TECHNESCAN™ HDP

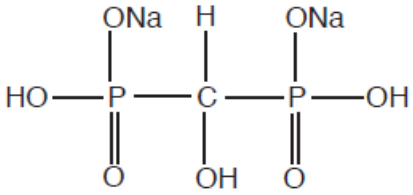
NAME OF THE MEDICINE

Technescan™ HDP Kit for the Preparation of Technetium (^{99m}Tc) Oxidronate intravenous diagnostic radiopharmaceutical agent.

DESCRIPTION

Technescan HDP is supplied as a lyophilised powder, packaged under nitrogen, in vials for intravenous administration after reconstitution with additive-free sodium pertechnetate (^{99m}Tc). Each vial contains 3.15 mg oxidronate sodium and 0.258 mg, minimum, stannous chloride ($SnCl_2 \bullet 2H_2O$), 0.297 mg, theoretical, stannous chloride ($SnCl_2 \bullet 2H_2O$), with 0.343 mg, maximum, tin chloride [stannous and stannic] dihydrate as $SnCl_2 \bullet 2H_2O$ as active ingredients. In addition, each vial contains 0.84 mg gentisic acid as a stabiliser and 30.0 mg sodium chloride. The pH is adjusted with hydrochloric acid and/or sodium hydroxide. The pH of the reconstituted drug is between 4.0 and 5.5. The contents of the vial are sterile and non-pyrogenic.

The chemical structure of oxidronate sodium is:



CAS number for oxidronate sodium: None

CAS number for stannous chloride: 7772-99-8

The radiopharmaceutical diagnostic agent, when reconstituted with additive-free sodium pertechnetate (^{99m}Tc) oxidronate complex of unknown structure.

Physical Characteristic

Technetium (^{99m}Tc) 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	Mean Percent/ Disintegration	Energy (keV)
Gamma-2	89.07	140.5

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

External Radiation

The specific gamma ray constant for technetium (^{99m}Tc) is 0.2108 mGy at 1 cm. The first half-value thickness of lead (Pb) for technetium (^{99m}Tc) is 0.017 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition.

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 this 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 (^{99m}Tc), 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

CLINICAL PHARMACOLOGY

General

This information is not available.

Pharmacokinetics

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 (^{99m}Tc) Oxidronate exhibits its greatest affinity for areas of altered osteogenesis and actively metabolizing bone.

Elimination

During the 24 hours following injection, (^{99m}Tc)-labeled Technescan HDP (Technetium (^{99m}Tc) Oxidronate) is rapidly cleared from blood and other non-osseous tissues and accumulates in the skeleton and urine in humans.

INDICATIONS

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

CONTRAINDICATIONS

None known.

PRECAUTIONS

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 (^{99m}Tc) Oxidronate and are not to be directly administered to the patient.

The contents of the kit are not radioactive. However, after the sodium pertechnetate (^{99m}Tc) is added, adequate shielding of the final preparation must be maintained to minimise 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 (^{99m}Tc) solutions which contain an oxidizing agent or saline solutions containing preservatives are not suitable for use in the preparation of Technetium (^{99m}Tc) Oxidronate. Technetium (^{99m}Tc) Oxidronate as well as other radioactive drugs, must be handled with care and appropriate safety measures should be used to minimise radiation exposure to 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.

Carcinogenicity, Genotoxicity, Effects on Fertility

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

Use in the Elderly

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

Use in Pregnancy

Since adequate reproduction studies have not been performed in animals to determine whether Technetium (^{99m}Tc) 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 Lactation

Technetium (^{99m}Tc) is excreted in human milk during lactation, therefore formula feedings should be substituted for breast feedings.

Paediatric Use

This information is not available.

Laboratory Test Interactions

This information is not available.

INTERACTIONS WITH OTHER MEDICINES

This information is not available.

ADVERSE REACTIONS

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.

Cardiovascular: this information is not available.

