

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

BOTOX® 50 / BOTOX® 100 / BOTOX® 200

Powder for solution for injection

Name and quantity of active ingredient:

botulinum toxin type A

Each vial of **BOTOX 50** contains:

50 Allergan units of botulinum toxin type A

Each vial of **BOTOX 100** contains:

100 Allergan units of botulinum toxin type A

Each vial of **BOTOX 200** contains:

200 Allergan units of botulinum toxin type A

Inactive ingredients and allergens: Please see section 6 'Additional information' and section 2 under 'Important information about some of this medicine's ingredients'.

Read the entire leaflet carefully before you start using this medicine.

This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

Nervous system disorders

- BOTOX is indicated for the treatment of **children** aged two years or older with cerebral palsy who can walk and who have a **foot deformity**, caused by persistent muscle spasms in the legs.
- **Adults and children aged 12 years or older**
 - persistent muscle spasms in the eyelid and half of the face.
 - crossed eyes.
- **Adults**
 - persistent muscle spasms in the wrist and hand.
 - persistent muscle spasms in the lower limb including ankle and foot.
 - persistent muscle spasms in the neck and in the shoulders (torticollis).
 - reducing the symptoms of chronic migraine in adults who have headaches on 15 or more days each month of which at least 8 days are with migraine, and who have not responded well to other preventative migraine medications.

Bladder disorders

BOTOX is indicated for treatment of the following conditions in **adults**:

- overactive bladder with leakage of urine, sudden urge to empty your bladder, and needing to go to the toilet more than usual when another medicine (called an anticholinergic) has not helped.
- leakage of urine due to bladder problems associated with spinal cord injury or multiple sclerosis.

Skin disorders

BOTOX is indicated for:

- reducing excessive sweating in the armpits in adults, when other treatments do not help.
- temporary improvement in the appearance of:
 - vertical lines between the eyebrows seen at maximum frown (glabellar lines)
 - and/or
 - fan-shaped lines from the corner of the eyes seen at maximum smile
 - and/or
 - forehead lines seen at maximum raised eyebrowswhen the severity of these facial lines has an important psychological impact in adults.

Therapeutic group: muscle relaxant.

BOTOX is a muscle relaxant used to treat a number of conditions within the body. The medicine contains the active ingredient 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 were injected and reducing excessive contractions of these muscles.

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 reduce leakage of urine (urinary incontinence).

In the case of chronic migraine (a condition affecting the nervous system in which patients usually have a headache often together with oversensitivity to light, noise or odors, as well as nausea and/or vomiting. These headaches occur on **15 days or more** each month, it is thought that BOTOX can block pain signals which indirectly blocks the development of a migraine. However, the way BOTOX works in chronic migraine is not fully established.

2. Before using this medicine

Do not use this medicine if:

- You are **sensitive** (allergic) to botulinum toxin type A or any of the other ingredients of this medicine (please see section 6 'Additional information').
- You have an **infection at the proposed injection site**.
- 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).
- You are being treated for leakage of urine and do not intend to begin using a catheter if required.
- Do not use this medicine for temporary improvement in appearance of facial lines if you are diagnosed with myasthenia gravis or Lambert-Eaton syndrome (chronic diseases affecting the muscles).

Special warnings about using this medicine

Talk to your doctor or pharmacist before BOTOX treatment if:

