DRN 4366 **TechneScan HDP Singapore**

DATASHEET/DIRECTIONS FOR USE

TRADE NAME OF THE MEDICINAL PRODUCT
TechneScan HDP

(Curium catalogue number: DRN 4366)

QUALITATIVE AND QUANTITATIVE COMPOSITION
Sodium Oxidronate 3.0 mg

PHARMACEUTICAL FORM
Powder for solution for injection

CLINICAL PARTICULARS

Therapeutic indications
After reconstitution with Sodium Pertechnetate (^{99m}Tc) Injection (Fission or Non-Fission) the agent may be used for bone scintigraphy, where it delineates areas of altered osteogenesis.

Posology and method of administration
The average activity administered by single intravenous injection is 500 MBq (300 – 700 MBq) in a 50 to 70 kg adult. Other activities may be justifiable. There is no special dosage regimen for the elderly patient. The dose to be administered to a child should be a fraction of the adult dose calculated from the body weight according to the following table.

3 kg = 0.1	4 kg = 0.14	6 kg = 0.19	8 kg = 0.23	10 kg = 0.27
12 kg = 0.32	14 kg = 0.36	16 kg = 0.40	18 kg = 0.44	20 kg = 0.46
22 kg = 0.50	24 kg = 0.53	26 kg = 0.56	28 kg = 0.58	30 kg = 0.62
32 kg = 0.65	34 kg = 0.68	36 kg = 0.71	38 kg = 0.73	40 kg = 0.76
42 kg = 0.78	44 kg = 0.80	46 kg = 0.82	48 kg = 0.85	50 kg = 0.88
52-54 kg = 0.90	56-58 kg = 0.92	60-62 kg = 0.96	64-66 kg = 0.98	68 kg = 0.99

In very young children (up to 1 year) a minimum dose of 40 MBq is necessary in order to obtain images of sufficient quality.

Images obtained shortly after injection (e.g. in the so-called "3-phase bone scan" procedure) will only partly reflect metabolic activity. Late phase static scintigraphy should be performed not earlier than 2 hours after injection. The patient should void before scanning.

Contra-indications
There are no specific contra-indications.

Special warnings and special precautions for use
In infants and children particular attention should be paid to the relatively higher radiation exposure of the epiphyses in growing bone. Appropriate precautions should be taken concerning the activity which is eliminated by the patients, to avoid any contamination. To

reduce the radiation exposure to the bladder wall, sufficient hydration of the patient and frequent voiding is recommended.
To avoid accumulation of tracer in the musculature it is advised that strenuous exercise is discouraged immediately after injection until satisfactory bone imaging has been effected. Inadvertent or accidental subcutaneous administration of technetium (^{99m}Tc) oxidronate should be avoided as perivascular inflammation has been described.
This radiopharmaceutical may be received, used and administered only by authorized persons in hospitals. Its receipt, storage, use, transfer and disposal are subject to the regulations and the appropriate licences of the local competent official organizations.
Radiopharmaceuticals intended for administration to patients should be prepared by the user in a manner which satisfies both radiological safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements of Good Pharmaceutical Manufacturing Practice for pharmaceuticals.

Interactions with other medicaments and other forms of interaction
The accumulation of technetium (^{99m}Tc) oxidronate in the skeleton, and thus the quality of the scintigraphic procedure, may be decreased after medication with chelates, with diphosphonates, after tetracycline or after iron containing drugs. Regular medication with aluminium containing drugs (notably antacids) may lead to abnormally high accumulation of ^{99m}Tc in the liver, presumably caused by the formation of labelled colloids.

Pregnancy and lactation
When it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty exists it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information.
Alternative techniques which do not involve ionising radiation should be considered. Radionuclide procedures carried out on pregnant women also involve radiation doses to the fetus. Only imperative investigations should be carried out during pregnancy when likely benefit exceeds the risk incurred by mother and fetus.
Administration of 700 MBq technetium (^{99m}Tc) oxidronate to a patient with normal bone uptake results in an absorbed dose to the uterus of 4.27 mGy. The dose decreases to 2.03 mGy in patients with high bone uptake and/or severely impaired kidney function. Doses above 0.5 mGy would be regarded as a potential risk for the fetus.
Before administering a radioactive medicinal product to a mother who is breast-feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast-feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, one breast feed should be banked prior to injection and the subsequent one discarded after injection. Breast-feeding can be restarted 4 hours post injection.

Effects on ability to drive and use machines
Effects on the ability to drive or to use machines have not been described.

Undesirable effects
Adverse drug effects are extremely rare following administration of technetium (^{99m}Tc) oxidronate injection. Onset of symptoms may be delayed 4 to 24 hours after administration.

Immune system disorders
Frequency unknown: Hypersensitivity/anaphylactoid reactions (e.g. rash, nausea, hypotension, arthralgia). Life-threatening hypersensitivity reactions have been reported.

