SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ABE botulinum antitoxin, 500 IU. + 500 IU. + 100 IU/m1, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One ampoule (10 ml) contains:
Botulinum antitoxin type A not less than 5,000 IU.
Botulinum antitoxin type B not less than 5,000 IU.
Botulinum antitoxin type E not less than 1,000 IU.

1 ml of solution contains:
Botulinum antitoxin type A not less than 500 IU.
Botulinum antitoxin type B not less than 500 IU.
Botulinum antitoxin type E not less than 100 IU.

The drug product contains less than 1 mmol (23 mg) of sodium per ml of solution, that is, the drug is considered "sodium-free."

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection
Colorless to pale straw-colored, clear solution.

4. CLINICAL DETAILS

4.1 Indications for use

The medicinal product Botulinum antitoxin ABE is used to neutralize botulinum toxin(s) types A, B and E in botulism.

4.2 Dosage and administration

The use of Botulinum Antitoxin ABE is decided by the doctor.

Before deciding to administer the drug product, a history should be taken (if the patient's condition allows) of the patient's allergies and receipt of horse antitoxin ever and taking antihistamines within 48 h.

Always perform a horse antitoxin (horse protein) sensitization test before using ABE Botulinum Antitoxin.

In the case of positive or doubtful results of sensitization tests, with concomitant indications of botulinum antitoxin ABE can be administered by desensitization.

You should always have a set of **ready-to-use antitoxin before performing a sensitization test and administering an animal antitoxin**.

Dosag

Profilaktveznie/zapobiettawezo:
Route of administration: intramuscularly.
Dosage: from 10 ml to 20 ml (one to two ampoules).

Therapeuti
Route of administration: intramuscularly, and in life-saving cases,
intravenously. Dose: 50 ml to 100 m1 (five to ten ampoules).
Note: Before administering the product intravenously, it should be warmed to 37°C.

Sensitization test
Perform one of the following sensitization tests (taking into account the history):
- Intradermal injection of 0.2 ml of product diluted 1:1,000 with sterile 0.9% sodium chloride solution or
- Intradermally inject 0.2 m1 of product diluted 1:100 with sterile 0.9% sodium chloride solution or
- Intradermally inject 0.1 ml of product diluted 1:10 with sterile 0.9% sodium chloride solution.

If no local or general reaction is found 30 minutes after intradermal administration, inject 0.2 ml of undiluted antitoxin subcutaneously.

If there is no local or general reaction within 30 minutes after subcutaneous injection of undiluted antitoxin, the antitoxin can be administered intramuscularly or intravenously.

Intramuscular administration:
To ensure slow release of the drug product, administer the antitoxin intramuscularly. If administered intramuscularly, it recommended that the antitoxin be injected into different areas of the body.

Application dożvlne:
To ensure that botulinum toxin is neutralized as quickly as possible in all tissues and body fluids, slow intravenous infusion of antitoxin is indicated.
Note: before administering antitoxin intravenously, it should be warmed to 37°C.

The occurrence of redness and blisters at the injection site after the sensitization test 30 minutes indicates sensitization to horse protein.

If the result is positive or uncertain, and the administration of botulinum antitoxin is necessary, it should be administered by desensitization.

Detection method dosage of botulinum antitoxin ABE

Desensitization involves subcutaneously injecting small volumes of the drug product, from 0.1 to 0.5 ml, at 30-40 minute intervals. Often the same doses need to be repeated due to questionable reactions.

Way piei wszv:
ABE botulinum antitoxin diluted 1:10 with sterile 0.9% sodium chloride is injected subcutaneously, at intervals of 30 minutes to 1 hour, from 0.1 to 0.5 ml, followed by undiluted 0.2 ml and 0.5 ml each.
Administer the remainder of the scheduled dose intramuscularly. It is recommended that the drug be injected into different areas of the body.

Sgosóh druki:
Inject subcutaneously the lowest dose tolerated in an intradermal test.

If there is no reaction 30 minutes, increase the dose every 30 minutes until 0.2 ml of undiluted antitoxin is injected subcutaneously.
Administer the remainder of the scheduled dose intramuscularly. It recommended that the drug be injected into different areas of the body.

4.3 Contraindications

Hypersensitivity to the active substance (horse protein) or to any of the excipients listed in section 6.1.

In svtuations **of severe poisoning and** the necessity a**;salting of botuIinowg|ntitoxin, you can** Administer ia by **desensitization** method or ood shielding fti. After the administration ofJ antiseizure agents.

4.4 Special warnings and precautions for use

The use of this medicinal product is decided by the doctor.
Before deciding on the use of this medicinal product, a history of the patient's history of allergy and ever receiving horse antitoxin and taking antihistamines 48 h should be taken.

W żadnym wypadku nie należy wykonywać próby śródskórnej ani wstrzykiwać produktu leczniczego bez gotowego do użycia zestawu przeciwwstrzą owl go.

Antitoxin administration should be carried out by personnel with experience in the management of anaphylactic shock and with access to a shock kit.

Taking antihistamines 48 h before an allergy test can inhibit the onset of an allergic reaction.
A negative sensitization test is not a complete guarantee that the patient is not susceptible to the antitoxin, so extreme caution should be exercised during any administration of this drug product and an anti-shock kit should be available.

If the patient is allergic to horse protein has previously received antitoxin or is allergic, ABE Botulinum Antitoxin should be administered according to the desensitizing route of administration described in section 4.2.