Digestive: nausea, vomiting.

Hemic and Lymphatic: this information is not available.

Metabolic and Nutritional: this information is not available.

Musculoskeletal: this information is not available.

Nervous System: this information is not available.

Respiratory System: this information is not available.

Skin and Appendages: allergic dermatological manifestations (erythema), urticaria, injection site inflammation/reaction.

Special Senses: this information is not available.

Urogenital: this information is not available.

DOSAGE AND ADMINISTRATION

The recommended adult dose of Technetium (^{99m}Tc)-labeled Technescan HDP is 555 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 (^{99m}Tc)-labeled Technescan HDP are shown in Table 4.

Preparation for Use

Technescan HDP contains no antimicrobial agent. Use aseptic technique and wear waterproof gloves throughout the entire preparation procedure.

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

The radiochemical purity of reconstituted Technetium (^{99m}Tc) Oxidronate Injection can be checked prior to administration to the patient by use of the method set out following the “Preparation Procedure”. This method includes the directions for performing the tests and the limits for acceptable radiochemical purity.

*Table 4. Estimated Absorbed Radiation Dose**

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

* Based on data in MIRD Dose Estimate Report No. 14. Bladder initially voided at 2.0 hours and then every 4.8 hours thereafter.
**See Dosage and Administration section.

Preparation Procedure

1. Remove plastic disc from Technescan HDP vial and cleanse top by swabbing with alcohol. To minimise volume injected and to insure 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.

2. Place vial in lead vial shield. Add appropriate amount of sodium pertechnetate (^{99m}Tc) for a single adult dose and shake gently. In choosing the amount of (^{99m}Tc) radioactivity to be used, 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 (^{99m}Tc) 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. Allow the vial to stand for a minimum of 5 minutes in order for the labeling reactions to go to completion. Parenteral drug 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 (^{99m}Tc)-labeled 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 below 30°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).

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 uL of the Technetium (^{99m}Tc) 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 1/3 of the distance from the origin to the solvent front. Methanol + Acetone system: cut the strip at a point 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 (^{99m}Tc) Oxidronate and any free (^{99m}Tc) 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 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 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%.

OVERDOSAGE

In the event of the administration of a radiation overdose with technetium (^{99m}Tc) 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.

PRESENTATION AND STORAGE CONDITIONS

Technescan HDP is supplied as a lyophilised powder, packaged under nitrogen, in vials for intravenous administration after reconstitution with additive-free sodium pertechnetate (^{99m}Tc). Each vial contains 3.15 mg oxidronate sodium and 0.258 mg, minimum, stannous chloride ($SnCl_2$•$2H_2O$), 0.297 mg, theoretical, stannous chloride ($SnCl_2$•$2H_2O$), with 0.343 mg, maximum, tin chloride [stannous and stannic] dyhydrate as $SnCl_2$•$2H_2O$ as active ingredients. In addition, each vial contains 0.84 mg gentisic acid as a stabiliser and 30.0 mg sodium chloride.

Kits containing 5 vials or 30 vials are available.

Storage

The drug should be stored below 30°C both prior to and following reconstitution with additive-free sodium pertechnetate (^{99m}Tc). The shelf life of the product is 6 months after manufacture.

Users of this product should observe the National Health and Medical Research Council (NHMRC) National Guidelines for Waste Management in the Health Industry (1999). (see www.nhmrc.gov.au/publications.)

NAME AND ADDRESS OF THE SPONSOR

Landauer Radiopharmaceuticals Pty Ltd
Level 3/69 Phillip Street
Parramatta NSW 2150
Australia

POISON SCHEDULE OF THE MEDICINE

Not scheduled. Not considered by committee.

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPUETIC GOODS

2 August 2000.

DATE OF MOST RECENT AMENDMENT

27 January 2016.

Revision Date: 11/2015

Manufactured by Mallinckrodt Inc., USA

Mallinckrodt™ Pharmaceuticals

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