® block pain signals which indirectly block the development of a migraine

When injected into the skin, Botox® works on sweat glands to reduce the amount of sweat produced.

When injected into the bladder wall, Botox® works on the bladder muscle to prevent leakage of urine (urinary incontinence) due to uncontrolled contractions of the bladder muscle.

1. BOTOX® can be injected directly into the muscles, and can be used to treat the following conditions:
   - **persistent muscle spasms** in the **ankle and foot** in **children** aged two years or older with cerebral palsy, who can walk, BOTOX is used to support rehabilitation therapy .
   - **Persistent muscle spasms** in the **wrist, hand, ankle or foot** of **adult** patients who have suffered a stroke
   - **Persistent muscle spasms** in the **eyelid** and **face** of **adult** patients;
   - **Persistent muscle spasms** in the **neck** and **shoulders** of **adult** patients

2. BOTOX® is used to **prevent** headaches in **adult** patients with **chronic migraine.**

Chronic migraine is a disease affecting the nervous system. To be diagnosed with chronic migraine, you must have headaches 15 days or more a month. In addition, on 8 or more days a month, your headaches must have at least two of the following characteristics:

- affect only one side of the head
- cause a pulsating pain
- cause moderate to severe pain
- are aggravated by routine physical activity

and they must cause at least one of the following:

- nausea, vomiting, or both
- sensitivity to light and sound.

BOTOX® has been shown to significantly reduce the frequency of days with headache and to improve the quality of life of patients suffering from chronic migraine. After two treatment sessions, approximately 47% of patients had a 50% or greater reduction from baseline in the number of days with headache they experienced.

3) When injected into the bladder wall, BOTOX® works on the bladder muscle to reduce leakage of urine (urinary incontinence) and control the following conditions in adults:
   - **overactive bladder with leakage of urine**, the sudden urge to empty your bladder and needing to go to the toilet more than usual;
   - **leakage of urine** due to bladder problems associated with spinal cord injury or multiple sclerosis.

   In patients who have not managed to control overactive bladder with leakage of urine with medicines called anticholinergics, BOTOX® has been shown to reduce leakage of urine from an average of about 5 episodes per day down to 2 after 12 weeks. 27% of patients had no leakage of urine at all.
   In patients with bladder problems associated with spinal cord injury or multiple sclerosis who have not managed to control leakage of urine with medicines called anticholinergics, BOTOX® has been shown to reduce leakage of urine, from an average of about 30 episodes per week down to 10 after 6 weeks. 37% of patients had no leakage of urine at all.

4) In adults, BOTOX® can be injected deep into the skin and can work on sweat glands to reduce **excessive sweating** of the **armpits**, which affects the activities of daily living when other local treatments do not help.

5) BOTOX® 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 BOTOX®

Do not use BOTOX®

- 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 have an **infection** at the proposed **site of injection**;
- when you are being treated for leakage of urine and have either a urinary tract infection or a

sudden inability to empty your bladder (and are not regularly using a catheter), or if you have bladder stones;
- if you are being treated for leakage of urine and are not willing to begin using a catheter if required.

Warnings and precautions

Talk to your doctor or pharmacist before using BOTOX®:

- if you have ever had problems with **swallowing** or **food** or **liquid accidentally going into your lungs,** especially if you will be treated for persistent muscle spasms (contractions) in the neck and shoulders;
- if you are **over 65 years of age** and have other serious illnesses;
- if you suffer from any other **muscle problems** or chronic diseases affecting your muscles (such as myasthenia gravis or Eaton Lambert Syndrome);
- if you suffer from certain **diseases** affecting your **nervous system** (such as amyotrophic lateral sclerosis or motor neuropathy);
- if you have significant **weakness** or **wasting of the muscles** which your doctor plans to inject;
- if you have had any **surgery** that may have in some way changed the muscle to be injected;
- if you have had any **problems with injections** (such as fainting) in the past;
- if you have **inflammation in the muscles** or **skin** area where your doctor plans to inject;
- if you have had problems in the past with previous botulinum toxin injections;
- if you suffer from cardiovascular disease (disease of the heart or blood vessels);
- if you suffer or have suffered from seizures;
- if you have an eye disease called closed-angle **glaucoma** (high pressure in the eye) or were told you are at risk for developing this type of glaucoma;
- if you will have an operation soon;
- if you are taking any blood thinning medicine.