- **You have ever had problems with swallowing or with food or liquid accidentally going into your lungs, especially if you will be treated with BOTOX in the neck or shoulder area.**
- You are **over 65 years of age** and have other **serious illnesses**.
- You suffer from any **muscle problems** or chronic diseases affecting your muscles (such as myasthenia gravis or Lambert-Eaton syndrome).
- You suffer from certain **diseases** affecting your **nervous system** (such as ALS or motor neuropathy).
- You have significant **weakness** or **wasting of the muscles** to be injected.
- You have had any **surgery** or **injury** that may have changed the muscle to be injected in some way.
- You have had any **problems with injections in the past** (such as fainting).
- You have **inflammation in the muscles** or **skin** area to be injected.
- You suffer from cardiovascular disease (disease of the heart or blood vessels).
- You suffer of have suffered from seizures.
- You have closed-angle **glaucoma** (high pressure in the eye) or were told you are at risk for developing this type of glaucoma.
- You are about to have surgery in the near future.
- You are about to be treated for an overactive bladder with leakage of urine and you are a male with signs and symptoms of urinary obstruction, such as difficulty in passing urine or a weak or interrupted stream.
- You had problems with previous botulinum toxin injections and are about to receive treatment for lines.
- You see no significant improvement in the appearance of your lines one month after your first course of treatment.
- You are about to receive this medicine to treat lines, and have had surgery or an injury in your head, neck, or chest.

After you have been given this medicine, contact your doctor immediately for medical attention in the following cases:

- **difficulty in breathing, swallowing, or speaking.**
- **allergic skin reaction (hives), swelling** including swelling of the face or throat, **wheezing**, feeling **faint** and shortness of **breath** (possible symptoms of severe allergic reaction).

General warnings

As with any injection, it is possible that the injection will cause infection, pain, swelling, abnormal skin sensations (like tingling or numbness), decreased skin sensation, tenderness, redness, bleeding/bruising at the site of injection and a drop in blood pressure or fainting. This may be the consequence of pain and/or anxiety associated with injection.

Side effects possibly related to the spread of toxin from the injection site have been reported with botulinum toxin (such as muscle weakness, difficulty swallowing, or unwanted food or liquid in the airways). These side effects can be mild to severe, may require treatment and in some cases may be fatal. This is a particular risk for patients with an underlying illness that makes them susceptible to these symptoms. Patients receiving recommended doses to temporarily improve the appearance of face lines may experience exaggerated muscle weakness.

Severe and/or immediate allergic reactions have been reported. The symptoms may include hives, swelling of the face or throat, shortness of breath, wheezing and fainting. Delayed allergic reactions (serum sickness) have also been reported, which may include symptoms such as fever, joint pain, and skin rash.

Side effects related to the cardiovascular system, including irregular heartbeat and heart attacks, have also been seen in patients treated with BOTOX, sometimes with a fatal outcome. However, some of these patients had a prior history of cardiac risk factors.

Seizures have been reported in adults and children treated with BOTOX, mostly in patients who are more prone to seizures. It is not known if BOTOX is the cause of these seizures. Seizures that were reported in children were mostly in cerebral palsy patients treated for persistent muscle spasms in the legs.

If you are given BOTOX too often or the dose is too high, you may experience muscle weakness and side effects related to the spread of toxin, or your body may start producing certain antibodies, which can reduce the effect of BOTOX.

When BOTOX is used to treat 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.

Patients who have not been physically active for a long time before the injection, are advised to start any physical activity gradually after the BOTOX injection.

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

Do not use BOTOX to treat persistent post-stroke ankle muscle spasms in adults if it is not expected to result in improvement in function (such as walking) or symptoms (such as pain) or to help with patient care. If your stroke was more than 2 years ago or if your ankle muscle spasm is less severe, improvement in activities such as walking may be limited. Furthermore, in patients who may be more likely to fall, their doctor will have to decide if this treatment is suitable.

BOTOX should only be used to treat ankle and foot muscle spasms after an evaluation by health care professionals experienced in rehabilitation

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, your doctor may advise treatment with eye drops, ointments, soft contact lenses, or even protective covering which closes the eye. Your doctor will tell you if any of this is required.

When BOTOX is used to control the leakage of urine, your doctor will prescribe antibiotics to be taken before and after the treatment to prevent urinary tract infection. You will be seen by your doctor approximately 2 weeks after the injection, if you were not using a catheter before the injection. You will be asked to pass urine and will then have the volume of urine left in your bladder measured using ultrasound. Your doctor will decide if you need to return during the next 12 weeks to repeat this test. 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 patients with leakage of urine due to bladder problems associated with spinal cord injury or multiple sclerosis, approximately one third who were not using a catheter before treatment may need to use a catheter after treatment. In patients with leakage of urine due to an overactive bladder, approximately 6 out of 100 patients may need to use a catheter after treatment.

