VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Radioactive iodine I-131 is used diagnostically to evaluate potential problems with the thyroid gland and as a therapeutic treatment of thyroid diseases, i.e. increased activity of the thyroid gland (Graves' disease) and enlargement of the thyroid gland (toxic multinodular goitre or autonomous nodules) and thyroid cancer.

Hyperthyroidism
The most common causes of hyperthyroidism are Graves' disease, followed by toxic multinodular goitre, whilst rarer causes include an autonomously functioning thyroid adenoma, or thyroiditis.

The incidence data available for overt hyperthyroidism in men and women from large population studies are comparable, at 0.4 per 1000 women and 0.1 per 1000 men, but the age-specific incidence varies considerably. The only available data in a black population, from Johannesburg, South Africa, also suggest a 10-fold lower annual incidence of hyperthyroidism (0.09 per 1000 women and 0.007 per1000 men) than in whites.[(1)]

Thyroid Cancer
Thyroid cancer is a cancerous tumour or growth in the thyroid gland. Cancer of the thyroid is more common in women than in men — almost three times as many women as men get thyroid cancer. Thyroid cancer strikes people at a younger age than most other cancers — most patients are between 20 and 54 years old. There is a twofold to fourfold higher incidence of new thyroid cancer cases in women than in men. [(2)] In Europe, thyroid cancer affects approximately 24,826 individuals annually, with an estimated mortality rate of 5,993 patients each year. [(3)]

The International Agency for Research on Cancer (IARC), which is part of the World Health Organization (WHO), estimates 24,800 new diagnoses of thyroid cancer in the European Countries in 2000. Although this cancer often has a good prognosis, it is estimated that approximately 3,890 European women and 2,103 European men may have died from thyroid cancer in the year 2000. [(4)]

VI.2.2 Summary of treatment benefits

Diagnostic Use of Radioactive Iodine
Radioactive I-131 is used extensively in *in vivo* diagnosis. The diagnostic implementations with I-131, like evaluation of thyroid functions (uptake), determination of the functionality of thyroid nodules (thyroid scintigraphy), evaluation of the thyroid tissue and metastasis in thyroid cancers (complete body scan) are very important as a guide in deciding on the therapy later on.
The procedures regarding diagnosis with radioactive I-131 has been published as guides by various Nuclear Medicine Groups and has become a part of routine practice over many years.

The radioiodine test has made it possible to measure the thyroid activity, directly and accurately. Moreover, it is used successfully in the treatment of certain types of thyroid cancers like tritoxicosis.

Therapeutic Use of Radioactive Iodine

The primary mechanism of action of radioactive iodine treatment is the concentration of iodine in the thyroid gland and inhibition of the follicular cell functions by impairment through radiation. It has beeen used since 1942 on more than one million patients, providing them with a simple, safe, cheap and effective treatment.

Radioiodine therapy is a well accepted therapy for hyperthyroidism and carcinoma of the thyroid. The dose of ^{131}I administered to the patients depends on the extent and type of the disease and can range from a few mCi to few hundred mCi.

VI.2.3 Unknowns relating to treatment benefits

Not applicable.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Radiation exposure	Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary effects. The radiation dose resulting from therapeutic exposure may result in higher incidence of cancer and mutations. In all cases it is necessary to ensure that the risks of the radiation are less than those of the disease itself. The radiation dose delivered (EDE) after therapeutic doses of sodium iodide I-131 is higher than 20 mSv.	Yes, by taking protective measures, handling and using the product according to instructions and following local regulations. Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisation.
Patients with dysphagia, oesophageal stricture, oesophageal stenosis, oesophagusdiverticulum, active gastritis, gastric	Product is contraindicated in patients with dysphagia, oesophageal stricture, oesophageal stenosis, oesophagusdiverticulum, active gastritis, gastric erosions and peptic ulcer.	No. Product is contraindicated in these patients.

