Package leaflet: **Information for the user**

Cyanokit / 5 g powder for solution for infusion
Active substance: hydroxocobalamin

Read all of this leaflet carefully before 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 your 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

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1. What Cyanokit is and what it is used for

Cyanokit contains the active substance hydroxocobalamin.

Cyanokit is is an antidote for the treatment of known or suspected cyanide poisoning in all age ranges.

Cyanokit is to be administered together with appropriate decontamination and supportive measures.

Cyanide is a highly poisonous chemical. Cyanide poisoning may be caused by exposure to smoke from household and industrial fires, breathing or swallowing cyanide, or contact with cyanide on skin.

2. What you need to know before Cyanokit is used

Warnings and precautions
Tell your doctor or other health care professional
- if you are allergic to hydroxocobalamin or vitamin B_{12}. They will have to take it into account before treating you with Cyanokit.
- that you have been treated with Cyanokit if you need to have the following:
  - any blood or urine tests. Cyanokit may modify the results of these tests.
  - burn assessement. Cyanokit may interfere with the assessment as it causes red coloration of the skin.
  - haemodialysis. Cyanokit may lead to shut down of haemodialysis machines until it is eliminated from the blood (at least 5.5 to 6.5 days).
  - monitoring of renal function: Cyanokit may lead to kidney failure and urine crystals.

Other medicines and Cyanokit
Tell your doctor or other health care professional if you are taking, have recently taken or might take any other medicines.

Detailed information for your doctor or other health care professional regarding simultaneous administration of Cyanokit with other medicines can be found at the end of this package leaflet (see 'Handling instructions').

Pregnancy and breast-feeding
This medicine is an emergency treatment. It can be administered during pregnancy and breast-feeding.

Tell your doctor as soon as possible if you were pregnant or think you may have been pregnant during treatment with Cyanokit.

Your doctor will recommend you to stop breast-feeding after treatment with Cyanokit.

3. How Cyanokit is used

Your doctor or health care professional will give you Cyanokit by infusion into a vein. You may need one or two infusions.

You will have the first infusion of Cyanokit over 15 minutes. For adults, the initial dose is 5 g. For children, it is 70 mg/kg body weight, up to a maximum dose of 5 g. If you need a second infusion, you will have it over 15 minutes to 2 hours. It depends on how serious the poisoning is. The maximum total recommended dose is 10 g for adults, and 140 mg/kg in children up to a maximum of 10 g.

Detailed instructions for your doctor or other health care professional on how to prepare the Cyanokit infusion and how to determine the dose can be found at the end of this package leaflet (see 'Handling instructions').

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may be expected (frequency cannot be estimated from the available data):

Allergy (hypersensitivity)
Tell your doctor **immediately** if you have the following symptoms during or after this treatment:
- swelling around the eyes, lips, tongue, throat or hands
- breathing difficulties, hoarseness, difficulty in speaking
- skin redness, nettle rash (urticaria) or itching.

Such side effects may be serious and need immediate attention.

Heart and blood pressure problems
- symptoms such as headache or dizziness, as they may be due to a rise in blood pressure. This rise in blood pressure especially occurs at the end of having this treatment and usually settles down within several hours
- irregular heart beat
- redness of the face (flush).

A decrease in blood pressure and a faster heart beat have also been observed in patients who have cyanide poisoning.

Breathing and chest problems
- fluid in the chest (pleural effusion)
- breathing difficulties
- a feeling of tightness in the throat
- dry throat
- chest pressure.

Renal and urinary problems
- kidney injuries such as acute kidney impairment and urine crystals.
- red colouration of the urine.

All patients will show a dark red colouration of the urine quite marked during the first three days following administration. Urine colouration may last up to 35 days after administration of Cyanokit. This red colouration has no other consequences on your body.

Gastrointestinal (digestive) problems
- discomfort in your stomach
- indigestion
- diarrhoea
- feeling sick (nausea)
- being sick (vomiting)
- difficulty in swallowing.

Eye problems
- swelling, irritation, redness.

Skin reactions
most patients will experience a reversible red colouration of the skin and membranes lining body cavities (mucous membranes) that may last up to 15 days after administration of Cyanokit.
- blister-like lesions on the skin (pustular rashes). These may last for several weeks, and affect mainly the face and the neck.
- inflammation in the part of the body where the medicine was infused.

Other side effects
- restlessness
- problems with memory
- dizziness
- headache
- swelling of ankles
- changes in the results of blood tests for certain white blood cells (lymphocytes)
- coloured plasma, which may cause artificial elevation or reduction in the levels of certain laboratory parameters.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Bundesinstitut für Arzneimittel und Medizin-produkte, 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 Cyanokit is stored

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 vial, the cardboard box and the carton after EXP.

Do not store above 25°C.

For the purpose of ambulatory use, Cyanokit may be exposed during short periods to the temperature variations of
- usual transport (15 days submitted to temperatures ranging from 5 to 40°C)
- transport in the desert (4 days submitted to temperatures ranging from 5 to 60°C) and
- freezing/defrosting cycles (15 days submitted to temperatures ranging from -20 to 40°C).