Warnings associated with use of BOTOX to temporarily improve the appearance of face lines

- The use of BOTOX is not recommended in patients with a history of dysphagia (difficulty to swallow) and impaired swallowing.
- The use of BOTOX to temporarily improve the appearance of lines is not recommended in individuals under 18 years.
- There is limited experience using BOTOX in patients over 65
- Too frequent or excessive dosing may enhance the risk of antibodies formation. Antibodies 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.
- Rarely, allergic reaction may occur after the injection of botulinum toxin.

- Drooping of the eyelid may occur after treatment.

Children and Adolescence

The safety and effectiveness of BOTOX has been established in children/adolescents over the age of two years for the treatment of foot deformity caused by persistent muscle spasms in the legs, associated with Cerebral Palsy.

Foot deformity caused by muscle spasms in the legs of children who have Cerebral Palsy	2 years
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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
crossed eyes (strabismus)	12 years
Persistent muscle spasms in neck and shoulder	12 years
Excessive sweating of the armpits	12 years (limited experience in adolescents between 12 and 17 years)

Other medicines with BOTOX

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- anti-platelets (aspirin-like products) and/or anti-coagulants (blood thinners)
- **antibiotics** (used to treat infections, for example aminoglycoside antibiotics or spectinomycin), anticholinesterase medicines, or **muscle relaxants**. Some of these medicines may increase the effect of BOTOX.
- **other medicine containing a botulinum toxin** (the active substance of BOTOX) at the same time or recently, as this may increase the effect of BOTOX too much.

Pregnancy and breastfeeding

The use of BOTOX is not recommended during pregnancy and in women of childbearing potential not using contraception, unless there is a need for it. BOTOX is not recommended in breastfeeding women.

If you are pregnant or breastfeeding, 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

Using this medicine 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.

Important information about some of this medicine's ingredients

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

3. How to use this medicine?

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

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

BOTOX will only be prescribed for you for chronic migraine if you have been diagnosed by a neurologist who is a specialist in this area. BOTOX will be administered under the supervision of a neurologist. BOTOX is not intended for use with acute migraine, chronic tension-type headache, or medication-overuse headache.

Method and route of administration

BOTOX is injected either into your muscles, into the bladder wall via a specific instrument (cystoscope) for injecting into the bladder, or into the skin. This medicine 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

Only your doctor will determine your dose and how you should take this medicine. **Do not exceed the recommended dose.**

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.

Dosage

Indication	Maximum dose (Units per affected area)		Minimal time between treatments
	First treatment	Next treatments	
Persistent muscle spasms in the legs of children who have cerebral palsy	4 Units/kg (hemiplegia) 6 Units/kg (diplegia)	4 Units/kg (hemiplegia) 6 Units/kg (diplegia)	3 months*
Persistent muscle spasms in the wrist and hand	The exact dosage and number of injection sites per hand/wrist are tailored to individual needs up to a maximum of 240 Units	The exact dosage and number of injection sites per hand/wrist are tailored to individual needs up to a maximum of 240 Units	12 weeks
Persistent muscle spasms in the ankle and foot	Your doctor may give multiple injections in the affected muscles. The total dose is 300 Units to 400 Units divided among up to 6 muscles in each treatment session	The total dose is 300 Units to 400 Units divided among up to 6 muscles in each treatment session.	12 weeks
Persistent muscle spasms of the eyelids and face	1.25-2.5 Units per injection site. Up to 25 Units per eye for eye spasms	Up to 100 Units for eye spasms	3 months for eye spasms
Crossed eyes	The exact dosage is tailored to individual needs up to a maximum of 25 Units per muscle	The exact dosage is tailored to individual needs up to a maximum of 25 Units per muscle	Not before the effect of the previous dose has disappeared
Persistent muscle spasms of the neck and shoulders	200 Units No more than 50 Units should be injected at any one site	Up to 300 Units	10 weeks
Headache in adults who have chronic migraine	155 to 195 Units No more than 5 units should be injected at any one site	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
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).	4 Units in each one of 5 injection sites (maximum total dose of 20 Units)	4 Units in each one of 5 injection sites (maximum total dose of 20 Units)	3 months
**Fan-shaped lines from the corner of the eyes seen at maximum smile	4 Units in each one of 6 injection sites (maximum total dose of 24 Units)	4 Units in each one of 6 injection sites (maximum total dose of 24 Units)	3 months
**Forehead lines seen at maximum raised eyebrows	4 Units in each one of 5 injection sites (maximum total dose of 20 Units)	4 Units in each one of 5 injection sites (maximum total dose of 20 Units)	3 months

