Octreoscan™ (\(^{111}\text{In}-\text{Pentetreotide}\))

Somatostatin receptor imaging for GEP neuroendocrine tumours
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

OctreoScan

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

OctreoScan contains hexachlorodisiloxane and sodium hydroxide. After reconstitution and labelling the solution contains 111In-pentetreotide 111 MBq/ml (111 MBq = 3.05 106 Bq).

3. PHARMACEUTICAL FORM

Vial A: 111In-pentetreotide 111 MBq/ml.
Vial B: Powder for solution for injection.
Vial C: A glass vial shielded with lead, containing a clear and colourless solution.
Vial D: A glass vial with grey rubber stopper and an aluminium crimp cap with orange flip off.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

4.2 Posology and method of administration

The activity to be administered for single photon emission tomography (SPECT) depends on the available equipment. In general, an activity of 110 to 220 MBq in one single intravenous injection should be sufficient. The activity for planar scintigraphy - if SPECT is not available - is 110 MBq available equipment. In general, an activity of 110 to 220 MBq in one single intravenous injection.

In a number of patients suffering from GEP or carcinoid tumours the receptor density is insufficient to allow visualisation with OctreoScan. Notably in approximately 50% of patients suffering from insuloma the tumour cannot be visualised.

4.3 Contraindications

There is limited experience on administrations in paediatric patients, but the activity to be administered in a child should be a fraction of the adult activity calculated according to the weight of the patient.

4.4 Special warnings and precautions for use

If the clinician responsible for the patient's therapeutic management considers withdrawal of octreotide therapy tolerable a three days withdrawal period is recommended.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions have been reported to date.

4.6 Pregnancy and lactation

There is no known interaction with the use of OctreoScan in pregnant women. Therefore, OctreoScan should not be used for pregnant women unless clearly necessary.

4.7 Effects on ability to drive and use machines

111In-pentetreotide does not affect the ability to drive or to use machines.

4.8 Undesirable effects

Adverse effects attributable to the administration of OctreoScan are uncommon (1/1000 to 1/100).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

No drug interactions have been reported to date.

5.2 Pharmacokinetic properties

In patients with significant renal failure administration of 40 g of pentetreotide resulted in a measurable but very limited activity is approximately 30% of the biological activity of natural somatostatin. The in vivo pharmacodynamic effects have been performed. The in vitro biological activity is approximately 30% of the biological activity of natural somatostatin. The in vivo biological activity, measured in rats, is less than that of equal amounts of octreotide. Intravenous administration of 20 g of pentetreotide resulted in some patients in a measurable but very limited decrease of serum gastrin and serum glucagon levels of less than 24 hours duration.

5.3 Preclinical safety data

No preclinical safety data are available. No detrimental effects have been observed. No drug interactions have been reported to date.

5.4 Pharmacokinetic properties

Within 24 hours after intravenous administration, approximately 80% of the radiolabelled pentetreotide is eliminated through the urinary system. After 48 hours 90% is excreted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Vial A: Hexachlorodisiloxane
Water for injections
Ferric Chloride hexahydrate.
Vial B: Sodium citrate dihydrate
Citric acid monohydrate
Inositol
Gentisic acid.

The ready-to-use solution does not contain a preservative agent.

6.2 Incompatibilities
Major incompatibilities: not known. After reconstitution and labelling Octreoscan may be diluted with 0.9% sodium chloride solution. Do not mix the injectate with any other solution in order to avoid possible incompatibilities.

6.3 Shelf life
Vial A and by consequence vial B of Octreoscan expire 24 hours after the activity reference time/date of the 111In.
After reconstitution: 6 hours. Store below 25°C.

6.4 Special precautions for storage
Store below 25°C.
For storage conditions of the reconstituted medicinal product, see section 6.3.

6.5 Nature and contents of the container
Both 10 ml vials comply with the requirements for glass Type I. The vial containing pentetreotide is closed with a butylrubber stopper. The vial containing 111In chloride is closed with a teflon-coated butylrubber stopper. Both vials are sealed with an aluminum crimp cap.

Octreoscan is supplied as one pack containing two vials that cannot be used separately, one of which has a lead shielding. Both vials are packed in a closed, folded tin. Enclosed in the tin is a Sterican Luer Lock 0.90 x 70 mm / 20 G x 2 4/5 needle to be used for the labeling procedure.

6.6 Special precautions for disposal and other handling
Radiopharmaceutical agents should only be used by qualified personnel with the appropriate government authorization for the use and manipulation of radionuclides.
This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisations.
Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements of Good Manufacturing Practice for pharmaceuticals.
The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. Therefore, radiation protection precautions in accordance with national regulations must be taken.

Instructions for waste disposal:
Unused 111In activity or unused Octreoscan should be allowed to decay until the activity has dropped to such a low level that, according to local regulations, it is no longer considered radioactive. Then it may be disposed of as harmless waste. Unused vials with lyophilized pentetreotide may be disposed of as harmless waste.
Waste must be disposed of according to national regulations for radioactive material.

7. MARKETING AUTHORISATION HOLDER
Mallinckrodt Medical B.V.
Westerduinweg 3
1755 LE Petten
The Netherlands

8. DATE OF REVISION OF THE TEXT
19. August 2011

9. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS
Do not use Octreoscan if you notice visible signs of deterioration.
Any unused product or waste material should be disposed of in accordance with local requirements.

Instructions for labelling:
1. Add the contents of vial A (111In chloride) to vial B (lyophilised pentetreotide) to obtain the product Indium (111In) pentetreotide; only the Sterican (0.90 x 70) needle supplied with the shipped patient dose should be used to remove the indium chloride from its vial.
2. Observe an incubation period of 30 minutes following the reconstitution.
3. The preparation may be diluted with 2-3 ml of 0.9% sodium chloride solution if a larger volume is desired for easier handling in the syringe.
4. The solution must be clear and colourless, this can be checked behind a lead wall containing a lead glass window. If the solution does not comply it should be discarded.
5. Use a tiny sample of this (diluted or not) volume for the quality control, which is described in the following paragraph.
6. The solution is ready for use. The solution must be used within 6 hours.

Note: for the reconstitution do not use any other 111In chloride solution than the one supplied in the same container that holds the lyophilised pentetreotide.
After reconstitution and labelling the pH of the aqueous solution is 3.8-4.3.

Instructions for quality control:
Analysis of 111In-bound peptides versus 111In-bound non-peptide compounds may be done on silicagel impregnated glass fiber strips (ITLC SG by GELMAN, cat nr.61885). Prepare a thorough dried strip, appr. 10 cm long and 2.5 cm wide by marking a starting line at 2 cm, with additional marks at 6 and 9 cm. Apply 5 to 10 l of the reconstituted and labelled solution to the starting line and develop in freshly prepared sodium citrate solution 0.1M, adjusted with HCl to pH 5. In approximately 2-3 min the front will have reached the 9 cm mark. Cut the strip at the 6 cm mark and measure the activity of both halves. Non-peptide bound 111In moves with the front. Requirement: The lower end of the chromatogram should contain > 98% of the applied activity.