Swiss Summary of the Risk Management Plan (RMP)

for

Tektrotyd®

(HYNIC-[D-Phe(1), Tyr(3)-octeotridum]trifluoroacetum)

DISCLAIMER:

Marketing Authorisation Holder: Heider AG, Schöftland

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in orderto further investigate and follow the risks as well as to prevent or minimise them. The RMP summary of Tektrotyd® (x) is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the "Arzneimittelinformation/Information sur le médicament" approved and published in Switzerland, eg, by mentioning risks occurring in populations or indications not included in the Swiss authorisation.

Please note that the reference document which is valid and relevant for the effective and safeuse of medicinal products in Switzerland is the "Arzneimittelinformation/Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic.

Rotop Pharmaka GmbH is fully responsible for the accuracy and correctness of the content of thepublished summary RMP of Tektrotyd.

Tektrotyd

Risk Management Plan Summary

Active substance(s) (INN or common name):	HYNIC-[D-Phe1, Tyr3-octreotide] TFA salt, 16 µg EDDA (Etylenediamine-N-N'-diacetic acid), 10 mg
Pharmaco-therapeutic group (ATC Code):	V09IA07
Name of Marketing Authorisation Holder or Applicant:	ROTOP Pharmaka GmbH Bautzner Landstraße 400 01328 Dresden Germany
Number of medicinal products to which this RMP refers:	1
Product(s) concerned (brand name(s)):	^{99m}Tc-Tektrotyd, 16 µg, Kit for radiopharmaceutical preparation

Part VI: Summary of the risk management plan by product

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Copy table from Part I: SVIII

Summary of safety concerns	
Important identified risks	Carcinogenicity and hereditary effects due to radiation exposure
Important potential risks	Hypersensitivity reactions
	Rebound effects in case of withdrawal of therapy with somatostatin analogues
Missing Information	Safety in paediatric patients
	Safety in breastfeeding/pregnant patients

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Not applicable

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable

VI.1.4 Summary table of Risk Minimisation Measures

Safety concern	**Routine risk minimisation measures SmPC**	**Other routine risk minimasation measures**	**Additional risk minimisation measures**
Carcinogenicity and hereditary effects	Text in section 4.2 Warning in section 4.4 Listed in section 4.8 General Warning in section 6.6	● Prescription only medicine ● Radiopharmaceuticals may only be used by trained and qualified personnel with an appropriate government authorization for the use and handling of radionuclides	---
Hypersensitivity reactions	Warning in section 4.3 Warning in section 4.4	● Use restricted to physicians and medical personnel trained and qualified in the use of radiopharmaceuticals ● Use always in presence of nuclear physician, who is able to take necessary actions in case of	---

Safety concern	Routine risk minimisation measures SmPC	Other routine risk minimasation measures	Additional risk minimisation measures
		emergency	
Rebound effects in case of withdrawal of therapy with somatostatin analogues	Warning in section 4.4 Warning in section 4.5	● Prescription only medicine ● Use always in presence of nuclear physician, observing and preventing the occurrence of potential interactions	---
Safety in paediatric patients	Recommendations in section 4.2 Posology and method of administration Warning in section 4.4	● Prescription only medicine ● Use always in presence of nuclear physician	---
Safety in breastfeeding / pregnant patients	Warning and recommendations in section 4.6 Fertility, Pregnancy, Breastfeeding	● Prescription only medicine ● Use always in presence of nuclear physician	---

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Gastro-entero-pancreatic neuroendocrine tumours (GEP-NETs) are tumors of the neuroendocrine system in the gut. This is where the nervous and hormonal system interact to control the digestive organs. GEP-NETs are debilitating as they often secrete hormones that may cause severe symptoms. But even those tumours which do not over-produce hormones are not harmless as they can grow and either affect surrounding organs or metastasize to vital organs. They are life-threatening if they spread to other organs in the body.

However GEP-NETs are very rare. Less than 1% of all malignant tumours are of neuroendocrine origin. In Europe 2-5 cases are newly diagnosed in 100.000 inhabitants per year, i.e. the number of patients suffering from this disease is very low.

VI.2.2 Summary of treatment benefits

Due to the small size and the absence of characteristic symptoms of GEP-NETs they are not easy to detect.

