PRODUCT MONOGRAPH

DRAXIMAGE® Xenon Xe 133

Xenon Xe 133, USP

Agent for the Study of Pulmonary Function and Cerebral Blood Flow

Gas for Inhalation
370 MBq/vial
740 MBq/vial

Diagnostic Use
ATC Code: V09EX03

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Date of Revision:
October 29, 2010
Control #

Control #: 142989

Date of Approval: December 31, 2010

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Inhalation	Gas of 370 MBq/vial Gas of 740 MBq/vial	None *For a complete listing see Dosage Forms, Composition and Packaging section.*

DESCRIPTION

DRAXIMAGE® Xenon Xe 133 is a carrier-free radioactive gas in air, suitable for inhalation in pulmonary ventilation studies. Greater than 99.5 % of the activity is Xe-133 with less than 0.01 % of the activity associated with Iodine I-131. Pressure in the vial is less than atmospheric.

Physical Characteristics
Xenon-133 is produced by fission of uranium-235 and decays with a physical half-life of 5.24 days by beta emission to stable cesium-133.[1] The 81.0 keV gamma ray listed in Table 1 is useful for detection in imaging studies.

Table #1 - Principal Radiation Emission Data

Radiation	Mean % per Disintegration	Mean Energy (keV)
Gamma-2	37.1	81.0
X-ray Kß	8.8	35.0
X-ray $K\alpha_1$	24.7	31.0
X-ray $K\alpha_2$	13.3	30.6
Total Beta	100.0	100.3
Conversion electron L-gamma 2	8.5	75.3
Conversion electron K-gamma 2	52.0	45.0

To correct for physical decay of this radionuclide, the fractions that remain at selected intervals from the time of calibration are shown in Table 2.

Table #2 - Physical Decay Chart of Xenon Xe-133

Half-Life: 5.24 Days					
Days	Fraction Remaining	Days	Fraction Remaining	Days	Fraction Remaining
-4	1.697	5	0.516	14	0.157
-3	1.487	6	0.453	15	0.138
-2	1.303	7	0.397	16	0.121
-1	1.141	8	0.347	17	0.106
0*	1.000	9	0.304	18	0.093
1	0.876	10	0.267	19	0.081
2	0.768	11	0.234	20	0.071
3	0.673	12	0.205	21	0.062
4	0.589	13	0.179		

* Calibration Time

External Radiation

The exposure rate constant for Xe-133 is 3.3 $\mu C \cdot kg^{-1} \cdot MBq^{-1} \cdot h^{-1}$ (0.50 R/mCi-hr) at 1 cm. The first half-value thickness of lead (Pb) is 0.0036 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from the interposition of various thicknesses of Pb is shown in Table 3. For example, the use of 0.203 cm of lead will attenuate the radiation emitted by a factor of about 1,000.

Table #3 - Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.0036	0.5
0.0366	10^{-1}
0.120	10^{-2}
0.203	10^{-3}
0.286	10^{-4}

Data supplied by Oak Ridge Associated Universities, Radiopharmaceutical Internal Dose Information Center, Oak Ridge, TN, 1987.

INDICATIONS AND CLINICAL USE

DRAXIMAGE® Xenon Xe 133 (Xenon Xe 133, USP) is indicated for:

- Evaluation of pulmonary function
- Imaging the lungs by means of inhalation studies
- Assessment of cerebral blood flow

The product should be administered under the supervision of a qualified health professional who is experienced in the use of radiopharmaceutical products.

Geriatrics: No data is available.

Pediatrics: No data is available.

CONTRAINDICATIONS

- Hypersensitivity to this agent.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.
- The content of the vial is radioactive and therefore adequate shielding of the radiopharmaceutical must be maintained.

General

The product should be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

The radiopharmaceutical product may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of local competent official organizations.

Exhaled Xenon Xe 133, USP should be controlled in a manner that is in compliance with the appropriate regulations of the government agency authorized to license the use of radionuclides.

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

Xenon Xe 133, USP delivery systems, i.e., respirators or spirometers, and associated tubing assemblies must be leak-proof to avoid loss of radioactivity into the laboratory environs not specifically protected by exhaust systems.

Xenon Xe 133, USP adheres to some plastics and rubber and should not be allowed to stand in tubing or respirator containers, for such unrecognized loss of radioactivity from the dose for administration may render the study non-diagnostic.

Carcinogenesis and Mutagenesis

No long term animal studies have been performed to evaluate carcinogenic or mutagenic potential in males or females.

Sexual Function/Reproduction
No adequate reproduction studies have been performed on animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse effects on the fetus.

Special Populations

Pregnant Women: Ideally examinations using radiopharmaceuticals, especially those elective in nature of women of childbearing capability should be performed during the first ten days following the onset of menses. This radiopharmaceutical preparation should not be administered to pregnant women unless it is considered that the benefits to be gained outweigh the potential hazards.

Nursing Women: It is not known if this agent is excreted in the human milk. Where an assessment of the risk/benefit ratio suggests the use of this product in lactating mothers, nursing should be stopped.