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

***The total dose for treating forehead lines (20 units) in conjunction with glabellar lines (20 units) is 40 units. If you are being treated for fan-shaped lines from the corner of the eyes at the same time as vertical lines between the eyebrows, you will receive a total dose of 44 units. If you are being treated for all 3 types of facial lines at the same time you will require a total dose of 64 units.*

Time to improvement and duration of effect

For **persistent muscle spasms in the legs of children who have cerebral palsy**, the improvement usually appears within the first 2 weeks after the injection.

For **persistent muscle spasms in the wrist and hand**, 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 in the ankle and foot**, when the effect starts to wear off you receive the treatment again if needed, but not more often than every 12 weeks.

For **persistent muscle spasms of the eyelids 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 **crossed eyes**, you will usually see an improvement within a day or two of the injection. The maximum effect is usually seen one week after treatment. The effect usually lasts for about 2 to 6 weeks after the injection.

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. The effect usually 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. The effect usually lasts approximately 8-9 months after the injection.

For **excessive sweating of the armpits**, you will usually see an improvement within the first week after the injection. On average the effect usually lasts 7.5 months after the first injection with approximately 1 out of 4 patients still experiencing the effect after one year.

With **vertical lines between the eyebrows seen at maximum frown** (glabellar lines) you will usually notice improvement within one week of treatment, and the maximum effect will be visible 5 to 6 weeks after injection. The treatment effect was visible for up to 4 months after injection. The efficacy and safety of repeated injections beyond 12 months have not been evaluated.

With **fan-shaped lines from the corner of the eyes seen at maximum smile**, you will usually see improvement within one week of treatment. The treatment effect was visible on average for up to 4 months after injection. The efficacy and safety of repeated injections beyond 12 months have not been evaluated.

With **forehead lines seen at maximum raised eyebrows**, you will usually see improvement within one week of treatment. The treatment effect was visible on average for up to 4 months after injection. The efficacy and safety of repeated injections beyond 12 months have not been evaluated.

If you have accidentally taken a higher dose

The signs of too much BOTOX may not appear for several days after the injection. In case 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. Your doctor 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
- generalized weakness

If you have any further questions about using this medicine, consult your doctor or pharmacist.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

4. Side effects

Like with all medicines, using BOTOX may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Side effects usually occur within the first few days following injection. They usually last only a short time, but they may last for several months or, in rare cases, even longer.

Approximately 1 out of 4 patients may experience side effects following BOTOX injection for the vertical lines between the eyebrows seen at maximum frown. Approximately 8% of patients may experience side effects following BOTOX 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 BOTOX injection for the forehead lines seen at maximum raised eyebrows when treated in conjunction with the treatment of vertical lines between the eyebrows seen at maximum frown. Approximately 14% of patients may experience side effects when treatment of forehead lines in conjunction with vertical lines is combined with treatment for fan-shaped lines from the corner of the eyes seen at maximum smile.

These side effects 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 BOTOX.

Contact your doctor for medical attention immediately in the following cases:

- **if you have difficulty in breathing, swallowing or speaking after receiving a BOTOX injection.**

- if you experience an allergic **skin reaction (hives)**, **swelling** including **swelling of the face or throat**, **wheezing**, feeling **faint**, and **shortness of breath**.