***After you have been given* BOTOX®**

You or your caregiver should contact your doctor and seek medical attention immediately if you experience any of the following:
- difficulty in **breathing, swallowing, or speaking;**
- **hives**, **swelling** including swelling of the face or throat, **wheezing**, feeling **faint** and shortness of **breath** (possible symptoms of severe allergic reaction).

If you have been treated for vertical and/or fan-shaped and/or forehead lines, please inform your doctor if you see no significant improvement of your lines one month after your first course of treatment.

General precautions

As with any injection, it is possible for the procedure to result in infection, pain, swelling, burning and stinging, increased sensitivity, tenderness, redness, and/or bleeding/bruising at the site of injection.

Side effects possibly related to the spread of toxin distant from the site of administration have been reported with botulinum toxin (e.g. muscle weakness, difficulty swallowing or unwanted food or liquid in the airways). This is a particular risk for patients with an underlying illness that makes them susceptible to these symptoms.

If you are given BOTOX® too often or the dose is too high, you may experience muscle weakness and side effect related to the spread of toxin, or your body may start producing some antibodies, which can reduce the effect of BOTOX®. To limit this risk, the interval between two treatments must not be less than three months depending on the indication.

When BOTOX® is used in the treatment of a condition that it is not listed in this leaflet, it could result in serious reactions, particularly in patients who already experience difficulty in swallowing or have significant debility.

If you have not done much exercise for a long time before receiving BOTOX® treatment, then after your injections you should start any activity gradually.

It is unlikely that this medicine will improve the range of motion of joints where the surrounding muscle has lost its ability to stretch.

When treating adults with post-stroke ankle muscle spasms, BOTOX® should only be used if it is expected to result in improvement in function (e.g. walking) or symptoms (e.g. spasms or pain) or to help with patient care. Furthermore, for patients who may be more likely to fall, your doctor will judge if this treatment is suitable.

When BOTOX® is used in the treatment of persistent muscle spasms in the eyelid, it could make your eyes blink less often, which may harm the surface of your eyes. In order to prevent this, you may need treatment with eye drops, ointments, soft contact lenses or even protective covering which closes the eye. Your doctor will tell you if this is required.

BOTOX® does not prevent headaches in patients with **episodic migraine**, which occur less than 15 days a month.

When BOTOX® is used for the treatment of vertical and/or fan-shaped and/or forehead lines drooping of the eyelid may occur after treatment.

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Other medicines with BOTOX®

Tell your doctor or pharmacist if:

- you are using any **antibiotics** (used to treat infections) , or any medicines that affect the nerves that control muscles (for example **anticholinesterase** medicines or **muscle relaxants)**. Some of these medicines may increase the effect of BOTOX®.
- you have recently been injected with a **medicine containing a botulinum toxin** (the active substance of BOTOX®), as this may increase the effect of BOTOX® too much.
- you are using any anti-platelet (aspirin-like products) and/or anti-coagulants (blood thinners).

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

Pregnancy and breast-feeding

The use of BOTOX® is not recommended during pregnancy and in women of childbearing potential not using contraception. BOTOX® is not recommended in breast-feeding women.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Driving and using machines

BOTOX® may cause dizziness, sleepiness, tiredness or problems with your vision. If you experience any of these effects, do not drive or use any machines. If you are not sure, ask your doctor for advice.

BOTOX contains Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. essentially "sodium free"

3. How to use BOTOX®

BOTOX® must only be injected by doctors with specific skills and experience on how to use the medicine.

