^{177}Lu octreotate

^{177}Lu-[DOTA^{0}-Tyr^{3}]-Octreotate

1. Indications

Not an approved product in The Netherlands for the ^{177}Lu precursor two licensed products are currently available.

Patients with Somatostatin receptor 2 (Sstr2)-expressing neuroendocrine tumours of the gastroentero-pancreatic and bronchial tract. Also patients with phaeochromocytoma, paraganglioma, neuroblastoma or medullary thyroid carcinoma which express Sstr2 in sufficient amounts. Conditions for PRRT are mentioned in the chapter "Peptide Receptor Radionuclide Therapy using ^{177}Lu-Octreotate".

2. Preparation

Peptide and Lutetium (^{177}Lu) chloride solution are mixed and heated during 30 min at 80°C. After filtration through a 0,2 µm filter, a DTPA solution is added. The adequate amount of labelled solution (x MBq) is added to 100 ml NaCl 0,9%.

3. Quality control

After each labeling the following quality controls are performed:
Visual control: clear and colourless solution.

Labellingspercentage (incorporation)

Plate	ITLC Silica gel plate
Test solution	The preparation to be examined
Mobile phase	Sodium citratebuffer 0,1 M pH 5,0
Application	2 µl
Identification of the spots	Rf = 0-0,1 ^{177}Lu octreotate Rf = 0,9-1 ^{177}Lu
Development	Over a path of 8 cm
Drying	In air
Limits	≥99% ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate

Radiochemical purity: Chromatography (UPLC)
Limit: ≥90% of intact ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate
Mobile phase: gradient A: 0,1% TFA in water, B: MeOH 100%
Collumn: HSS C_{18} 1,8 µm, 2,1x50 mm

4. Interactions

No interaction studies have been performed with ^{177}Lu Octrotate.

Radiolabelling of carrier molecules, such as monoclonal antibodies, peptides or other substrates, with Lutetium (^{177}Lu) chloride is very sensitive to the presence of trace metal impurities.

It is important that all glassware, syringe needles etc, used for the preparation of the radiolabelled medicinal product are thoroughly cleaned to ensure freedom from such trace metal impurities. Only syringe needles (for example non-metallic) with proven resistance to dilute acid should be used to minimize trace metal impurity levels.

5. Contraindications

^{177}Lu-Octreotate is contraindicated in the following cases:

Hypersensitivity to the active substance or to any of the excipients

Established or suspected pregnancy or when pregnancy has not been excluded

6. Adverse reactions

Nausea and vomiting are the most frequent acute toxicities observed in 25% of treatments (WHO grade 1-2). Abdominal pain is observed in 10% of treatments. In most cases, the symptoms resolved within the first 24 h. Also, temporary hair loss, but no baldness (WHO grade 1) is observed in 62% of patients.

Platelet, lymphocyte and leukocyte counts as well as haemoglobin were monitored as indicators for haematological toxicity. The incidence of grade-3 and -4 haematological adverse events are summarized below:

Thrombocytopenia CTC grade-3 and -4 occurred in 29 of the 325 Dutch on-protocol patients; in 2 cases this was considered to be unrelated to ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate therapy.

Anaemia CTC grade-3 occurred in 15 of the 325 Dutch on-protocol patients; in 4 cases this was considered to be unrelated to ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate therapy. No cases of grade-4 anaemia were recorded.

Leukocytopenia CTC grade-3 and -4 occurred in 22 of the 325 Dutch on-protocol patients; in 2 cases this was considered to be unrelated to ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate therapy.

Pancytopenia was reported for 26 of the 325 Dutch on-protocol patients.

MDS was reported for 3 of the 325 Dutch on-protocol patients with median follow-up of 34 months after the last therapy. One of these cases was in the group in which bone marrow dosimetry was performed. This patient was treated with a cumulative amount of radioactivity of only 18,5 GBq (500 mCi) and the bone marrow radiation dose for this patient was 0,39 Gy. An additional MDS occurred in the 42 Dutch off-protocol patient group.

Acute leukaemia was reported for 2 of the Dutch on-protocol patients. In one it was diagnosed 3,5 years after the last ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate treatment (29,6 GBq (800 mCi) cumulative administered activity) and in the second patient it was diagnosed 7 years after the last treatment (22,2 GBq (600 mCi) cumulative administered activity).

7. Biodistribution & pharmacokinetics

The biodistribution of ^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate shows a fast clearance from the circulation with 91% of the administered radioactivity having a plasma half-life of 24 min and 8% with a plasma half-life of 4,6 h.
^{177}Lu-DOTA^{0}-Tyr^{3}-Octreotate is cleared via the kidneys; on average 69% of the radioactivity clears with a half-life of 3,0 h.

8. Stability

The shelf-life of this product is 1 year from the date of manufacture.
Store in freezer at -20°C.

9. Literature

- SmPC DOTA0-Tyr3-Octreotate, version 1;09/2012.