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

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

Side effects are classified by frequency, as follows:

Very common	affect more than one in ten users
Common	affect 1-10 in 100 users
Uncommon	affect 1-10 in 1,000 users
Rare	affect 1-10 in 10,000 users
Very rare	affect less than one in 10,000 users
Frequency not known	Frequency cannot be estimated from the available data

Below are lists of side effects by the part of the body in which BOTOX is injected. **If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor or pharmacist.**

Injections in the legs of children with cerebral palsy

Very common	Viral infection, ear infection.
Common	Sleepiness, problems with walking, numbness, rash, muscle pain, muscle weakness, pain in the extremities such as the hands and fingers, urinary incontinence (leakage of urine), feeling generally unwell, pain where the injection was given, feeling of weakness, fall.

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 patients who have had a stroke

Common	Increased muscle tension, bruising and bleeding under the skin causing red patches (ecchymosis or purpura), pain in the hand and fingers, muscle weakness, pain where the injection was given, fever, flu symptoms, bleeding or burning where the injection was given.
Uncommon	Depression, difficulty in sleeping (insomnia), decreased skin sensation, headache, numbness, lack of coordination of movements, loss of memory, feeling of dizziness or “spinning”

	(vertigo), fall in blood pressure on standing up which causes dizziness, lightheadedness or fainting, nausea, numbness around the mouth, inflammation of the skin (dermatitis), itching, rash, joint pain or inflammation, general weakness, pain, increased sensitivity where the injection was given, feeling generally unwell, swelling of the extremities such as the hands and feet.
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Some of these uncommon side effects may also be related to your disease.

Injections in the ankle and foot of 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.
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Injections in the eyelid and face including crossed eyes

Very common	Drooping of the eyelid, problem with eye motion
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, skin irritation, swelling of the face.
Uncommon	Dizziness, weakness of the face muscles, drooping of the muscles on one side of the face, inflammation of the cornea (transparent surface covering the front of the eye), abnormal turning of the eyelids inwards or outwards, double vision, difficulties in seeing clearly, blurred vision, rash, tiredness, bleeding behind the eyeball, perforation of the white of the eye, dilated pupil.
Rare	Swelling of the eyelid, bleeding in the vitreous fluid of the eye.
Very rare	Ulcer, damage to the cornea (transparent surface covering the front of the eye), high pressure in the eye.

Injections in the neck and shoulder

Very common	Difficulty in swallowing, muscle weakness, pain.
Common	Swelling and irritation inside the nose (rhinitis), blocked or runny nose, cough, sore throat, tickle or irritation in the throat, dizziness, increased muscle tension (cramps), decreased skin sensation, sleepiness, headache, dry mouth, nausea, stiff or sore muscles, feeling of weakness, flu syndrome, feeling generally unwell.
Uncommon	Double vision, fever, drooping of the eyelid, shortness of breath, changes in your voice.

Injections in the head and neck for the treatment of headache in patients who suffer from chronic migraine

Common	Headache, migraine and worsening of migraine, weakness of the face muscles, drooping of the eyelid, rash, itching, neck pain,
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	muscle pain, muscle spasms, muscle stiffness, muscle tightness, muscle weakness, pain where the injection was given.
Uncommon	Difficulty in swallowing, skin pain, jaw pain.
Frequency not known	“Mephisto sign” (raising of the outer eyebrows).

Injections in the bladder wall for leakage of urine due to overactive bladder

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

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

**This side effect is only related to the injection procedure.

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

Very common	Urinary tract infection, inability to empty your bladder (urinary retention).
Common	Difficulty in sleeping (insomnia), constipation, muscle weakness, muscle spasm, blood in the urine after the injection*, painful urination after the injection*, bulge in the bladder wall (bladder diverticulum), tiredness, problems with walking (gait disturbance), possible uncontrolled reflex reaction of your body (such as profuse sweating, throbbing headache or increase in pulse rate) around the time of the injection (autonomic dysreflexia)*, fall.

