Summary of Risk Management Plan for MADDACOL

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Rationale for submitting an update of the summary RMP: periodic 2022 update, submission of document for AIFA request.

Summary of significant changes in this RMP: no changes.

QPPV name: Dott. Fabio Geremia

QPPV signature: 

Table of contents

Summary of the risk management plan 4

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This is a summary of the risk management plan (RMP) for MADDACOL. The RMP details important risks of MADDACOL, how these risks can be minimised and how more information will be obtained about MADDACOL risks and uncertainties.

MADDACOL summary of product characteristics (SPC) and its package leaflet give essential information to healthcare professionals and patients on how MADDACOL should be used.

Important new concerns or changes to the current ones will be included in updates of MADDACOL RMP.

I - Medicinal product and what it is used for:

The product MADDACOL (Fluoromethylcholine (^{18}F)) is a positron emission radiopharmaceutical, detectable by Positron Emission Tomography, PET.

[^{18}F]-Fluoromethylcholine chloride is a choline analogue (precursor to phospholipid biosynthesis). Choline is transported across the cell membrane by specific carriers and is phosphorylated by the enzyme choline kinase. Subsequently, phosphorylcholine is converted to cytidine-diphosphate-choline [(CDP)-choline] and there is incorporation of phosphatidylcholine, which is a component of the cell membrane. The over expression of choline kinase and its increased enzymatic activity has been observed in prostate carcinoma, this explains the increased accumulation of [^{18}F]-Fluoromethylcholine in tumor cells.

Current Therapeutic indications:
Medication for diagnostic use only. The use of fluorocholine (^{18}F) chloride is indicated in positron emission tomography (PET).
MADDACOL is used for imaging in patients undergoing oncologic diagnosis and not for the description of organ function or metabolism based on the rationale of increased choline influx into specific organs or tissues.

The following indications for PET with [18F]-Fluoromethylcholine chloride have been sufficiently documented:

Prostate cancer
In staging, for the search for any distant metastases, in the biochemical recurrence of the disease after first-line therapies (BR) and in patients resistant to hormone castration (mCRPC)

Study of the Parathyroid Glands
In primary hyperparathyroidism, recognition and preoperative localization of adenomas single or glandular hyperplasia with previous non-diagnostic imaging (scintigraphy with sestamibi or inconclusive MRI). Staging of disease in patients with cancer of the parathyroid glands.

Hepato-Cellular Carcinoma (HCC):
- Characterization of lesions with radiological features of HCC
- Localization of well-differentiated hepatocellular carcinoma lesions.
- In addition to PET with FDG, characterization of liver nodules and/or staging of ascertained
- very likely hepatocellular carcinoma, when PET with FDG is inconclusive or when surgery or transplant is planned

- Evaluation of the response to local HCC treatments (radioembolization with 90Y microspheres, thermal ablation etc.)

II - Risks associated with the medicine and activities to minimise or further characterise the risks:

Safety concern	Risk minimisation measures	Pharmacovigilance activities
Important identified risks		
Reactions around point of injection (local tolerance)	Routine risk minimisation measures: notes in the SPC, use of the product by professional physicians	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection
Hypersensitivity (allergy)	Routine risk minimisation measures: notes in the SPC, use of the product by professional physicians	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection
Important potential risks		
Injection of the medicine outside of a vein (extravasation)	Routine risk minimization measures: notes in the SPC, use of the product by professional physicians	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection
Risk due to contact with radiation (carcinogenic and hereditary risk)	Routine risk minimization measures: notes in the SPC, use of the product by professional physicians	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection
PET scan interpretation errors	Routine risk minimization measures: use of the product by professional physicians and training of PET scan readers with educational material	Not applicable

No additional risk minimization measures are needed.

II.A – List of important risks and missing information:

Important identified risks - Reactions around point of injection (local tolerance) - Hypersensitivity (allergy)
Important potential risks - Risk due to contact with radiation (carcinogenic and hereditary risk) - Injection of the medicine outside of a vein (extravasation) - PET scan interpretation errors
Missing information - Safety in patients with reduced kidney function - Safety in patients with reduced liver function - Safety in patients pediatric patients

II.B – Summary of important risks:

The safety information in the proposed Product Information is aligned to the reference medicinal product.

II.C Post-authorisation development plan

Not applicable. There are no studies required for MADDACOL.

II.C.1 Studies which are conditions of the marketing authorisation

Not applicable. There are no studies which are conditions of the marketing authorisation or specific obligation of MADDACOL.

II.C.2 Other studies in post-authorisation development plan

Not applicable. There are no studies required for MADDACOL.