Package leaflet/ Summary of Product Characteristics

Toxogonin®
Solution for injection

Active substance: Obidoximchloride

Read all of this leaflet carefully before you start taking 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.
- 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 Toxogonin is and what it is used for

Toxogonin is an injectable antidote against poisoning with organophosphates.

Toxogonin is used against insecticide poisoning with substances belonging to the organophosphate group (alkyl phosphates, alkyl thiophosphates, phosphoric acid esters, thiophosphoric acid esters), e.g. parathion = E 605® forte, in which the inhibited acetylcholinesterases may be reactivated by the specific antidote Toxogonin.

Pharmacotherapeutic group: antidote - obidoxime –: ATC code V03B13

Symptoms of acute organophosphate poisoning

Poisoning with organophosphate insecticides is suspected in the presence of signs of parasympathetic stimulation such as miosis (may also be absent!), bronchospasm, diarrhea with vomiting, bradycardia, colics and collapse; also convulsions or fibrillary twitches, respiratory depression, pulmonary edema and coma.

In less severe cases the following symptoms may well give reason to suspect organophosphate poisoning: dizziness, blurred vision, weakness, asthma, nausea, sweating and vomiting

2. What you need to know before you take Toxogonin

Do not use Toxogonin :
- if you are allergic to obidoxime or any of the other ingredients of this medicine (listed in section 6).
- in case of poisoning with insecticides from the carbamate group (e.g. Aldicarb = Temik® 5G). Toxogonin is ineffective here, or it may even increase the carbamate effect. In these cases only atropine and symptomatic treatment should be considered.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Toxogonin.

Children and adolescents
Not applicable

Other medicines and Toxogonin
Not known to date.
Since obidoxime chloride is exclusively eliminated via the kidneys, interactions with other renally eliminated medicinal products are theoretically possible.
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Toxogonin with food, drink and alcohol
Not applicable

Pregnancy, breast-feeding and fertility
No sufficient experience with the use of Toxogonin during pregnancy has been gained up to date. In one case the administration of obidoxime (1250 mg in 24 hours) to a woman five months pregnant did not result in any adverse effects in the mother or the infant.
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 taking this medicine.

Driving and using machines
Not applicable.

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

3. How to take Toxogonin

General measures of emergency care and initial doses of atropine are to proceed any administration of Toxogonin! As the measures taken within the first 15 minutes are decisive for the survival of the poisoned patient *treatment must be commenced before admission to hospital**!***

The following measures should be taken as soon as possible:

General measures
After oral ingestion
of poisons gastric lavage needs to be performed, followed by instillation of activated charcoal, to be repeated as required.

After skin contact
clothes need to be removed and the patient's entire body washed with a solution of sodium bicarbonate or polyethylene glycol.

Generally: Clearing and keeping open of airways (intubation), aspiration of secretions, and, if necessary, artificial ventilation. Immediate intravenous access, volume replacement (plasma expander). In the case of pulmonary edema (excessive bronchial secretions!) immediate administration of high-dose atropine.

Administration of atropine
Administer atropine as soon as possible: 2-5 mg intravenously, to be repeated at intervals of 5-15 minutes until the atropine effect is clearly manifest (check dryness of the mouth or, in the case of intubated patients, the amount of bronchial secretion). Atropine tolerance is extremely high in organophosphate poisoning. Single doses of 1-3 mg in children.

Systematic treatment with atropine must be started prior to transferring the patient to hospital. It is a measure to combat imminent cardiac arrest in bradycardia. Atropine should be given until signs of overdosage appear (hot, dry skin, dry mouth, mild tachycardia).

Administration of Toxogonin
Note: On no account does administration of Toxogonin replace administration of atropine!

Specific antidote treatment with Toxogonin is initiated after the first doses of atropine.

Initial dose in adults: 1 ampoule (250 mg), initial dose in children: 4–8 mg/kg body weight, slowly intravenously.

This drug is administered as a continuous infusion at a dose of 750 mg/24 h and in children at a dose of 10 mg/kg BW daily as long as reactivation of acetylcholinesterase is still possible.

