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EPAR summary for the public

Methylthioninium chloride Proveblue

methylthioninium chloride

This is a summary of the European public assessment report (EPAR) for Methylthioninium chloride Proveblue. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Methylthioninium chloride Proveblue

For practical information about using Methylthioninium chloride Proveblue, patients should read the package leaflet or contact their doctor or pharmacist.

What is Methylthioninium chloride Proveblue and what is it used for?

Methylthioninium chloride Proveblue is used in adults and children of all ages as an antidote to treat symptoms of methaemoglobinaemia caused by the use of certain medicines or chemicals.

Methaemoglobinaemia is a condition where there is too much of an abnormal form of haemoglobin (called methaemoglobin) in the blood that is not able to transport oxygen effectively. Substances that may cause methaemoglobinaemia include some antibiotics, local anaesthetics, nitrates in drinking water and pesticides.

Methylthioninium chloride Proveblue is a 'hybrid medicine'. This means that it is similar to a reference medicine, containing the same active substance but in a different concentration. The reference medicine for Methylthioninium chloride Proveblue is Methylthioninium Chloride Injection USP 1% w/v.

Methylthioninium chloride Proveblue contains the active substance methylthioninium chloride.



How is Methylthioninium chloride Proveblue used?

Methylthioninium chloride Proveblue is available as a solution for injection (5 mg/ml), which is injected slowly into a vein over a period of five minutes. It can only be obtained with a prescription and must be given by a healthcare professional.

The usual dose for adults and children aged above three months is 1 to 2 mg per kilogram (kg) body weight. A repeat dose may be given one hour after the first dose if symptoms persist or come back, or if the level of methaemoglobin in the blood stays higher than normal.

The dose in children aged three months or less is 0.3 to 0.5 mg/kg. They may also be given a repeat dose after one hour.

How does Methylthioninium chloride Proveblue work?

To carry oxygen in the blood, haemoglobin needs to contain an atom of iron in the 'ferrous' form (Fe^{2+}). Exposure to certain medicines or chemicals can cause the iron in the haemoglobin to change to the 'ferric' form (Fe^{3+}) seen in methaemoglobinaemia which is less able to transport oxygen.

The active substance in Methylthioninium chloride Proveblue, methylthioninium chloride (also called methylene blue), helps speed up the conversion of abnormal haemoglobin back into normal haemoglobin. It does this by accepting negatively charged electron particles through an enzyme called 'NADPH methaemoglobinaemia reductase'. The electrons are then transferred to the iron atoms in the abnormal haemoglobin, converting them into the normal ferrous form.

What benefits of Methylthioninium chloride Proveblue have been shown in studies?

Because methylthioninium chloride has been used in the European Union for several decades to treat methaemoglobinaemia, the company presented data on its use from the published literature, which confirmed that methylthioninium chloride is effective in treating methaemoglobinaemia that has been caused by exposure to a medicine or chemical in adults and children.

What are the risks associated with Methylthioninium chloride Proveblue?

The most common side effects with methylthioninium chloride are dizziness, paraesthesia (unusual sensations like 'pins and needles'), dysgeusia (taste disturbances), nausea (feeling sick), skin discoloration, chromaturia (abnormal colouration of the urine), sweating and pain at the site of injection or in a limb. For the full list of all side effects reported with methylthioninium chloride, see the package leaflet.

Methylthioninium chloride Proveblue must not be used in people who are hypersensitive (allergic) to methylthioninium chloride, or to any other thiazine dyes (the group to which methylthioninium chloride belongs). It must not be used in patients with the following conditions:

- glucose-6-phosphate dehydrogenase deficiency (G6PD),
- methaemoglobinaemia caused by nitrite during treatment of cyanide poisoning,
- methaemoglobinaemia caused by chlorate poisoning,
- deficiency in the enzyme NADPH reductase.

Why is Methylthioninium chloride Proveblue approved?

The Committee concluded the long experience with the active substance, methylthioninium chloride, shows that it is effective in treating methaemoglobinaemia. The CHMP decided that the medicine's benefits are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of Methylthioninium chloride Proveblue?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Methylthioninium chloride Proveblue have been included in the summary of product characteristics and the package leaflet.

Other information about Methylthioninium chloride Proveblue

The European Commission granted a marketing authorisation valid throughout the European Union for Methylthioninium chloride Proveblue on 6 May 2011.

The full EPAR for Methylthioninium chloride Proveblue can be found on the Agency's website: [ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports](http://ema.europa.eu/Find%20medicine/Human%20medicines/European%20Public%20Assessment%20Reports). For more information about treatment with Methylthioninium chloride Proveblue, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 10-2016.