Technescan™ HDP Kit for the Preparation of Technetium Tc 99m Oxidronate

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AUSTRALIAN PRODUCT INFORMATION TECHNESCAN™ HDP (OXIDRONATE) POWDER FOR INJECTION

1 NAME OF THE MEDICINE

Sodium oxidronate.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Technescan™ HDP is a Kit for the Preparation of Technetium Tc 99m Oxidronate, a diagnostic radiopharmaceutical agent.

Technescan HDP is supplied as a sterile, non-pyrogenic, lyophilised powder, packaged under nitrogen, in vials for intravenous administration after reconstitution with additive-free Sodium Pertechnetate Tc 99m. Each vial contains 3.15 mg oxidronate sodium.

For the full list of excipients, see section **6.1 LIST OF EXCIPIENTS**.

Physical Characteristics
Technetium Tc 99m decays by isomeric transition with a physical half-life of 6.02 hours.[1] The principal photon that is useful for detection and imaging is listed in **Table 1**.

Table 1. Principal Radiation Emission Data[1]

Radiation M	Mean Percent/ Disintegration	Energy (keV)
Gamma-2	89.07	140.5

External Radiation
The specific gamma ray constant for Technetium Tc 99m is 0.2108 mGy at 1 cm. The first half-value thickness of lead (Pb) for Technetium Tc 99m is 0.017 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in **Table 2**.

Table 2. Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10^{-1}
0.16	10^{-2}
0.25	10^{-3}
0.33	10^{-4}

To correct for physical decay of the radionuclide, the fractions that remain at selected time intervals after the time of calibration are shown in **Table 3**.

Table 3. Physical Decay Chart: Technetium Tc 99m, Half-life 6.02 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

*Calibration Time

3 PHARMACEUTICAL FORM

Powder for Injection.
Technescan HDP is a white lyophilised powder in a glass vial intended for intravenous injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Technescan HDP is a diagnostic skeletal imaging agent used to demonstrate areas of altered osteogenesis in adult patients.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage
The recommended adult dose of Technetium Tc 99m-labelled Technescan HDP is 555 megabecquerel (MBq) with a range of 370 to 740 MBq. The maximum total dose to be injected is 740 MBq. The radioactivity of each dose should be measured by a suitable radiation calibration system just prior to administration. The dose should be given intravenously by slow injection. For optimal results imaging should be performed 1 to 4 hours post-injection.

Radiation Dosimetry
The estimated absorbed radiation doses in an average patient (70 kg) from an intravenous injection of 740 MBq Technetium Tc 99m-labelled Technescan HDP are shown in **Table 4**.

Table 4. Estimated Absorbed Radiation Doses

Ages	Newborn		1 year old		5 year old		10 year old		15 year old		Adult	
Weight (kg)	3.5		12.1		20.3		33.5		55.0		70.0	
Maximum Recommended Dose	45.5 MBq (1.2 mCi)		157.3 MBq (4.2 mCi)		263.9 MBq (7.1 mCi)		435.5 MBq (11.7 mCi)		715.0 MBq (19.3 mCi)		740.0 MBq (20.0 mCi)	
Tissue	Estimated Absorbed Radiation Doses											
	mGy	Rads	mGy	Rads	mGy	Rads	mGy	Rads	mGy	Rads	mGy	Rads
Kidneys	3.0	0.30	4.2	0.42	4.0	0.40	4.4	0.44	5.2	0.52	4.4	0.44
Ovaries	1.5	0.15	2.5	0.25	2.4	0.24	2.6	0.26	3.0	0.30	2.4	0.24
Red Marrow	10.9	1.09	12.9	1.29	10.6	1.06	10.0	1.00	10.0	1.00	9.6	0.96
Bone Surfaces	104.6	10.46	113.3	11.33	79.2	7.92	78.4	7.84	78.7	7.87	64.4	6.44
Testes	1.2	0.12	2.0	0.20	1.8	0.18	1.9	0.19	2.1	0.21	1.6	0.16
Bladder Wall	11.4	1.14	17.3	1.73	15.6	1.56	17.4	1.74	19.3	1.93	15.5	1.55
Total Body	1.8	0.18	2.7	0.27	2.6	0.26	2.7	0.27	3.0	0.30	2.5	0.25

mCi = millicurie; mGY = milligray; rads = unit of absorbed radiation dose.

* Based on data in MIRD Dose Estimate Report No. 14. Bladder initially voided at 2 hours and then every 4.8 hours thereafter.

Make all transfers of radioactive solutions with an adequately shielded syringe and maintain adequate shielding around the vial during the useful life of the radioactive product.

