VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Neuroendocrine tumours (NETs) are neoplasms of the 'neuroendocrine system' in the gut. This is where the nervous and hormonal systems interact to control the digestive organs. 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 metastasise to vital organs. They are life-threatening if they spread to other organs in the body.

However NETs are very rare. Less than 1% of all malignant tumors 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, although the prevalence of the disease is increasing.

VI.2.2 Summary of treatment benefits

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 a radioactive element, technetium (^{99m}Tc), attached to the product Tektrotyd, which is similar to a natural hormone called somatostatin. Many receptors for the natural hormone somatostatin are found on the surface of NETs cells. Once injected into a vein, ^{99m}Tc-Tektrotyd binds to these receptors on the cells of NETs. The emitted radiation can be detected by special cameras allowing the tumour diagnosis.

Due to the small size and the absence of characteristic symptoms of NETs they are difficult to detect. The efficiency of medical and surgical treatment for therapy of NET depends on the successful pre-treatment tumour location.

The identification and localization of neuroendocrine tumors may be carried out by scintigraphic technique after administration of Tektrotyd labeled with ^{99m}Technetium.

Using ^{99m}Tc-Tektrotyd for the diagnosis of neuroendocrine tumours leads to a high tumour detection rate. It allows the detection of the tumour size and spread and predicts which treatment is likely to be the most promising.

Scintigraphy with ^{99m}Tc-Tektrotyd with the option of radio-guided surgery improves the efficacy of the treatment of NETs and contributes to the selection of optimal accessible therapeutic procedure.

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.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Carcinogenity 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 20mSv 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	Like all medicines, Tektrotyd can potentially cause

Risk	What is known (Including reason why it is considered a potential risk)
	hypersenstitivity reactions, although no case has been reported.

Risk	What is known (Including reason why it is considered a potential risk)
Inhibition of glucagon secretion	Octreotide inhibits secretion of growth hormone, glucagon, and insulin what may affect glucose regulation. Postprandial glucose tolerance may be impaired and hypoglycaemia has also been reported. Octreotide, because of its greater relative potency in inhibiting the secretion of GH and glucagon than that of insulin, and because of the shorter duration of its inhibitory action on insulin, may increase the depth and prolong the duration of hypoglycaemia in patients with insulinomas. These patients should be closely monitored during initiation of octreotide therapy and at each change of dosage. Due to possible inhibition of hyperglycaemic hormones, insulin requirements of patients with type I diabetes mellitus may be reduced by administration of octreotide. In turn, in non-diabetics and type II diabetics with partially intact insulin reserves, octreotide administration can result in postprandial increases in glycaemia. ^{99m}Tc-EDDA/HYNIC-TOC retains high specific binding to somatostatin receptors capability similar to that of the unlabelled peptide conjugates. Therefore, although the dose of HYNIC-Tyr^3-octreotide injected with ^{99m}Tc-Tektrotyd is significantly lower than that used for octreotide therapy, caution should be exercised when administering this medicinal product to patients with diabetes mellitus and more frequent monitoring of glucose level can be recommended in these patients.

Missing information

There is no missing information

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
Not applicable			Initial submission