SUMMARY OF PRODUCT CHARACTERISTICS

Radiogardase®-Cs

1. NAME OF THE MEDICINAL PRODUCT

Radiogardase-Cs 500 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 hard capsule contains 500 mg ferric hexacyanoferrate(II) (68 % $Fe_4[Fe(CN)_6]_3$) (Prussian blue insoluble).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule
Blue, transparent hard capsule, 21.5 - 22.1 mm long and with the imprint " " on the capsule cap and "PB" on the capsule base; filled with crystalline, blue-violet, fine- to coarse-grained powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Decorporation or avoidance of absorption of radiocaesium (e.g., ^{134}Cs, ^{137}Cs).

4.2 Posology and method of administration

Posology
The dosage depends on the severity of the caesium intoxication.

Adults, children and adolescents
- 6 to 40 hard capsules of Radiogardase-Cs [3 to 20 g ferric hexacyanoferrate(II)] orally each day. The daily dose should be distributed evenly over the 24-hour period (e.g., 3 x 6 hard capsules daily) to interrupt the enterohepatic circulation of the caesium optimally.
- In cases of acute intoxication, where the radiocaesium is still present in the stomach or upper parts of the intestinal tract, an initial dose of at least 6 hard capsules [3 g ferric hexacyanoferrate(II)] should be taken in one dose.

Method of administration
For oral use.
The hard capsules should be taken with liquid.

Patients, who cannot swallow the capsules, may open them. The ingredient may be taken mixed with food or be drunk dispersed in fluid (e.g., in warm water). This may result in blue discoloration of the mouth and teeth.

The administration of the suspension can also follow gastric lavage via stomach intubation.

If oral intake is not possible, the content of the hard capsules can be suspended in water or a mannitol solution and administered by stomach or duodenal tube.

The hard capsules should be taken during mealtimes since food stimulates bile secretion and the enterohepatic circulation (possible stimulation of caesium excretion).

Duration of treatment
Treatment with Radiogardase-Cs should be initiated as soon as possible. If Radiogardase-Cs is not available immediately, treatment is still effective and reasonable even after time has elapsed since exposure.

Treatment should take at least 30 days and depends on the severity of contamination and the judgement of the treating physician. During treatment, regular (weekly) controls of the radioactivity in the faeces and urine are important since the duration of treatment depends on the detection of radiocaesium in the faeces. The long biological half-life of the radiocaesium should be borne in mind.

If the detected radioactivity of caesium has decreased significantly, the dosage of Radiogardase-Cs may be reduced to 2 to 4 hard capsules daily [1 to 2 g ferric hexacyanoferrate(II)] to improve gastrointestinal tolerance.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

None known so far.
Radiogardase-Cs contains less than 1 mmol (23 mg) of sodium per hard capsule, meaning it is virtually "sodium free."

4.5 Interaction with other medicinal products and other forms of interaction

Radiogardase-Cs can bind to other oral administered drugs and essential nutrients. Therefore, the drug levels and the response to therapy should be monitored.

Radiogardase-Cs may inhibit the absorption of tetracyclines.

Radiogardase-Cs can bind to electrolytes in the gastrointestinal tract (e.g., potassium), which can result in lowered serum potassium levels (asymptomatic hypokalaemia). Therefore, serum electrolytes should be monitored regularly during therapy. Caution is advised especially in patients with pre-existing cardiac arrhythmias and electrolyte imbalances.

The co-administration of other drugs for treatment of contamination with radioactive substances does not affect the effectiveness of Radiogardase-Cs for radiocaesium.

4.6 Fertility, pregnancy and lactation

There are no objections to the use during pregnancy and lactation.

Since Radiogardase-Cs is practically not absorbed, it does not penetrate the placental barrier and does not enter breast milk. In contrast, radiocaesium is transferred both to the unborn child as to the breast milk. Therefore, the risk by radiocaesium is much higher than the risk of treatment with Radiogardase-Cs.

Contaminated mothers should not breastfeed in general.

4.7 Effects on ability to drive and use machines

None known so far.

4.8 Undesirable effects

Undesirable effects are due to overdose.

Gastrointestinal disorders
The intake of Radiogardase-Cs can cause constipation. This may be treated with a high-fibre diet or fibre-based laxatives.
In high dosage therapy (20 g ferric hexacyanoferrate(II) daily) undefined gastric distress may occur.
Note: Dark coloration of the faeces is harmless; it is due to the colour of the active ingredient Prussian blue.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, Website: www.bfarm.de.

4.9 Overdose

Overdoses of Radiogardase-Cs have not been described.

Symptoms of overdose may be constipation, obstruction, or severe decrease in electrolytes.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antidote, ATC code: V03AB31

Mechanism of action
Caesium is subject to enterohepatic circulation. During this process, absorbed caesium reaches the intestines via the liver and the bile. There, partial reabsorption through the intestinal mucosa takes place, which results in a renewed intoxication.

Ferric hexacyanoferrate(II) (Prussian blue insoluble) is not absorbed by intact mucosa after oral administration. It binds monovalent cations, where the strength of binding rises with increasing ionic radius: $Na^+ < K^+ < NH_4^+ < Rb^+ < Tl^+ < Cs^+$.

Prussian blue binds to the caesium present in the intestine and prevents its absorption or reabsorption. So, the enterohepatic circulation is interrupted. The caesium is excreted in the faeces together with the antidote. By the enhanced faecal excretion of caesium, the retention time in the body is reduced and the radiation exposure of the organism by the radionuclide is lowered.

Due to the decreased excretion of radiocaesium into the bile Radiogardase-Cs may be less effective in individuals with impaired liver function (but is not contraindicated in this group).

In self tests on humans, the daily oral administration of 3 g of Prussian blue reduced the biological half-life of radiocaesium from 110 to 115 days to approximately 40 days.

5.2 Pharmacokinetic properties

Absorption
The solubility product of Prussian blue is extremely small, and it is practically not absorbed after oral administration. Thus, it is not subject to pharmacokinetics in its proper meaning.

Elimination
Prussian blue is excreted in the stool together with the bound caesium.

5.3 Preclinical safety data

Acute toxicity
Overdose and poisoning by ferric hexacyanoferrate(II) are so far unknown (see section 4.9). The LD_{50} in rats via oral administration doses is > 10 g/kg body weight, for long term application > 1 g/kg body weight.

Chronic toxicity / subchronic toxicity
Ferric hexacyanoferrate(II) is not metabolized in the intestines. The long-term administration of 1 % Prussian blue in the feed does not lead to pathological changes in the rat.

Mutagenic and carcinogenic potential
Studies with Prussian blue to assess the carcinogenicity and mutagenicity have not been performed. Since the active ingredient is not absorbed, no effects are expected.

Reproductive toxicity
Prussian Blue was negative in an *in vitro* micronucleus assay. No further studies were performed to evaluate the mutagenicity and carcinogenicity of Prussian blue. As the active substance is not absorbed, no effects are expected *in vivo*.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Gelatine, Indigo carmine (E132), sodium dodecyl sulfate, purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and contents of container

White plastic bottle containing 36 hard capsules

6.6 Special precautions for disposal and other handling

No special requirements for disposal of unused capsules.

Radiocaesium is excreted in the faeces and the urine. The contamination of other persons should be avoided by special preventive measures.

Please note that the content of the hard capsules has a strong coloration effect.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

6813163.00.00

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 24 September 1997
Date of latest renewal: 15 May 2009

10. DATE OF REVISION OF THE TEXT

February 2025

11. PRESCRIPTION STATE

By prescription only