Parenteral products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

Procedure for the Preparation of Technetium Tc 99m Oxidronate

1. Remove plastic disc from Technescan HDP vial and cleanse top by swabbing with alcohol.
   Note: If dose is for a single-adult patient, see unit dose preparation method below.

2. Place vial in lead vial shield. Add 3 to 6 mL of Sodium Pertechnetate Tc 99m solution and secure with a fitted lead cover. In choosing the amount of Tc 99m radioactivity to be used, the number of doses desired, the activity of each dose (recommended adult dose is 555 MBq [15 mCi] with a range of 370 to 740 MBq) and radioactive decay must be taken into account. The recommended range of 1.11 GBq to 11.1 GBq of Tc 99m radioactivity should be used to reconstitute the vial of Technescan HDP.
   Note: The contents of the vial are now radioactive. Maintain adequate shielding using the lead vial shield and fitted lead cover during the life of the radioactive preparation.

3. Shake the vial gently, for approximately 30 seconds to assure complete dissolution. Parenteral products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit.

4. Record the time, date of preparation and the activity of the Technetium Tc 99m-labelled Oxidronate Injection on the radioassay information label and affix to the vial.

5. Use within eight (8) hours of preparation. To reduce microbiological hazard, use as soon as practicable after reconstitution/ preparation. The preparation should be stored between 15 to 25°C. The disposal of all radioactive wastes should be carried out in accordance with the NHMRC 9 Code of Practice for the Disposal of Radioactive Wastes by the User (1985).

Unit Dose Preparation
To minimise volume injected and to ensure optimum solution concentration, reconstitute the vial contents in 3 to 6 mL of sterile, non-pyrogenic normal saline containing no preservatives. Shake the vial gently for approximately 30 seconds to assure complete dissolution, withdraw and discard all but approximately 1 mL of the solution. Add appropriate amount of Sodium Pertechnetate Tc 99m for a single adult dose and shake gently. Proceed with steps 4 and 5.

The radiochemical purity of reconstituted Technetium Tc 99m Oxidronate Injection can be checked prior to administration to the patient by use of the method set out below. This method includes the directions for performing the tests and the limits for acceptable radiochemical purity.

Instructions for Determining Radiochemical Purity

Required Materials:
ITLC-SG (silica gel strips)
0.9% Sodium Chloride Injection
Methanol
Acetone

Procedure

1. On each of two ITLC strips, place approximately 20 to 30 µL of the Technetium Tc 99m Oxidronate injection approximately 2 to 3 cm from the end of the strip.

2. Develop one strip by ascending chromatography using a solvent system consisting of 0.9% Sodium Chloride Injection. Allow the solvent front to move about 8 cm from the origin.

3. Develop the second strip by ascending chromatography using a mixture of 1:1 methanol and acetone. Allow the solvent front to move about 8 cm from the origin.

4. Determine the radioactivity distribution on each strip by cutting the strips as described below and counting the sections in a suitable ionization chamber. Saline system: cut the strip at a point one third (1/3) of the distance from the origin to the solvent front. Methanol + Acetone system: cut the strip at a point two thirds (2/3) of the distance from the origin to the solvent front.

5. In the saline system hydrolyzed-reduced technetium remains at the origin (Rf 0 to 0.1) while the complex Tc 99m oxidronate and any free Tc 99m pertechnetate move to the solvent front (Rf 0.85 to 1.0). The percentage of hydrolyzed-reduced technetium is calculated by dividing the activity on the bottom one third (1/3) (origin section) of the strip by the total activity of both sections of the strip and multiplying by 100%.

6. In the 1:1 Methanol + Acetone system, the complex plus any hydrolyzed-reduced technetium remain at the origin (Rf 0 to 0.1), while the free pertechnetate moves to the solvent front (RF 0 to 1.0). The percentage of free technetium is calculated by dividing the activity on the top one third (1/3) (solvent front section) of the strip by the total activity of both sections of the strip and multiplying by 100%.

7. The sum of the percentage of radioactivity at the origin in the saline system (the hydrolyzed-reduced technetium) plus the percentage of radioactivity at the solvent front in the Methanol + Acetone system (free pertechnetate) must not be greater than 10%.

4.3 CONTRAINDICATIONS

None known.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

This class of compounds is known to complex cations such as calcium. Particular caution should be used with patients who have or who may be predisposed to hypocalcemia (i.e. alkalosis).

The contents of the Technescan HDP kit are intended only for use in the preparation of Technetium Tc 99m Oxidronate and are not to be directly administered to the patient.

The contents of the kit are not radioactive. However, after the Sodium Pertechnetate Tc 99m is added, adequate shielding of the final preparation must be maintained to minimize radiation exposure to occupational workers and patients.