Method and route of administration

BOTOX® is injected into your muscles (intramuscularly), into the bladder wall via a specific instrument (cystoscope) to inject into the bladder or into the skin (intradermally). It is injected directly into the affected area of your body; your doctor will usually **inject BOTOX® into several sites within each affected area**.

General information about dosage

- The number of injections per muscle and the dose vary depending on the indications. Therefore, your doctor will decide how much, how often, and in which muscle(s) BOTOX® will be given to you. It is recommended that your doctor uses the lowest effective dose.

- Dosages for older people are the same as for other adults.

The dosage of BOTOX® and the duration of its effect will vary depending on the condition for which you are treated. Below are details corresponding to each condition.

The safety and effectiveness of BOTOX® has been established in children/adolescents over the age of two years for the treatment of persistent muscle spasms in the ankle and foot, associated with cerebral palsy.

Limited information is available on the use of BOTOX in the following conditions in children/adolescents over the age of 12 years. No recommendation on dosage can be made for these indications.

Persistent muscle spasms in the eyelid and face	12 years
Persistent muscle spasms in the neck and shoulder	12 years
Excessive sweating of the armpits	12 years (limited experience in adolescents between 12 and 17 years, speak to your doctor for further information)

In addition, there is limited experience of using BOTOX in the treatment of vertical and/or fan-shaped and/or forehead lines in patients older than 65 years.

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

Dosage

The dosage of BOTOX and the duration of its effect will vary depending on the condition for which you are treated. Below are details corresponding to each condition.

Indication	**Maximum dose (Units per affected area)**		**Minimal time between treatments**
	First treatment	**Following treatments**	
Persistent muscle spasms in the ankle and foot in children who have cerebral palsy	Ankle & foot: 4 to 8 Units/kg or 300 Units, whichever is lower	When treating the ankle & foot of both legs the maximum dose is not to exceed the lower of 10 Units/kg or 340 Units	12 weeks*
Persistent muscle spasms in the wrist and hand of adult patients who have had a stroke	The exact dosage and number of injection sites per hand/wrist is tailored to individual needs up to a maximum of 240 Units	The exact dosage and number of injection sites is tailored to individual needs up to a maximum of 240 Units	12 weeks
Persistent muscle spasms in the ankle and foot of adult patients who have had a stroke	Multiple injections in the affected muscles. The total dose is 300 Units to 400 Units divided among up to 6 muscles	The total dose is 300 Units to 400 Units divided among up to 6 muscles for each treatment session	12 weeks
Persistent muscle spasms of the eyelid and face	Up to 25 Units per eye	Up to 100 Units	3 months
Persistent muscle spasms of the neck and shoulders	Up to 200 Units	Up to 300 Units	10 weeks
Headache in adults who have chronic migraine	155 to 195 Units	155 to 195 Units	12 weeks
Overactive bladder with leakage of urine	100 Units	100 Units	3 months
Leakage of urine due to bladder problems associated with spinal cord injury or multiple sclerosis	200 Units	200 Units	3 months The effects of more than two treatment sessions have not been evaluated.
Excessive sweating of the armpits	50 Units per armpit	50 Units per armpit	16 weeks
Vertical lines between the eyebrows seen at maximum frown (glabellar lines)	20 Units**	Up to 50 Units	3 months The effects of more than four treatment sessions have not been

			evaluated.
Fan-shaped lines from the corner of the eyes seen at maximum smile (crow's feet lines)	24 Units**)	24 Units	3 months
Forehead lines seen at maximum raised eyebrows	20 Units***		3 months

** The doctor may select a dose that would mean the treatment may be up to 6 months apart.*
*** 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*

Information for patients treated for leakage of urine

Your doctor will give you antibiotics around the time of the injection to help prevent urinary tract infection. The injection will be administered by a procedure called cystoscopy. An instrument with a light source at the end will be introduced into your bladder through the opening by which you let out the urine (called urethra). This enables the doctor to see the inside of the bladder and place the injections into the bladder wall. Please ask your doctor to explain further details of the procedure to you.