The first Toxogonin dose should be given as soon as possible. Even in delayed initiation of therapy within one week after poisoning, reactivation of acetylcholinesterase can still be expected.

Toxogonin may also be given by intramuscular injection.

Lack of marked short-term improvement after Toxogonin injection in insecticide poisoning most probably is an indication for non-organophosphate poisoning manageable with Toxogonin or for acetylcholinesterases that are already irreversibly inactivated and that can no longer be reactivated with Toxogonin. In such cases no further injections of Toxogonin should be given.

Depending on the individual intoxication situation, particularly the type and quantity of ingested organophosphates as well as other factors, it is not possible to predict with certainty the antidotal efficacy achieved by Toxogonin in the individual case. Use of Toxogonin is generally indicated in organophosphate poisoning within the overall scope of treatment to ensure the best possible management of poisoning. Overdosage is to be avoided. When given as recommended, Toxogonin treatment incurs no additional risks for the poisoned person.

Since animal studies have indicated certain irritations in intra-arterial injection of Toxogonin, this drug must be given strictly according to instructions by intravenous injection.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Because of the nature of the product no clinical trial data are available which would allow estimation of frequencies for adverse reactions.

In healthy volunteers symptoms resolved spontaneously within 2 hours.

Regarding side effects labelled with * in patients with organophosphorous intoxications, a relationship to Toxogonin cannot be excluded.

Not known (cannot be estimated from the available data):

<u>Nervous system disorders</u>
Dysgeusia (taste of menthol), hypoaesthesia

<u>Cardiac disorders</u>
Cardiac arrhythmia*

<u>Gastrointestinal disorders</u>
Dry mouth

<u>Hepatobiliary disorders</u>
Jaundice cholestatic* (with doses exceeding 3000-10000 mg within 1-3 days), hepatic function abnormal* (with doses exceeding 2000 mg)

<u>Musculoskeletal and connective tissue disorders</u>
Muscular weakness

General disorders and administration site conditions
Feeling hot, feeling cold

Investigations
Heart rate increased, blood pressure increased, Electrocardiogram change*

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. You can also report side effects directly via Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, Website: www.bfarm.de. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Toxogonin

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton after "Verwendbar bis/ EXP". The expiry date refers to the last day of that month.

Do not refrigerate or freeze.
Do not store above 25 °C.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

6. Contents of the pack and other information

What Toxogonin contains
- The active substance is:

Obidoxime chloride…… ……250,00 mg
For 1ml ampoule

- The other ingredients are: sodium hydroxide solution, hydrochloric acid, water for injection

What Toxogonin looks like and contents of the pack
5 ampoules containing 1 ml each of solution for injection.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
SERB SA
Avenue Louise 480
1050 Brussels
Belgium
E-mail: infomed@serb.eu
Phone: + 32 2 792 05 00

Co-promotion ("Mitvertrieb"):

Heyl Chem.-pharm. Fabrik GmbH & Co. KG
Kurfürstendamm 178-179
10707 Berlin
Germany
E-mail: info@heyl-berlin.de
Phone: +49 30 81696-0
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Manufacturer:
Cenexi
52 rue Marcel et Jacques Gaucher
94120 Fontenay-Sous-Bois
France

This leaflet was last revised in December 2025.

The following information is intended for healthcare professionals only:

Legal category
Medicinal product subject to medical prescription.

Overdose
If the recommended single and total Toxogonin doses are by far exceeded, the resultant effect may be contrary to the intended leading to further inhibition of acetylcholinesterases and aggravation of the symptoms of poisoning. Risk situations like this may result from the interaction of high concentrations of Toxogonin with large organophosphate quantities in the body. As in severe organophosphate poisoning countermeasures to be considered here are haemoperfusion or exchange transfusions.

Furthermore, when the appropriate Toxogonin doses are severely exceeded, the possibility of the substance being connected with transient disturbances in liver function cannot be ruled out.