Examinations using radiopharmaceuticals, especially those elective in nature, of women of childbearing capability, should be performed during the first 10 days following the onset of menses.

The components of the kit are sterile and non-pyrogenic. It is essential that the user follow the directions carefully and adhere to strict aseptic procedures during preparation. Sodium Pertechnetate Tc 99m solutions which contain an oxidizing agent or saline solutions containing preservatives are not suitable for use in the preparation of Technetium Tc 99m Oxidronate.

Technetium Tc 99m Oxidronate should be formulated within eight (8) hours prior to clinical use. Optimal imaging results are obtained one to four hours after administration.

Technetium Tc 99m Oxidronate as well as other radioactive agents, must be handled with care and appropriate safety measures should be used to minimise radiation exposure to the patients consistent with proper patient management and to ensure minimum radiation exposure the occupational workers.

Radiopharmaceuticals should be used only by medical practitioners who are qualified by specific training in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorised to license the use of radionuclides.

To minimise radiation dose to the bladder, the patients should be encouraged to drink fluids and to void immediately before the examination and as often thereafter as possible for the next four to six hours.

Since adequate reproduction studies have not been performed in animals to determine whether Technetium Tc 99m Oxidronate affects fertility in males or females, has teratogenic potential, or has other adverse effects on the foetus, this radiopharmaceutical preparation should not be administered to pregnant women. Any woman who has missed a period should be assumed to be pregnant unless proven otherwise.

Use in the elderly
There is no special safety or dosing information available for use in the elderly.

Paediatric use
This information is not available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

This information is not available.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility
No data available.

Use in pregnancy
No data available.

Use in lactation
Technetium Tc 99m is excreted in human milk during lactation, therefore formula feedings should be substituted for breast feedings.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

The incidence of total adverse events reported to the FDA over a one year period was less than 0.004%.

Body as a Whole: hypersensitivity reactions, including life-threatening reaction.

Gastrointestinal: nausea, vomiting.

Skin and Appendages: allergic dermatological manifestations (erythema), urticaria.

General Disorders and Administration site: Injection site reaction, injection site inflammation.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

In the event of the administration of a radiation overdose with Technetium Tc 99m Oxidronate the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and bladder voiding.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action
This information is not available.

Clinical trials
No data available.

5.2 PHARMACOKINETICS PROPERTIES

Absorption
This information is not available.

Distribution
Blood levels are about 10% of the injected dose at one hour post-injection and continue to fall to about 6%, 4% and 3% at 2, 3 and 4 hours respectively. When measured at 24 hours following its administration, skeletal retention is approximately 50% of the injected dose. Technetium Tc 99m Oxidronate exhibits its greatest affinity for areas of altered osteogenesis and actively metabolising bone.

Metabolism
This information is not available.

Excretion
During the 24 hours following injection, Technetium Tc 99m Oxidronate is rapidly cleared from blood and other non-osseous tissues and accumulates in the skeleton and urine in humans.

5.3 PRECLINICAL SAFETY DATA

No long term animal studies have been performed to evaluate carcinogenic or mutagenic potential, or whether Tc 99m-labelled Technescan HDP (Technetium Tc 99m Oxidronate) affects fertility in males and females.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Gentisic acid
Sodium chloride
Stannous chloride dihydrate.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

Before reconstitution: 12 months from date of manufacture.
After reconstitution: The reconstituted vial must be used within eight (8) hours of preparation.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Before and After reconstitution: Technescan HDP should be stored between 15 to 25°C with additive-free Sodium Pertechnetate Tc 99m.

6.5 NATURE AND CONTENTS OF CONTAINER

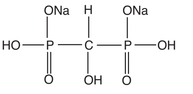
Glass vial.
Kits contain 5 vials or 30 vials.
Not all presentations may be available.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure
The chemical structural formula of oxidronate sodium is:



CAS number
CAS number for oxidronate sodium:
14255-61-9

The radiopharmaceutical diagnostic agent, when reconstituted with additive-free Sodium Pertechnetate Tc 99m forms a complex of unknown structure.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Not scheduled. Not considered by committee.

8 SPONSOR

Landauer Radiopharmaceuticals Pty Ltd
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Parramatta NSW 2150
Australia
Contact Number: (02) 8651 4000

9 DATE OF FIRST APPROVAL

2 August 2000

10 DATE OF REVISION

15 April 2020

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Summary Table of Changes

Section changed	Summary of new information
All sections	Adopted new TGA approved PI form throughout the document with no change to previously approved TGA text. New text added were necessary to comply with the new PI form.

[1] Kocher, David C., "Radioactive Decay Data Tables," DOE/TIC-11026, 108 (1981).