If you were not using a catheter (a soft, hollow tube that is inserted into your urethra to help empty urine from the bladder) before treatment with BOTOX®, you should be seen by your doctor approximately 2 weeks after the injection. You will be asked to pass urine and will then have the volume of urine left in your bladder measured. If your doctor assesses you have too much urine left in your bladder you will be instructed to use a catheter to empty your bladder. Your doctor will decide if and when you need to return for the same test.

For overactive bladder with leakage of urine

You may be given a local anaesthetic before the injections (your bladder would be filled with anaesthetic solution for a while and then drained). You may also be given a sedative.

You will be observed for at least 30 minutes after the injection before you can leave to see if you can pass urine spontaneously.

You must contact your doctor if at any time you are unable to pass urine because it is possible that you may need to start using a catheter. In clinical trials, approximately 6 out of 100 patients not using a catheter before treatment may need to use a catheter after treatment.

For leakage of urine due to bladder problems associated with spinal cord injury or multiple sclerosis
You may be given a local or general anaesthetic before the procedure.
You will be observed for at least 30 minutes after the injection before you can leave. At the time of the injection, due to the procedure by which the injection is delivered into your bladder, you may experience possible uncontrolled reflex reaction of your body (e.g. profuse sweating, throbbing headache or increase in pulse rate).

You must contact your doctor if at any time you are unable to pass urine because it is possible that you may need to start using a catheter. In clinical trials, approximately one fifth of patients reported an inability to completely empty their bladder after BOTOX® treatment. At least one third of patients not using a catheter before treatment may need to use a catheter after treatment.

Time to Improvement and Duration of Effect

For **persistent muscle spasms in the ankle and foot in children two years and older**, the improvement usually appears within the first 2 weeks after the injection.

For **persistent muscle spasms in the wrist and hand of adult patients who have had a stroke,** you will usually see an improvement within the first 2 weeks after the injection. The maximum effect is usually seen about 4 to 6 weeks after treatment.

For **persistent muscle spasms of the eyelid and face**, you will usually see an improvement within 3 days after the injection and maximum effect is usually seen after 1 to 2 weeks.

For **persistent muscle spasms of the neck and shoulders,** you will usually see an improvement within 2 weeks after the injection. The maximum effect is usually seen about 6 weeks after treatment.

For **leakage of urine due to overactive bladder,** you will usually see an improvement within 2 weeks after the injection. Typically patients find the effect lasts approximately 6-7 months after the injection.

For **leakage of urine due to bladder problems associated with spinal cord injury or multiple sclerosis,** you will usually see an improvement within 2 weeks after the injection. Typically patients find the effect lasts approximately 9-10 months after the injection.

For **excessive sweating of the armpits**, you will usually see an improvement within the first week after injection. On average the effect usually lasts 4-7 months after the first injection.

For **vertical lines between the eyebrows seen at maximum frown**, you will usually see an improvement within 1 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.

For **fan-shaped lines from the corner of the eyes seen at maximum smile**, you will usually see an improvement within 1 week after treatment. The treatment effect has been demonstrated for an average of 4months after injection.

For **forehead lines seen at maximum eyebrow elevation** you will usually see an improvement within 1 week after treatment. The treatment effect has been demonstrated for an average of 4 months after injection.

If you have received more BOTOX® than you should

The signs of too much BOTOX® may not appear for several days after the injection. Should you swallow BOTOX® or have it accidentally injected, you should see your doctor who might keep you under observation for several weeks.
If you have received too much BOTOX®, you may have any of the following symptoms and you must contact your doctor immediately. He/she will decide if you have to go to hospital:

- muscle weakness which could be local or distant from the site of injection;
- difficulty in breathing, swallowing or speaking due to muscle paralysis;

- food or liquid accidentally going into your lungs which might cause pneumonia (infection of the lungs) due to muscle paralysis;
- drooping of the eyelids, double vision;
- generalised weakness.