Pharmacological properties

Pharmacodynamic properties
Toxogonin is a causal antidote since it counteracts the causes of the symptoms of poisoning induced by organophosphates (inhibition of acetylcholinesterases and subsequent accumulation of acetylcholine). Toxogonin is an effective adjunct to the symptomatic and absolutely essential treatment of organophosphate poisoning with atropine.

Obidoxime chloride can reactivate blocked acetylcholinesterases where their function has been inhibited by organophosphates. (alkyl phosphates, alkyl thiophosphates, phosphoric acid esters, thiophosphoric acid esters). This does not apply to phosphoramidate, like Tabun or Fenamiphos.

A significant reactivation can be expected at blood plasma levels of 10-20 micromol obidoxime chloride. At high concentrations, not achieved when recommended doses are administered, obidoxime chloride itself causes a weak inhibition of cholinesterase.

Pharmacokinetic properties
Generally, Toxogonin is administered by the intravenous route thus ensuring its bioavailability. After intravenous administration of an initial bolus dose of 250 mg obidoxime chloride followed by continuous infusion of 750 mg/24 hours, plasma levels of 3.6-7.2 mg/l (10-20 micromol/l) were determined in patients with organophosphate poisoning.

After intramuscular injection of one ampoule of Toxogonin (0.25 g equivalent to about 3 mg obidoxime chloride / kg of body weight) to subjects maximum obidoxime concentrations in the blood were about 6 µg/ml after 20 to 40 minutes.

Obidoxime is not noticeably bound to plasma proteins. The distribution volume corresponds with approximately 0.171 l/kg to those of the extracellular space, however, may reach 0.32 l/kg in patients with organophosphate intoxication.

Obidoxime chloride is mainly eliminated renally. With a half-life in the range of 2 hours the unchanged substance was excreted with the urine. After 2 hours 52% and after 8 hours 87% of the injected dose had been eliminated.

Preclinical safety data

According to animal studies obidoxime chloride is an active substance with relatively slight intrinsic toxicity and a large therapeutic index. Symptoms of overdosage are seen in animals after intravenous doses starting with 50 mg obidoxime chloride/kg of body weight. The acute symptoms of poisoning are muscle weakness, states of motor paralysis and excitation, dyspnoea and respiratory paralysis.

Rats tolerated intraperitoneal injection of 68 mg obidoxime chloride/kg of body weight daily for a period of 30 days without any recognisable impairment to their state of health. After daily injections of 113 mg/kg of body weight over this period 30% of the study animals died, and after 158 mg/kg of body weight the corresponding figure was 100%. Death of the animals was probably due to respiratory paralysis; no organic lesions were found.

In vitro investigations with obidoxime chloride have not revealed any mutagenic properties.

In vivo investigations on mutagenic potential as well as investigations on chronic toxicity, on reproduction toxicity as well as carcinogenicity with obidoxime chloride are not available.

Bioavailability
Generally, Toxogonin is administered by the intravenous route thus ensuring its bioavailability. No further experience is available on the bioavailability of this drug after intramuscular administration besides the information given in the section on pharmacokinetics.

Incompatibilities
Most important incompatibilities and compatibility with solutions for infusion

Incompatibilities are unknown to date. Toxogonin (250 mg) is compatible with 250 ml of Glucosteril (5%) or 250 ml of physiological saline solution for a period of 24 hours.

Shelf life
5years

Holder of marketing authorization in Germany:
SERB SA
Avenue Louise 480
1050 Brussels
Belgium

Marketing Authorisation Number in Germany
6102841.00.00

Date of first authorisation / renewal of the authorization
05.11.1998 / 20.11.2012

Holder of marketing authorisation in Switzerland:
Curatis AG
4410 Liestal

Marketing Authorisation Number in Switzerland:
Reg.no. 31`514 (Swissmedic), Abgabekategorie B

Holder of marketing authorisation in the the Netherlands:
SERB SA
Avenue Louise 480
1050 Brussels

Marketing Authorisation Number in the Netherlands
RVG 04562