For storage conditions of the reconstituted medicine, see 'Handling instructions' at the end of this package leaflet.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines no longer used. These measures will help protect the environment.

6. Contents of the pack and other information

What Cyanokit contains

- The active substance is hydroxocobalamin. The vial contains 5 g of hydroxocobalamin. After reconstitution with 200 mL of diluent, each mL of the reconstituted solution contains 25 mg of hydroxocobalamin.
- The other ingredient is hydrochloric acid (for pH adjustment).

How Cyanokit looks like and contents of the pack

Cyanokit powder for solution for infusion is a dark red crystalline powder supplied in a glass vial closed with bromobutyl rubber stopper and an aluminium cap with a plastic lid.

Each pack contains one vial packed in one cardboard box, one sterile transfer device, one sterile intravenous infusion set and one sterile short catheter for administration to children.

Marketing authorisation holder

SERB S.A.
Avenue Louise 480
1050 Brussels
Belgium

Manufacturer

Merck Santé s.a.s. / SEMOY
2, rue du Pressoir Vert
45400 Semoy
France

This leaflet was last revised July 2017

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

The following information is intended for medical or healthcare professionals only:

Handling instructions

Treatment of cyanide poisoning must include immediate attention to airway patency, adequacy of oxygenation and hydration, cardiovascular support, and management of seizures. Consideration must be given to decontamination measures based on the route of exposure.

Cyanokit does not substitute oxygen therapy and must not delay the set up of the above measures.

The presence and extent of cyanide poisoning are often initially unknown. There is no widely available, rapid, confirmatory cyanide blood test. However, if a cyanide blood level determination is planned, it is recommended to draw the blood sample before initiation of treatment with Cyanokit. Treatment decisions must be made on the basis of clinical history and/or signs and symptoms of cyanide intoxication. If there is clinical suspicion of cyanide poisoning, it is strongly recommended that Cyanokit be administered without delay.

Preparation of Cyanokit

The vial is to be reconstituted with 200 mL of diluent using the supplied sterile transfer device. Sodium chloride 9 mg/mL (0.9%) solution for injection is the recommended diluent. Only when sodium chloride 9 mg/mL (0.9%) solution for injection is not available, Lactated Ringer solution or glucose 50 mg/mL (5%) solution for injection can also be used.

The Cyanokit vial is to be rocked or inverted for at least 1 minute to mix the solution. It must not be shaken as shaking the vial may cause foam and therefore may make checking reconstitution less easy. Because the reconstituted solution is a dark red solution, some insoluble particles may not be seen. The intravenous infusion set provided in the kit must then be used as it includes an appropriate filter and is to be primed with the reconstituted solution.

Posology

Initial dose

Adults: The initial dose of Cyanokit is 5 g (200 mL, complete volume of reconstituted solution).

Paediatric population: In infants to adolescents (0 to 18 years old), the initial dose of Cyanokit is 70 mg/kg body weight not exceeding 5 g.

Body weight in kg	5	10	20	30	40	50	60
Initial dose in g	0.35	0.70	1.40	2.10	2.80	3.50	4.20
in mL	14	28	56	84	112	140	168

Subsequent dose

Depending upon the severity of the poisoning and the clinical response, a second dose may be administered

Adults: The subsequent dose of Cyanokit is 5 g (200 mL, complete volume of reconstituted solution).

Paediatric population: In infants to adolescents (0 to 18 years old), the subsequent dose of Cyanokit is 70 mg/kg body weight not exceeding 5 g.

Maximum dose

Adults: The maximum total recommended dose is 10 g.

Paediatric population: In infants to adolescents (0 to 18 years old), the maximum total recommended dose is 140 mg/kg not exceeding 10 g.

Renal and hepatic impairment

No dose adjustment is required in these patients.

Method of administration

Initial dose of Cyanokit is administered as an intravenous infusion over 15 minutes.

The rate of intravenous infusion for the second dose ranges from 15 minutes (for patients extremely unstable) to 2 hours based on patient condition.

Simultaneous administration of Cyanokit and other products

Cyanokit must not be mixed with diluents other than sodium chloride 9 mg/mL (0.9%) solution for injection or Lactated Ringer solution or glucose 50 mg/mL (5%) solution for injection.

As physical and chemical incompatibilities were observed with a number of selected medicinal products that are frequently used in resuscitation efforts, these and other medicinal products must not be administered simultaneously in the same intravenous line as hydroxocobalamin.

If blood products (whole blood, packed red cells, platelet concentrate and fresh frozen plasma) and hydroxocobalamin are administered simultaneously, use of separate intravenous lines (preferably on contralateral extremities) is recommended.

Combination with another cyanide antidote

Chemical incompatibility was observed with sodium thiosulfate and sodium nitrite. If the decision is made to administer another cyanide antidote with Cyanokit, these medicinal products must not be administered concurrently in the same intravenous line.

In-use stability of the reconstituted solution

Chemical and physical in-use stability of the reconstituted solution with sodium chloride 9 mg/mL (0.9%) has been demonstrated for 6 hours at a temperature between 2°C to 40°C.

From a microbiological point of view, the medicinal 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 6 hours at 2°C to 8°C.