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

4. Possible side effects

If you have any difficulty in breathing, swallowing or speaking after receiving BOTOX®, contact your doctor immediately.

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

Like all medicines, this medicine can cause side effects, although not everybody gets them. In general, side effects occur within the first few days following injection.
They usually last only for a short time, but they may last for several months and in rare cases, longer.

As expected for any injection procedure, pain/burning/stinging, swelling and/or bruising may be associated with the injection.

The side effects are classified into the following categories, depending on how often they occur:

Very common	may affect more than 1 in 10 people
Common	may affect up to 1 in 10 people
Uncommon	may affect up to 1 in 100 people
Rare	may affect up to 1 in 1,000 people
Very rare	may affect up to 1 in 10,000 people

Below are lists of side effects which vary depending on the part of the body where BOTOX® is injected. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Injections for children with persistent muscle spasms in the ankle and foot

Common	• Stretching or tearing of ligaments, shallow wound to the skin • Problems with walking, pain where the injection was given • Rash.
Uncommon	• Muscle weakness

There have been rare spontaneous reports of death sometimes associated with aspiration pneumonia in children with severe cerebral palsy after treatment with BOTOX®.

Injections in the wrist and hand of adult patients who have had a stroke

Common	• Muscle weakness , increased muscle tension • Bruising and bleeding under the skin causing red patches (ecchymosis or purpura) • Pain in the hand and fingers • Bleeding, burning, pain where the injection was given, • Fever, flu manifestations
Uncommon	• Depression, difficulty in sleeping (insomnia) • Lack of coordination of movements, loss of memory, decreased skin sensation, headache, numbness • Feeling of dizziness or "spinning" (vertigo) • A fall in blood pressure on standing up which causes dizziness, light headedness or fainting • Feeling sick, numbness around the mouth, • Inflammation of the skin (dermatitis), itching, rash, increased sensitivity where the injection was given • Joint pain or inflammation • General weakness, , feeling generally unwell • Pain, swelling of the extremities such as the hands and feet.

Some of these uncommon side effects may also be related to your disease.

Injections in the ankle and foot of adult patients who have had a stroke

Common	• Rash • Joint pain or inflammation, stiff or sore muscles, muscular weakness • Swelling of the extremities such as the hands and feet • Fall

Injections in the eyelid and face for muscle spasms

Very Common	• Drooping of the eyelid.
Common	• Pinpoint damage of the cornea (transparent surface covering the front of the eye), difficulty in completely closing the eye, dry eyes, sensitivity to light, eye irritation, overflow of tears • Bruising under the skin • Irritation, • Swelling of the face.
Uncommon	• Dizziness, weakness of the face muscles, drooping of the muscles on one side of the face • Visual disturbance, inflammation of the cornea (transparent surface covering the front of the eye), abnormal turning of the eyelids outwards or inwards, double vision, blurred vision, • Rash • Tiredness.
Rare	• Swelling of the eyelid.
Very Rare	• Damage to the cornea (transparent surface covering the front of the eye) including ulcer and perforation

Injections in the neck and shoulder

Very Common	• Difficulty in swallowing • Muscle weakness • Pain.
Common	• Swelling and irritation inside the nose (rhinitis), signs of infection of the nose or throat (blocked or runny nose, cough, sore throat) • Dizziness, sleepiness, headache • Muscle cramps, stiff or sore mucles, increased muscle tension • Decreased skin sensation • Feeling of weakness or generally unwell, flu manifestations. • Feeling sick, dry mouth
Uncommon	• Double vision, drooping of the eyelid • Fever, • Shortness of breath, changes in voice.

Injections in the head and neck to prevent headache in patients who suffer from chronic migraine

Common	• Increase in headache, migraine and worsening of migraine • Weakness of the face muscles • Drooping of the eyelid • Rash, itching • Neck pain, muscle pain or cramp, muscle stiffness or tightness, muscle weakness • Pain where the injection was given.
Uncommon	• Difficulty in swallowing • Swollen eyelid • Skin pain • Jaw pain.