Pediatrics: Adequate studies do not exist to support the use of this radiopharmaceutical in pediatric patients. The benefit to risk ratio should be assessed before consideration is given to the use of this product in this age group.

Geriatric: No data is available. The benefit to risk ratio should be assessed before consideration is given to the use of this product in this age group.

ADVERSE REACTIONS

Adverse Drug Reaction Overview
To date, no adverse reaction specifically attributable to the use of Xenon Xe 133, USP has been reported.

DRUG INTERACTIONS

Overview
None known.

Drug-Drug Interactions
None known.

Drug-Food Interactions
Interactions with food have not been established.

Drug-Herb Interactions
Interactions with herbal products have not been established.

Drug-Laboratory Interactions
Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Dosing Considerations
None

Dosage
The suggested activity range to be employed for the average (70 kg) adult patient is:
- 74 to 740 MBq (2 to 20 mCi) for evaluation of pulmonary function by inhalation;
- 74 to 740 MBq (2 to 20 mCi) for imaging the lungs by inhalation;
- 370 to 1,110 MBq (10 to 30 mCi) for assessment of cerebral blood flow.

There are no recommendations available for pediatric and geriatric populations.

Administration
Xenon Xe 133, USP is administered by *inhalation only* from closed respirator systems or spirometers. The patient dose should be measured by a suitable radioactivity calibration system prior to administration.

Image Acquisition and Interpretation
Ventilation imaging is performed as the patient inhales the radioactive xenon. Successive images are obtained while the patient holds his or her breath (single-breath-hold image) and during various phases of breathing (rebreathing and washout from lungs).

Instructions for Preparation and Use
DRAXIMAGE® Xenon Xe 133 is ready for diagnostic use by inhalation administration.

The vial is designed to be used with most delivery systems available. Maintain adequate shielding around the vial during the useful life of the radioactive product.

Directions for Quality Control
None required.

RADIATION DOSIMETRY

The estimated absorbed radiation doses[2] to various organs of an average adult (70 kg) for a single breath study and an equilibrium breathing study are shown in Table 4.

Table #4 - Estimated Absorbed Radiation Doses in Adult

Organ	With Single Inhalation (30 sec breath-hold)		With Inhalation (rebreathing from closed spirometer)			
			For 5 minutes		For 10 minutes	
	mGy/ MBq	rad/ mCi	mGy/ MBq	rad/ mCi	mGy/ MBq	rad/ mCi
Lungs	0.00077	0.0029	0.0011	0.0041	0.0012	0.0044
Bone surfaces	0.00012	0.00044	0.00080	0.0030	0.0013	0.0048
Breast	0.00012	0.00044	0.00083	0.0031	0.0014	0.0052
Red marrow	0.00012	0.00044	0.00084	0.0031	0.0014	0.0052
Small intestine	0.00011	0.00041	0.00074	0.0027	0.0012	0.0044
Large intestine wall (upper)	0.00011	0.00041	0.00074	0.0027	0.0012	0.0044
Large intestine wall (lower)	0.00011	0.00041	0.00074	0.0027	0.0012	0.0044
Liver	0.00011	0.00041	0.00073	0.0027	0.0012	0.0044
Pancreas	0.00011	0.00041	0.00074	0.0027	0.0012	0.0044
Spleen	0.00011	0.00041	0.00073	0.0027	0.0012	0.0044
Uterus	0.00011	0.00041	0.00074	0.0027	0.0012	0.0044
Adrenals	0.00010	0.00037	0.00071	0.0026	0.0012	0.0044
Bladder wall	0.00010	0.00037	0.00073	0.0027	0.0012	0.0044
Stomach wall	0.00010	0.00037	0.00072	0.0027	0.0012	0.0044
Kidneys	0.00010	0.00037	0.00072	0.0027	0.0012	0.0044
Ovaries	0.00010	0.00037	0.00073	0.0027	0.0012	0.0044
Testes	0.000099	0.00037	0.00069	0.0026	0.0011	0.0041
Thyroid	0.000099	0.00037	0.00069	0.0026	0.0011	0.0041
Other tissue	0.00010	0.00037	0.00070	0.0026	0.0012	0.0044
Effective Dose	0.00019 mSv/MBq 0.00070 rem/mCi		0.00080 mSv/MBq 0.0030 rem/mCi		0.0013 mSv/MBq 0.0048 rem/mCi	

OVERDOSAGE

None known.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Not applicable.

Pharmacodynamics
Not applicable.

Pharmacokinetics
Xenon-133 is a chemically inert and pharmacologically inactive gas at the concentrations used for diagnostic studies. It is neither a natural product of the body, nor is it utilized.

Absorption: Xenon Xe 133, USP is readily diffusible, passing through cell membranes and exchanging between blood and tissue. It has limited solubility in aqueous media, exhibiting a preferential solubility in body fats over blood or plasma. Xenon Xe 133, USP will cross the alveolar wall after inhalation, and will enter the venous circulation via the pulmonary capillary bed.