erosions and peptic ulcer.		
Patients with suspected reduced gastrointestinal motility.	Product is contraindicated in patients with suspected reduced gastrointestinal motility.	No. Product is contraindicated in these patients.
Use in pregnancy and lactation.	Pregnancy The use of Sodium iodide I-131 is contraindicated during established or suspected pregnancy or when pregnancy has not been excluded, due to transplacental passage of sodium iodide I-131 which can cause severe and possibly irreversible hypothyroidism in neonates (the absorbed dose to the uterus for this medicinal product is likely to be in the range 11-511 mGy, and the foetal thyroid gland avidly concentrates iodine during the second and third trimesters). Should differentiated thyroid carcinoma be diagnosed during pregnancy, radioactive iodine treatment must be postponed until after the pregnancy. Breastfeeding Before administering radiopharmaceuticals to a mother who is breast-feeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding, and what is the most appropriate choice of radiopharmaceutical, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be discontinued after Sodium Iodide I-131 administration.	No. Product is contraindicated in these patients.
Frequently occurring adverse reactions; Hypothyroidism, leukemia, bone marrow suppression.	Frequently occurring adverse reactions are: hypothyroidism, transient hyperthyroidism, salivary and lacrimal gland disorders, and local radiation effects. In cancer treatment additionally gastro-intestinal adverse reactions and bone marrow suppression may frequently occur.	No. However, in order to reduce the frequency of the salivary gland inflammation, salivary glands can be stimulated by eating or drinking

	Thyroid and parathyroid gland disorders: Dose dependent hypothyroidism may occur as a late consequence of radioiodine treatment of hyperthyroidism. This may manifest itself weeks or years after treatment, requiring suitable timed measurement of thyroid function and appropriate thyroid replacement. Hypothyroidism is generally not seen until 6-12 weeks after sodium iodide I-131 administration. In treatment of malignant disease hypothyroidism is frequently reported as an adverse reaction, which, however, is being accounted for by the preceding thyroidectomy. The destruction of thyroid follicles caused by the radiation exposure of sodium iodide [^{131}I] may lead to exacerbation of an already existing hyperthyroidism after 2 – 10 days or even to thyrotoxic crisis. Occasionally, an immune hyperthyroidism may develop after initial normalisation (latency period 2 – 10 months). With high dose radioiodine treatment, the patient may experience transient inflammatory thyroiditis and tracheitis 1-3 days after administration, with a possibility of severe tracheal constriction, especially where there is existing tracheal stenosis. In rare cases, a temporary hyperthyroidism could be found even after treatment of functional thyroid carcinoma. Cases of transient hypoparathyroidism have been observed after radioiodine; they must be monitored accordingly and treated with replacement therapy *Bone marrow depression:* As a late consequence, reversible bone marrow depression may develop, presenting with isolated thrombocytopenia or	acidic foods.

	erythrocytopenia which may be fatal. Bone marrow depression is more likely to occur after one single administration of more than 5000 MBq, or after repeat administration in intervals below 6 months. *Secondary malignancies* After higher activities, typically those used in the treatment of thyroid malignancies, an increased incidence of leukaemia has been observed. There is also evidence for an increased incidence of secondary solid cancers at high activities (more than 7.4 GBq).	

Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Potential for hypersensitivity or anaphylactic reactions	In patients with known hypersensitivity for gelatine and/ or its metabolites the use of sodium iodide [^{131}I] solution should be preferred for radioiodine treatment.
Use in significant renal impairment (increased radiation exposure)	The therapeutic administration of 131I capsules in patients with significant renal impairment, in which an activity adjustment is necessary, requires special attention.
Fertility impairment	After radioiodine therapy of thyroid carcinoma, a dose dependent impairment of fertility may occur in men and women. Depending on the activity dose, a reversible impairment of the spermatogenesis could be verified in doses above 1850 MBq; clinical relevant effects including oligospermia and azoospermia and elevated serum FSH levels have been described after administration greater than 3700 MBq.
Interaction with other medicinal products and other forms of interaction (reduced thyroid uptake of (^{131}I) iodide)	Many pharmacologically active substances are known to interact with radioiodide. These may happen by a variety of mechanisms which can affect the protein binding, the pharmacokinetics or influence the dynamic effects of labelled

	iodide. As a consequence, it should be considered that the thyroid uptake might be reduced. It is therefore necessary to take a full drug history and ascertain whether any medicinal products are required to be withheld prior to the administration of sodium iodide I-131.

Missing information

Risk	**What is known**
Not available	Not available

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

Not applicable.

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

Not applicable.