Injections in the bladder wall for overactive bladder with leakage of urine

Very Common	• Urinary tract infection, painful urination after the injection*.
Common	• Bacteria or white blood cells in the urine • Inability to empty your bladder (urinary retention), incomplete emptying of the bladder, frequent daytime urination

** This side effect may also be related to the injection procedure.*

Injections in the bladder wall for leakage of urine due to bladder problems associated with spinal cord injury or multiple sclerosis

Very Common	• Urinary tract infection (in about half the patients) • Inability to empty your bladder (urinary retention; see section 3).
Common	• Muscle spasm, • Bulge in the bladder wall (bladder diverticulum) The following side effects have only be reported in multiple sclerosis: • Difficulty in sleeping (insomnia) • Tiredness, problems with walking (gait disturbance) • Consitpation • Muscle weakness, fall The following side effects are related to the injection procedure: • Blood in the urine after the injection • Uncontrolled reflex reaction of your body (e.g. profuse sweating, throbbing headache or increase in pulse rate) around the time of the injection (autonomic dysreflexia; see section 3)

Injections for excessive sweating of the armpits

Very Common	• Pain where the injection was given
Common	• Headache, numbness • Hot flushes • Increased sweating at sites other than the armpit, abnormal skin odour, itching, lump under the skin • Hair loss • Pain in the extremities such as the hands and fingers • Pain, reaction where the injection was given such as swelling, bleeding, burning or increased sensitivity
Uncommon	• Muscle weakness, muscle pain, , problem with the joints. • Feeling weak • Feeling sick

Injections in the forehead lines and/or vertical lines and/or fan-shaped lines from the corner of the eyes

Possible Side Effects	**Injection in the forehead for vertical lines**	**Injections in the fan-shaped lines from the corner of the eyes, when treated with or without vertical lines between the eyebrows seen at frown**	**Injections 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**
• Headache	Common	n/a	Common

• Drooping of the eyelid	Common	n/a	Common[1]
• Localised muscle weakness	Common	n/a	n/a
• Face pain	Common	n/a	n/a
• Skin redness	Common	n/a	n/a
• Injection site haematoma*	n/a	Common	Common
• Injection site bruising*	n/a	n/a	Common
• Skin tightness	Uncommon	n/a	Common
• Infection	Uncommon	n/a	n/a
• Anxiety	Uncommon	n/a	n/a
• Numbness, dizziness	Uncommon	n/a	n/a
• Inflammation of the eyelid, eye pain, visual disturbance	Uncommon	n/a	n/a
• Swelling (face, around the eyes), skin sensitivity to light, dry skin, itching	Uncommon	n/a	n/a
• Eyelid swelling	Uncommon	Uncommon	n/a
• Feeling sick, dry mouth	Uncommon	n/a	n/a
• Muscle twitching	Uncommon	n/a	n/a
• Fever, flu manifestations, feeling weak	Uncommon	n/a	n/a
• Injection site bleeding*	n/a	Uncommon	n/a
• Injection site pain*	n/a	Uncommon	Uncommon
• Injection site tingling or numbness	n/a	Uncommon	n/a
• Drooping eyebrow[2]	n/a	n/a	Common

n/a – not reported as possible side effect

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

[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

General information about other side effects

The following list describes **additional side effects** reported for BOTOX®, in any disease, since it has been marketed:

Affecting the immune system

- sudden allergic reactions, which can be serious (swelling of the face or throat, difficulty in breathing, feeling faint)
- delayed reaction which may include fever, skin reaction, joint pain (serum sickness)
- hives

Affecting metabolism
- loss of appetite

Affecting the nervous system

- nerve damage (brachial plexopathy)
- slurred speech, speech problems
- weakness or drooping of the muscles on one side of the face
- decreased skin sensation
- muscle weakness
- chronic disease affecting the muscles (myasthenia gravis)
- difficulty moving the arm and shoulder
- numbness; tingling and pain in hands and feet
- pain/numbness/or weakness starting from the spine
- seizures and fainting