The product TEKTROTYD is an agent to be used for an imaging method called somatostatin receptor scintigraphy. The product is used to prepare a solution for injection consisting of the radioactive element technetium (^{99m}Tc) attached to the product TEKTROTYD. The drug substance is similar to a natural hormone called somatostatin. Many receptors for the natural hormone somatostatin are found on the surface of GEP-NETs cells. Once injected into a vein, the drug substance binds to these receptors on the cells of GEP-NETs. The emitted radiation can be detected by using special cameras, which produce images of the tumour site and size.

This diagnostic procedure allows the detection of the tumour size and spread. The procedure provides information on the need for surgical and/or medical treatment.

VI.2.3 Unknowns relating to treatment benefits

In the supporting publications for the main indications nearly all patients were white Caucasians. However from the mechanism of transport and accumulation of the radiopharmaceutical there is no reason to presume that diagnostic performance would be any different in none-white patients.

Data reporting the use in paedatric/breastfeeding/pregnant patients is very limited. According to the SmPC there are no clinical data on safety and efficacy of technetium (99mTc) tektrotyd for the use in paediatric patients.

This is a consequence of the low incidence and hence sporadic occurrence in children, adolescents and breastfeeding or pregnant women. However scintigraphic localisation of neuroendocrine tumours is actually undergone in the paediatric population in daily practice.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Carcinogenicity and hereditary effects	Exposure to ionisation radiation is linked with cancer induction and a potential for development of hereditary defects. For most diagnostic investigations using a nuclear medicine procedure the effective dose is less than 20 mSv, so these adverse effects will occur with low probability. The effective dose of 20 mSv is not higher than the exposure to ionization radiation during a computer tomographic examination and is equivalent to the natural annual exposure to ionization radiation.	For each patient, exposure to ionising radiation is justified on the basis of the expected diagnostic benefit in relation to the risk from radiation exposure. The activity administered is as low as necessary to achieve the diagnostic result. The product is always used in compliance to the law regarding protective measures for the use of radioactive pharmaceuticals. Radiopharmaceuticals may be used only 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 authorized persons in designated clinical settings.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Rebound effects in case of withdrawal of therapy with somatostatin analogues	The withdrawal of therapy with somatostatin analogues as a preparatory step to scintigraphy might provoke severe adverse effects, generally of the nature of a return of the symptoms seen before this therapy was started. The nuclear medicine doctor supervising the procedure will decide, whether the withdrawal of somatostatin analogues for therapy is appropriate.
Hypersensitivitiy reaction	In patients who are allergic to TEKTROTYD (or any of the excipients) hypersensitivity (allergic) reactions may occur after injection of the medicine. Such a reaction may even evolve to an anaphylactic reaction (severe allergic reaction), which can be life-threatening.

Missing information

Risk	What is known
Safety in paediatric patients	According to the SmPC there are no data on safety and efficacy of technetium (99mTc) tektrotyd for the use in paediatric patients. This is a consequence of the low incidence and hence sporadic occurrence in children and adolescents. Because of the potential hazard of ionising radiation, technetium (^{99m}Tc) tektrotyd should not be used in children under 18 years of age, unless the value of the expected clinical information is considered to outweigh the possible risk from radiation.
Safety in breastfeeding/ pregnant patients	Radionuclide procedures carried out on pregnant women also involve radiation dose to the foetus. Only essential investigations should therefore be carried out during pregnancy, when the likely benefit far exceeds the risk incurred by the mother and foetus. Before administering radiopharmaceuticals to a mother who is breastfeeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding, and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breastfeeding should be interrupted for 24 hours and the expressed feeds discarded.

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

A post authorisation development plan will not be carried out.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
01.1	24.08.2012	---	Initial submission
01.2	17.04.2014	● Carcinogenicity and hereditary effects (identified risk) ● Hypersensitivity reactions (potential risk) ● Rebound effects in case of withdrawal of therapy with somatostatin analogues (potential risk)	Update according new pharmacovigilance legislation, GVP module V
01.3	31.08.2015	● Carcinogenicity and hereditary effects (identified risk) ● Hypersensitivity reactions (potential risk) ● Rebound effects in case of withdrawal of therapy with somatostatin analogues (potential risk) ● Safety in Paediatric Patients	Update according RMS assessment of 20.08.2015, Day 120 of the procedure
01.4	13.11.2015	● Carcinogenicity and hereditary effects (identified risk) ● Hypersensitivity reactions (potential risk) ● Rebound effects in case of withdrawal of therapy with somatostatin analogues (potential risk) ● Safety in Paediatric Patients	Update according RMS assessment of 02.11.2015, Day 180 of the procedure: Correction Module VI.1.4 Correction of the section effectiveness of risk minimisation measures Correction of the section VI.2.3