4.5 Interactions with other medicinal products and other types of interactions

No studies have been conducted on the interaction of Botulinum Antitoxin ABE with other drugs.

4.6 Effects on fertility, pregnancy and lactation

There are insufficient data on the use of Botulinum Antitoxin ABE in pregnant and lactating women.
Caution should be exercised when prescribing this medicinal product to pregnant and lactating women.

4.7 Effects on the ability to drive and operate machinery

ABE botulinum antitoxin has no effect on the ability to and operate machinery.

4.8 Side effects

There are insufficient data from clinical trials on the incidence of side effects.

Based on literature data, the following undesirable effects have been reported. As after the administration of other antitoxins of animal origin, serious general reactions of allergic , i.e. anaphylactic shock and (or) post-surgical disease, observed not very often. Sickness between 7 and 20 days after administration of the product and manifests itself as swelling at the injection site, enlargement of lymph nodes, elevation of body temperature, swelling of joints, urticaria, in acute cases kidney damage.
Very rarely, neurologicme complications may occur in the form of inflammation of the nerves of the brachial plexus, cranial and peripheral nerves (i.e. encephalopathy) or Guillan-Barre syndrome (acute idiopathic polyneuritis). Symptoms of the disease resolve when the antigen is removed from the body.

Very rarely, swelling and pain1 at the site of administration

may occur. Reporting of suspected side effects
Once a medicinal product is approved for marketing, it is important to report suspected adverse reactions. This allows continuous monitoring of the benefit-risk ratio of the medicinal product. Professional medical personnel should report any suspected adverse reactions through the Adverse Drug Reactions Monitoring Department of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products:
Al. Jerozolimskie 181C
02-222 Warsaw,
tel. +48 22 49 21 301, fax. +48 22 49 21 **309,** e-mail: ndl@urpl.gov.pl.

4.9 Overdose

Avoid giving higher doses than necessary.
A higher dose may exacerbate the adverse reactions listed in Section 4.8, such allergic reactions or neurological symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: drugs for infections; antisera
and immunoglobulins; antisera; botulinum antitoxin, ATC code: J06AA04.

The drug product contains a mixture of three horse *botulinum* antitoxins that neutralize individual types of toxin A, B and E produced by *Clostridium botulinum* bacteria. Each of the antitoxins contains purified F(ab)fragments from specific class G immunoglobulins. The F(ab)2 fragments are obtained using a modified Pop's thermal method, which involves enzymatic proteolysis of proteins with pepsin, precipitation of labile proteins by thermocoagulation and selective salting out with ammonium sulfate. This process allows the elimination of ballast proteins and Fc fragments of the IgG molecule responsible for the ability to form aggregates, bind complement or induce skin reactions. Such purification of the product contributes to the reduction of adverse reactions after administration of heterologous immunoglobulins.

Botulinum antitoxin ABE neutralizes the action of botulinum toxins types A, B and E through a specific antigen (toxin) - antibody (antitoxin) type reaction. The complexes formed are gradually captured by the macrophage system, and partially deposited in the vascular endothelium, in the basement membrane of the renal glomeruli, joints and muscles.

Due to the content of proteins of animal origin, the medicinal product may cause severe adverse allergic reactions associated with the administration of foreign protein.

The drug product has been manufactured in Poland for more than 55 years. The clinical evaluation is retrospective.

5.2 Pharmacokinetic properties

After intramuscular injection, the peak serum concentration of antitoxin is obtained within 1 to 2 days.
After intravenous administration, the peak serum concentration of antitoxin is obtained immediately after the end of the infusion.
Absorption from the intramuscular injection site is by simple diffusion from the tissue into the plasma. The antigen (toxin) - antibody (antitoxin) complex undergoes phagocytosis. The half-life of the complex is 2 - 3 days.
Complete elimination occurs in 8 - 12 days.

5.3 Preclinical safety data

Non-clinical data from pharmacological studies on safety of use, repeated dose toxicity, genotoxicity, potential carcinogenicity and reproductive toxicity do not reveal the presence of any special hazard for humans.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Phenol
Sodium chloride
Water for injection
Sodium hydroxide and hydrochloric acid - in small amounts to determine pH

6.2 Pharmaceutical incompatibilities

Not applicable.

6.3 Validity period

3 years.
The medicinal product should be used immediately after opening.

6.4 Special precautions during storage

Store in the refrigerator (2°C - 8°C). Do not freeze.
Store in original packaging to protect from light.

6.5 Type and content of packaging

Glass ampoules in a cardboard box. The package contains 1 or 5 ampoules of 10 ml each.

Not all package sizes need to be on the market.

6.6 Special precautions for disposal and preparation of the medicinal product for use

Before administering the product intravenously, it should be warmed to 37°C.

Dispose of any unused medicinal product residue or waste accordance with local regulations.

7. MARKETING AUTHORIZATION HOLDER RESPONSIBLE PARTY

Wytwórnia Surowic i Szczepionek BIOMED Sp. z o.o.
30/34 Chelmska St.
00-725 Warsaw
tel. +48 22 841 40 71

8. MARKETING AUTHORIZATION NUMBER

R/0530

9. DATE OF FIRST MARKETING AUTHORIZATION /DATE OF PERMIT RENEWAL

Date first marketing authorization: November 15, 1974 Date of last authorization renewal: August 8, 2014.

10. DATE OF APPROVAL OR PARTIAL AMENDMENT OF THE TEXT OF THE SUMMARY OF PRODUCT CHARACTERISTICS

May 28, 2019.