Affecting the eyes
- increase in eye pressure
- drooping eyelid
- difficulty in completely closing the eye
- strabismus (squint);
- blurred vision;
- visual disturbance
- dry eye
- swelling of the eyelid

Affecting the ears
- decreased hearing;
- noises in the ear;
- feeling of dizziness or “spinning” (vertigo)

Affecting the cardiovascular system
- heart problems including heart attack

Affecting the respiratory system
- aspiration pneumonia (lung inflammation caused by accidentally breathing in food, drink, saliva or vomit)
- breathing problems, respiratory depression and/or respiratory failure

Affecting the gastrointestinal system
- abdominal pain;
- diarrhoea, constipation;
- dry mouth;

- difficulty swallowing;
- feeling sick, vomiting

Affecting the skin
- hair loss; loss of eyebrows
- drooping eyebrow
- itching;
- different types of red blotchy skin rashes;
- excessive sweating;
- rash

Affecting the muscles
- muscles pain, loss of nerve supply to/shrinkage of injected muscle
- localised muscle twitching/involuntary muscle contractions

Affecting the body
- feeling generally unwell;
- fever

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store BOTOX®

Keep out of the sight and reach of children.

Your doctor should not use BOTOX® after the expiry date which is stated on the label after 'EXP'. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C – 8°C), or store in a freezer (at or below -5°C).
After the solution is made up, immediate use of the solution 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 BOTOX® contains

• The active substance is: Botulinum toxin type A from Clostridium botulinum. Each vial contains 100 Allergan Units of Botulinum toxin type A.
• The other ingredients are human albumin and sodium chloride.

What BOTOX® looks like and contents of the pack

BOTOX® is presented as a thin white powder 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 sodium chloride 9 mg/ml (0.9%) solution for injection.

Each pack contains 1, 2, 3 or 6 vials.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Allergan Pharmaceuticals Ireland
Castlebar Road
Westport
County Mayo
Ireland

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To report any side effect(s):

Saudi Arabia:

The National Pharmacovigilance Centre (NPC):

- SFDA Call Center: 19999
- E-mail: npc.drug@sfda.gov.sa
- Website: https://ade.sfda.gov.sa/

- Other GCC States:
  - Please contact the relevant competent authority.

Council of Arab Health Ministers

THIS IS A MEDICAMENT
▪ Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you. ▪ Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament. ▪ The doctor and the pharmacist are experts in medicines, their benefits and risks. ▪ Do not by yourself interrupt the period of treatment prescribed for you. ▪ Do not repeat the same prescription without consulting your doctor. ▪ Keep all medicaments out of reach of children.
Council of Arab Health Ministers Union of Arab Pharmacists

This patient information leaflet is approved by the Saudi Food and Drugs Authority

ALLERGAN®
Westport, Co. Mayo, Ireland
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The following information is intended for medical or healthcare professionals only:

Please refer to the Summary of Product Characteristics for complete prescribing information for BOTOX®.

For all indications:

Side effects related to spread of toxin distant from the site of administration have been reported, sometimes resulting in death, which in some cases was associated with dysphagia, pneumonia and/or significant debility. The symptoms are consistent with the mechanism of action of botulinum toxin and have been reported hours to weeks after injection. The risk of symptoms is probably greatest in patients who have underlying conditions and comorbidities that would predispose them to these symptoms, including children and adults treated for spasticity, and are treated with high doses. Patients treated with therapeutic doses may also experience exaggerated muscle weakness.

Pneumothorax associated with injection procedure has been reported following administration of BOTOX® near the thorax. Caution is warranted when injecting in proximity to the lung, particularly the apices or other vulnerable anatomic structures.