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

Injections for excessive sweating of the armpits

Very common	Injection site pain.
Common	Headache, numbness, hot flushes, increased sweating at sites other than the armpit, abnormal skin odor, itching, lump under the skin, hair loss, pain in the extremities such as the hands and fingers, pain, reactions and swelling, bleeding or burning and increased sensitivity where the injection was given, general weakness.
Uncommon	Nausea, muscle weakness, feeling of weakness, muscle pain, problem with the joints.

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

Common	Headaches, drooping eyelid, skin redness, localized muscle weakness, face pain, numbness, nausea, skin tightness, injection site swelling, injection site pain, bruising under the skin, injection site irritation.
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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 symptoms, lack of strength, fever, “Mephisto sign” (raising of the outer eyebrows).
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Injections for the temporary improvement in the appearance of fan-shaped lines from the corner of the eyes, when treated with or without vertical lines between the eyebrows

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 appearance of forehead lines and of 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, injection site bruising*, injection site haematoma*, drooping eyebrow ² , “Mephisto sign” (raising of the outer eyebrows).
Uncommon	injection site pain*

**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.

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

- allergic reaction, including reactions to injected serum or proteins;
- severe allergic reaction (swelling under the skin, difficulty in breathing);
- swelling of the deeper layers of the skin;
- rash;
- hives;
- eating disorders, loss of appetite;
- nerve damage (brachial plexopathy);
- voice and speech problems;
- drooping of the muscles on one side of the face;
- weakness of the face muscles;
- decreased skin sensation;
- muscle weakness;
- chronic disease affecting the muscles (myasthenia gravis);
- difficulty moving the arm and shoulder;
- numbness;
- pain, numbness, or weakness starting from the spine;
- seizures and fainting;
- increase in eye pressure;
- difficulty in completely closing the eye;
- crossed eyes (strabismus);

- drooping eyelid/eyebrow;
- blurred vision;
- difficulties in seeing clearly;
- decreased hearing;
- noises in the ear;
- feeling of dizziness or spinning (vertigo);
- heart problems including heart attack;
- 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;
- diarrhea, constipation;
- dry mouth;
- difficulty swallowing;
- nausea, vomiting;
- hair loss;
- Itching;
- psoriasis-like skin patches (red, thick, dry and scaly);
- different types of red blotchy skin rashes;
- excessive sweating;
- loss of eyelashes/eyebrows;
- muscle wasting;
- muscle pain, loss of nerve conduction to the injected muscle, shrinkage of injected muscle;
- malaise;
- feeling generally unwell;
- fever;
- dry eye (associated with injections around the eye);
- localized muscle twitching/involuntary muscle contractions;
- Swelling of the eyelid.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:

<https://sideeffects.health.gov.il>

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.

- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C – 8°C), or in a freezer (-20°C to -5°C).
- After the solution is made up, immediate use of the solution is recommended; however, it can be stored in a refrigerator (2°C – 8°C) for up to 24 hours from the time it was made up.

6. Additional information

In addition to the active ingredient, this medicine also contains inactive ingredients:

Sodium chloride, human albumin.

What the medicine looks like and contents of the pack: Each pack of BOTOX contains one vial with a thin white powder that may be difficult to see on the bottom of transparent glass vial.

Prior to injection, the product must be dissolved in a sterile unpreserved normal saline solution (0.9% sodium chloride solution for injection).

For stability information and full reconstitution instructions, please refer to the Prescribing Information.

Manufacturer's name and address:

Allergan Pharmaceuticals Ireland Westport, Mayo County, Ireland.

Registration holder's name and address:

AbbVie Biopharmaceuticals Ltd., 4 Haharash St., Hod Hasharon, Israel.

Revised in March 2023 according to MOH guidelines.

Registration number of the medicine:

BOTOX 50: 145-33-32005

BOTOX 100: 057-68-27328

BOTOX 200: 149-45-33538