VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

XENETIX is an iodine-containing medicine which is intended for use in CT scans. It may be used in patients of all ages and all conditions (from the very healthy to patients with multiple diseases). There are no restrictions on its use expect for patients with hypersensitivity to iobitridol (the active ingredient in Xenetix), patients who have overactive thyroid glands or female patients who are pregnant who require certain types of x-ray investigation of their uterine cavity and fallopian tubes.

As XENETIX has a very wide target patient population, patients receiving Xenetix may also be taking concomitant medications or have other disorders or diseases in addition to the ones requiring investigation with Xenetix.

VI.2.2 Summary of treatment benefits

The efficacy of Xenetix as a contrast agent has been evaluated extensively both during pre-clinical and clinical development.

The number and size of clinical trials involving of Xenetix as a contrast agent in various kind of X-ray examination is listed below:

- Intravenous urography
    - 5 comparator (iohexol, iopromide, iopamidol) studies sponsored by Guerbet (420 patients)
- Brain and whole body CT
    - 7 comparator (iohexol, iopromide) studies sponsored by Guerbet (619 patients)
- Intravenous and intra-arterial DSA
    - 2 comparator (iohexol, iopromide) studies sponsored by Guerbet (160 patients)
- Angiocardiography
    - 5 comparator (iohexol, iopamidol, iopromide) studies sponsored by Guerbet (750 patients)
    - 1 non-comparator study sponsored by Guerbet (351 patients)
- Venography
    - 1 comparator (iohexol) study sponsored by Guerbet (70 patients)
- Arteriography

- 7 comparator (iohexol, iopromide, iopamidol) studies sponsored by Guerbet (380 patients)
- Arthrography
  - 1 comparator (ioxaglate) study sponsored by Guerbet (186 patients)
- Hysterosalpyngography
  - 1 comparator (ioxaglate) study sponsored by Guerbet (181 patients)

In these studies, the proportion of Xenetix images considered good or excellent quality was at least 70% with no images classified as poor or fair. The proportion of Xenetix images that contributed to the diagnosis or provided all the diagnostic information necessary was at least 87%.

Xenetix was compared in the above studies to a range of other iodinated contrast agents (iohexol, iopamidol, iopromide and ioxaglate). In all studies there were no significant differences in efficacy between Xenetix and these agents.

VI.2.3 Unknowns relating to treatment benefits

XENETIX has been used for a long time in a range of CT procedures and for a wide variety of patients (both sexes, and from children to the elderly). The efficacy and safety profile of XENETIX have been demonstrated in a general population of more than 163,700 patients.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Cardiac disorders either on their own or along with hypersensitivity: Cardiac arrest (blood flow ceasing because the heart is not contracting properly) Myocardial infarction (injury to the heart muscle because it is not receiving enough blood) particularly after injection of Xentix into the coronary artery Angina pectoris (chest pain caused by the heart muscle not receiving enough oxygen) Arrhythmia (change in the frequency of heartbeat, change in the rhythm of heartbeat) the body)	Change in the frequency of heartbeat or change in the rhythm of heartbeat may occur following the use of iobitridol: Frequency: Very rare	Do not use the product in patients with a high risk for changes in the frequency and rhythm of heartbeat. Careful weighing up of the benefits and risks. All equipment and drugs necessary to counter any cardiac disorder which may occur should be made ready for use beforehand
Leakage of Xenetix from the injection site (Extravasation). Any injuries as a result are likely to be	Leakage from the injection site may occur following the use of	Use of correct technique by healthcare professionals when

Risk	What is known	Preventability
minor, but severe injuries may occur and include: Skin ulceration Death of the surrounding tissue (tissue necrosis) Insufficient blood to supply reaching the affected area (compartment syndrome).	iobitridol: Frequency: very rare to rare	administering Xenetix, and checking the injection site prior to, during and after the injection of XENETIX

Important missing information

Risk	What is known (Including reason why it is considered a potential risk)
Birth defects (Use in pregnant women)	Xenetix is unlikely to have any effect on an unborn child, but there is no sufficient data available in exposed human pregnancies to confirm this. Xenetix should be used during pregnancy only if the benefit to the mother justifies the potential risk to the foetus. Furthermore, exposure to radiation from x-rays and CT scans during pregnancy should be avoided as much as possible

VI.2.5 Summary of additional 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.

The Summary of Product Characteristics and the Package leaflet for XENETIX can be found in the product's EPAR page.

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

Version	Date	Safety Concerns	Comment
1	3 October 2011	Cardiac disorders in and out a context of hypersensitivity: cardiac arrest, myocardial infarction (more frequent after intracoronary injection), angina pectoris, arrhythmia (including ventricular fibrillation and Torsade de Pointes) Teratogenicity	Creation of RMP following PSUR assessment report from 3-Year PSUR evaluation; signal of cardiovascular risk

Version	Date	Safety Concerns	Comment
2	6 February 2012	Cardiac disorders in and out a context of hypersensitivity: cardiac arrest, myocardial infarction (more frequent after intracoronary injection), angina pectoris, arrhythmia (including ventricular fibrillation and Torsade de Pointes) Teratogenicity	No new information Reformat according to volume 9A requirements and EU Template for RMP Presentation of risks by categories (identified, potential and missing information)
3	25 April 2013	Cardiac disorders in and out a context of hypersensitivity: cardiac arrest, myocardial infarction (more frequent after intracoronary injection), angina pectoris, arrhythmia (including ventricular fibrillation and Torsade de Pointes) Extravasation Teratogenicity	Inclusion of extravasation in identified risk Update of RMP format
4	01May2015	Cardiac disorders in and out a context of hypersensitivity. Extravasation Allergic/hypersensitivity/anaphylactic type reacions Contrast induced nephropathy Bronchospasm/ Asthma Dysthyroidism Throbmotic vascular events Acute pancreatitis (after ERCP) Thrombophlebitis Use in pregnant women	Inclusion of: Allergic/hypersensitivity/anaphylactic type reacions, Contrast induced nephropathy, Bronchospasm/ Asthma, Dysthyroidism, Throbmotic vascular events, Acute pancreatitis (after ERCP), Thrombophlebitis, Use in pregnant women