Distribution: Following a single breath, Xenon Xe 133, USP distributes through the lungs and the blood stream.

Metabolism: Not applicable.

Excretion: Following a single breath, the majority of the Xenon Xe 133, USP that enters the blood stream will be quickly returned to the lungs and will be exhaled. Xenon Xe 133, USP is eliminated by the lungs into the expired air with a biological half-life of about 5 minutes.

Special Populations and Conditions
None

STORAGE AND STABILITY

Store at room temperature with proper radiation shielding. The expiry date is 20 days from the date of manufacture.

SPECIAL HANDLING INSTRUCTIONS

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

The residual materials may be discarded in the ordinary trash, provided the radioactivity in the vials and syringes measures no more than background with an appropriate low-range survey meter. All identifying labels should be destroyed before discarding.

DOSAGE FORMS, COMPOSITION AND PACKAGING

DRAXIMAGE® Xenon Xe 133 is a carrier-free radioactive gas in air, suitable for inhalation in pulmonary ventilation studies. Greater than 99.5 % of the activity is Xe-133 with less than 0.01 % of the activity associated with Iodine I-131. Pressure in the vial is less than atmospheric.

There is no clinically relevant non medicinal ingredient related to this product.

DRAXIMAGE® Xenon Xe 133 (Xenon Xe 133, USP) is ready for diagnostic use by inhalation administration and is available in 3 mL single-dose vials containing either 370 or 740 MBq per vial.

Product No. 502740

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PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Xenon-133

Chemical name: Xenon-133

Molecular formula and molecular mass: Xe, 133 g/mol

Structural formula: None

Physicochemical properties: A colorless, odorless, tasteless, inert and radioactive gas.

Product Characteristics

DRAXIMAGE® Xenon Xe 133 for diagnostic use is a colorless, odourless, tasteless, relatively inert, monoatomic gas.

CLINICAL TRIALS

Not applicable

DETAILED PHARMACOLOGY

Not applicable

TOXICOLOGY

Not applicable

REFERENCES

1. Martin, M. J., Nuclear Decay Data for Selected Radionuclides, ORNL-5114. Oak Ridge National Laboratory, Oak Ridge, Tennessee, March 1976.
2. Data based on the International Commission on Radiological Protection (ICRP) Publication 53 – Radiation dose to patients from radiopharmaceuticals, 1987.

PART III: CONSUMER INFORMATION

DRAXIMAGE® Xenon Xe 133
Xenon Xe 133, USP

This leaflet is part III of a three-part "Product Monograph" published when DRAXIMAGE® Xenon Xe 133 was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about DRAXIMAGE® Xenon Xe 133. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
- Diagnosis of lung disease;
- Assessment of cerebral blood flow.

The product should be administered under the supervision of a qualified health professional who is experienced in the use of radiopharmaceutical products.

What it does:
When very small doses of xenon-133 are given, the radioactivity is taken up by the lungs and can cross the blood-brain barrier. An image of the lungs or brain on film or on computer screen can be provided to help with the diagnosis.

When it should not be used:
DRAXIMAGE® Xenon Xe 133 is contraindicated in patients who are hypersensitive to this agent.

What the medicinal ingredient is:
Xenon-133

What the important nonmedicinal ingredients are:
None
For a full listing of nonmedicinal ingredients see Part 1 of the product monograph.

What dosage form it comes in:
Each 3 mL unit dose vial of DRAXIMAGE® Xenon Xe 133 contains 370 or 740 MBq/vial of Xenon-133.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions
- Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to licence the use of radionuclides.

BEFORE you receive DRAXIMAGE® Xenon Xe 133 talk to your doctor or pharmacist if:
- You are a woman of childbearing capability (examination should be performed during the first ten days following the onset of menses).
- You are a nursing woman (formula feeding should be substituted for breast feeding).
- You are hypersensitive to this agent.

INTERACTIONS WITH THIS MEDICATION

No known drugs are known to interact with DRAXIMAGE® Xenon Xe 133 by interfering with the uptake of Xenon-133.

PROPER USE OF THIS MEDICATION

DRAXIMAGE® Xenon Xe 133 will be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

None known.

If you have any unexpected effects after receiving DRAXIMAGE® Xenon Xe 133, contact your doctor or pharmacist.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345
toll-free fax: 866-678-6789
By email: cadrmp@hc-sc.gc.ca

By regular mail:
National AR Centre
Marketed Health Products Safety and Effectiveness
Information Division
Marketed Health Products Directorate
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:
http://www.draximage.com/catalogue-can.html
or by contacting the sponsor, Jubilant DraxImage Inc.. at:
1-800-361-2356

The HPFB (BGTD and TPD) website:
http://www.hc-sc.gc.ca/hpfb-dgpsa/tpd-dpt/index_e.html
Sponsor website: http://www.draximage.com

This leaflet was prepared by Jubilant DraxImage Inc.

Last revised: October 29, 2010.