Package leaflet: Information for the user

NUCEIVA 50 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 the end of section 4 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, pharmacist, or healthcare practitioner.
- 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 have any side effects, talk to your doctor, pharmacist, or healthcare practitioner. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What NUCEIVA is and what it is used for

NUCEIVA contains the active substance botulinum toxin type A.
It prevents muscles from contracting, leading to a temporary paralysis. It works by blocking the nerve impulses to the muscles in which it has been injected.

NUCEIVA is used for the temporary improvement in the appearance of vertical lines between the eyebrows. It is used in adults less than 65 years of age in whom those facial lines have an important psychological impact.

2. What you need to know before NUCEIVA is used

NUCEIVA must not be used:
- if you are allergic to botulinum toxin type A or any of the other ingredients of this medicine (listed in section 6);
- if you have myasthenia gravis or Eaton Lambert syndrome (chronic diseases affecting the muscles);
- if you have an infection or inflammation at the proposed injection sites.

Warnings and precautions
Side effects possibly related to the spread of botulinum toxin from the site of injection can occur very rarely (e.g. muscle weakness, difficulty in swallowing or food or liquid entering the airways). Patients receiving recommended doses may have exaggerated muscle weakness.

Visit your doctor, pharmacist, or healthcare practitioner immediately if you find it difficult to swallow, to speak or to breathe after treatment.

- NUCEIVA is not recommended in patients who have had problems swallowing (dysphagia) and breathing.
- Too frequent or excessive dosing may lead to antibody formation. Antibody formation can stop botulinum toxin type A from working even for other uses. To prevent this, there must be a gap of at least three months between doses.
- Very rarely, an allergic reaction can occur after the injection of botulinum toxin.
- Drooping of the eyelid may occur after treatment.

Please tell your doctor, pharmacist, or healthcare practitioner if:
- you had problems 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 a bleeding disorder as injection may lead to bruising.

Children and adolescents
The use of NUCEIVA is not recommended in individuals under 18 years.

Other medicines and NUCEIVA
Tell your doctor, pharmacist, or healthcare practitioner if you are taking, have recently taken or might take any other medicines.

The use of botulinum toxin is not recommended in association with aminoglycoside antibiotics, spectinomycin or other medicines that interfere with nerve impulses to the muscle.

Tell your doctor, pharmacist, or healthcare practitioner if you have recently been injected with a medicine containing botulinum toxin (the active substance of NUCEIVA), as this may increase the effect of NUCEIVA excessively.

Pregnancy and breast-feeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby ask your doctor, pharmacist, or healthcare practitioner for advice before you receive this medicine.

The use of NUCEIVA is not recommended during pregnancy and in women able to have children who are not using contraception.

NUCEIVA is not recommended in breast-feeding women.

Driving and using machines
Muscle weakness, dizziness, and visual disturbance with this medicine could make driving or the use of machines dangerous. Do not drive or use machinery until such effects have cleared.

NUCEIVA contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose; this means it is essentially ‘sodium- free’.

3. How to use NUCEIVA

Unit doses for NUCEIVA are not interchangeable with those used for other preparations of botulinum toxin.

NUCEIVA should only be injected by doctors or other healthcare practitioners with appropriate qualifications and expertise in the treatment of glabellar lines at maximum frown.

The usual dose of NUCEIVA is 20 Units. You will be injected with the recommended volume of 0.1 millilitre (ml) (4 Units) of NUCEIVA into each of 5 injection sites.

Improvement of severity of the lines between the eyebrows generally occurs within a few days of treatment.

The interval between treatments will be decided by your doctor or healthcare practitioner.

How NUCEIVA is injected

NUCEIVA is injected into your muscles (intramuscularly), directly into the affected area above and between the eyebrows.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
In general, side effects occur within the first few days after injection and are temporary. Most side effects are of mild to moderate severity.

If you have any difficulty in breathing, swallowing or speaking after receiving NUCEIVA contact your doctor or healthcare practitioner immediately.

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

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

Common (May affect up to 1 in 10 people)	Headache, muscle imbalance resulting in elevated or asymmetrical eyebrows, eyelid drooping, injection site bruise
Uncommon (May affect up to 1 in 100 people)	Sensory disturbance, head discomfort, dry eye, eyelid swelling, eye swelling, muscle twitching, injection site: redness, pain, tingling

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, or healthcare practitioner. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme, Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

5. How to store NUCEIVA

Keep out of the sight and reach of children.