Serious adverse events including fatal outcomes have been reported in patients who had received off-label injections of BOTOX® directly into salivary glands, the oro-lingual-pharyngeal region, oesophagus and stomach. Some patients had pre-existing dysphagia or significant debility.

There have been rare spontaneous reports of death sometimes associated with aspiration pneumonia in children with severe cerebral palsy after treatment with botulinum toxin, including following off-label use (e.g. neck area). Extreme caution should be exercised when treating paediatric patients who have significant neurologic debility, dysphagia, or have a recent history of aspiration pneumonia or lung disease.

Treatment in patients with poor underlying health status should be administered only if the potential benefit to the individual patient is considered to outweigh the risks.

Refer to the Summary of Product Characteristics for complete information for BOTOX®.

Reconstitution of the medicinal product:

It is good practice to perform vial reconstitution and syringe preparation over plastic-lined paper towels to catch any spillage.

Reconstitute BOTOX® only with sterile unpreserved normal saline (0.9% sodium chloride for injection). Draw up an appropriate amount of diluent (see dilution table or instructions below) into a syringe.

Dilution table for BOTOX® 100 Allergan Units vial size for all indications except bladder disorders:

	100 Unit vial
Resulting dose (Units per 0.1 ml)	**Amount of diluent (sterile unpreserved normal saline (0.9% sodium chloride for injection)) added in a 100 Unit vial**
20 Units	**0.5 ml**
10 Units	**1 ml**
5 Units	**2 ml**
4 Units	**2.5 ml**
2.5 Units	**4 ml**
1.25 Units	**8 ml**

Since BOTOX is denatured by bubbling or similar vigorous agitation, inject the diluent gently into the vial. Discard the vial if a vacuum does not pull the diluent into the vial. Reconstituted BOTOX is a clear colourless to slightly yellow solution free of particulate matter. The reconstituted solution should be visually inspected for clarity and absence of particles prior to use. When reconstituted in the vial, BOTOX® may be stored in a refrigerator (2◦C - 8◦C) for up to 24 hours prior to use.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2◦C - 8◦C.

Dilution instructions for treatment of urinary incontinence due to overactive bladder:

Reconstitute a 100 Unit vial of BOTOX® with 10 ml of sterile unpreserved normal saline (0.9% sodium chloride for injection) and mix the vial gently. Draw 10 ml from the vial into a 10 ml syringe. This will result in a 10 ml syringe containing a total of 100 Units of reconstituted BOTOX®. Use immediately after reconstitution in the syringe. Dispose of any unused saline.

This product is for single use only and any unused reconstituted product should be disposed of.

Dilution instructions for treatment of urinary incontinence due to neurogenic detrusor overactivity:

Reconstitute **two 100 Unit vials** of BOTOX® , each with 6 ml of sterile sterile unpreserved normal saline (0.9% sodium chloride for injection) and mix the vials gently. Draw 4 ml from each vial into each of two 10 ml syringes. Draw the remaining 2 ml from each vial into a third 10ml syringe. Complete the reconstitution by adding 6 ml of sterile unpreserved normal saline (0.9% sodium chloride for injection) into each of the 10 ml syringes, and mix gently. This will result in three 10 ml syringes containing a total of 200 Units of reconstituted BOTOX®. Use immediately after reconstitution in the syringe. Dispose of any unused saline.

This product is for single use only and any unused reconstituted product should be disposed of.

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

For safe disposal, unused vials should be reconstituted with a small amount of water and then autoclaved. Any used vials, syringes, and spillages etc. should be autoclaved, or the residual BOTOX® inactivated using dilute hypochlorite solution (0.5%) for 5 minutes.

Identification of the product

In order to verify receipt of actual BOTOX® product from Allergan, look for a tamper-evident seal that contains a translucent silver Allergan logo on the top and bottom flaps of the BOTOX cartons and 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 BOTOX 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 BOTOX vial label, the word "USED" will show, which is to provide you with further assurance that you are using an authentic BOTOX product manufactured by Allergan.

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