Unopened vial

Do not use NUCEIVA after the expiry date which is stated on the vial and the carton after EXP.

6. Contents of the pack and other information

What NUCEIVA contains
- The active substance is: 50 Units botulinum toxin type A.
- The other ingredients are human albumin and sodium chloride.

What NUCEIVA looks like and contents of the pack
NUCEIVA is presented as a white powder for solution for injection in a transparent glass vial.
Each pack contains 1 vial.

Marketing Authorisation Holder and Manufacturer
Evolus Pharma B.V.
Apollolaan 151
1077 AR Amsterdam
The Netherlands

For any information about this medicine, please contact the Marketing Authorisation Holder (medicalinformation@evolus.com).

This leaflet was last revised in June 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 units are different from other botulinum toxin preparations.

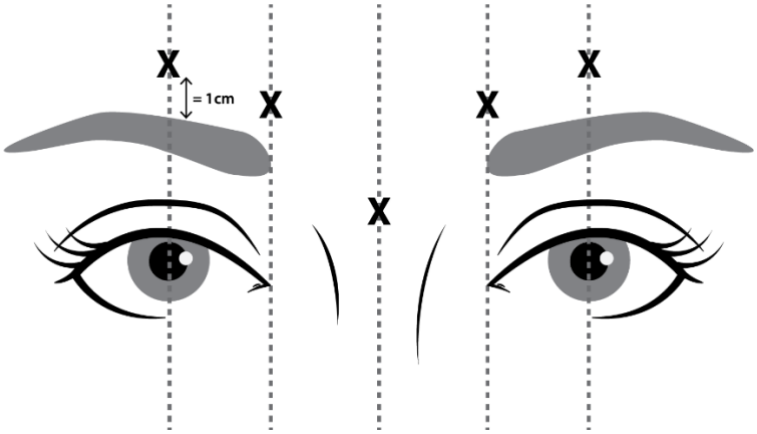
Reconstitution should be performed in accordance with good clinical practice, particularly with respect to aseptic technique. NUCEIVA is reconstituted with sodium chloride 9 mg/ml (0.9%) solution for injection. 1.25 mL of sodium chloride 9 mg/ml (0.9%) solution for injection is drawn up into a syringe in order to obtain a reconstituted solution for injection at a concentration of 4 Units/0.1 mL.

Amount of solvent added to 50 Unit vial (sodium chloride 9 mg/ml (0.9%) solution for injection)	Resulting dose (Units per 0.1 mL)
1.25 mL	4.0 U

The central part of the rubber cap should be cleaned with alcohol. Inject the diluent slowly into the vial with a needle through the rubber stopper 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 solution free of particulate matter.

Reconstituted NUCEIVA (50 Units/1.25 mL) is injected using a sterile 30 gauge needle. Four Units (4 U/ 0.1 mL) are administered in each of the 5 injection sites (see Figure 1): 2 injections in each corrugator muscle (inferior medial and superior medial aspect) and 1 injection in the procerus muscle for a total dose of 20 Units.

Figure 1: Injection Points



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

- Avoid injection near the levator palpebrae superioris, particularly in patients with larger brow depressor complexes.
- Lateral corrugator injections should be placed at least 1 cm above the bony supraorbital ridge.
- Ensure the injected volume/dose is accurate and where feasible kept to a minimum.

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

Immediately after use, unused reconstituted NUCEIVA solution for injection in the vial and/or the syringe must be inactivated, prior to disposal, with 2 mL of dilute sodium hypochlorite solution at 0.5% or 1% available chlorine. Following inactivation, dispose 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 handling the product, whether in the vacuum-dried state or reconstituted, the appropriate measures described below must be initiated immediately.

- The toxin is very sensitive to heat and certain chemical agents.

- 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, carefully collect the pieces of glass and wipe up the product as stated above, avoiding cuts to the skin.

- If splashed, wash with a solution of sodium hypochlorite and then rinse thoroughly with plenty of water.

- If splashed into the eyes, rinse eyes 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.

<u>These instructions for use, handling and disposal should be strictly followed</u>.