General disorders and administration site conditions
Frequency unknown: Injection site reactions

For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic result. Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred.
For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (EDE) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

Overdose
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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties
At chemical concentrations of radiopharmaceuticals and excipients used for diagnostic procedures technetium (^{99m}Tc) oxidronate does not appear to exert any pharmacodynamic effect. ATC code: V09B A01.

Pharmacokinetic properties
Intravenously administered technetium (^{99m}Tc) oxidronate is rapidly distributed throughout the extracellular space. Skeletal uptake begins almost immediately and proceeds rapidly. 30 minutes post injection 10 % of the initial dose is still present in whole blood. At 1 hour, 2 hours, 3 hours and 4 hours after injection these values are resp. 5 %, 3 %, 1.5 % and 1 %. Clearance from the body takes place via the kidneys. Of the administered activity approximately 30 % is cleared within the first hour, 48 % within two hours and 60 % within 6 hours.

Preclinical safety data
This agent is not intended for regular or continuous administration. Reproduction, mutagenicity studies and long-term carcinogenicity studies have not been carried out.
Minimal liver abnormalities are seen at the level of 30 mg/kg in rats. In subacute toxicity studies rats do not react to the administration of 10 mg/kg/day for 14 days, dogs show histological changes in the liver (microgranuloma) after 3 and 10 mg/kg/day for 14 days.
In dogs, treated for 14 consecutive days long-lasting indurations at the site of injection were observed.

Radiation dosimetry

For this product the effective dose equivalent resulting from an administered activity of 700 MBq is typically 5.6 mSv (per 70 kg individual).
For an administered activity of 700 MBq the typical radiation dose to the target organ (bone) is 44.1 mGy and the typical radiation dose to the critical organ (bladder wall) is 35 mGy.
In cases of high bone uptake and/or severely impaired kidney function, the effective dose equivalent resulting from an administered activity of 700 MBq of technetium (^{99m}Tc) oxidronate is 5.7 mSv. The typical radiation dose to the target organ is 84 mGy and the typical radiation dose to the critical organ (red marrow) is 12.6 mGy.
(^{99m}Tc) Technetium disintegrates with the emission of gamma radiation with an energy of 140 keV and a half-life of 6 hours to (^{99m}Tc) Technetium which, in view of its long half-life of 2.13×10^5 years, can be regarded as quasi stable.

The dosimetry data were quoted from ICRP publication 53 for phosphonates.

Radiation exposure in normal bone uptake
(absorbed dose/injected activity (mGy/MBq).

Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.0019	0.0027	0.0039	0.0060	0.011
Bladder wall	0.050	0.062	0.090	0.13	0.24
Bone surface	0.063	0.082	0.13	0.22	0.53
Breast	0.00088	0.00088	0.0014	0.0022	0.0042
Stomach wall	0.0012	0.0015	0.0025	0.0037	0.0070
Small intestine	0.0023	0.0028	0.0044	0.0066	0.012
Upper large intestine	0.0020	0.0025	0.0038	0.0062	0.011
Lower large intestine	0.0038	0.0047	0.0072	0.010	0.017
Kidneys	0.0073	0.0089	0.013	0.018	0.033
Liver	0.0013	0.0016	0.0024	0.0038	0.0070
Lungs	0.0013	0.0016	0.0024	0.0036	0.0069
Ovaries	0.0035	0.0046	0.0066	0.0097	0.016
Pancreas	0.0016	0.0020	0.0030	0.0046	0.0085
Red marrow	0.0096	0.013	0.020	0.038	0.075
Spleen	0.0014	0.0018	0.0028	0.0043	0.0081
Testes	0.0024	0.0033	0.0055	0.0084	0.016
Thyroid	0.0010	0.0016	0.0022	0.0035	0.0056
Uterus	0.0061	0.0076	0.012	0.017	0.028
Other tissue	0.0019	0.0023	0.0033	0.0050	0.0089
Effective dose equivalent (mSv/MBq)	**0.0080**	**0.010**	**0.015**	**0.025**	**0.050**

Radiation exposure in high bone uptake and/or severely impaired kidney function
(absorbed dose/injected activity (mGy/MBq).

Organ	**Adult**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.0035	0.0050	0.0072	0.011	0.021
Bladder wall	0.0025	0.0035	0.0054	0.0074	0.015
Bone surface	0.12	0.16	0.26	0.43	1.0

Breast	0.0021	0.0021	0.0032	0.0051	0.0096
Stomach wall	0.0026	0.0032	0.0051	0.0073	0.014
Small intestine	0.0031	0.0038	0.0057	0.0085	0.016
Upper large intestine	0.0029	0.0036	0.0053	0.0086	0.015
Lower large intestine	0.0034	0.0042	0.0065	0.0096	0.018
Kidneys	0.0030	0.0037	0.0056	0.0087	0.016
Liver	0.0027	0.0033	0.0049	0.0075	0.014
Lungs	0.0030	0.0037	0.0053	0.0081	0.015
Ovaries	0.0029	0.0041	0.0059	0.0089	0.016
Pancreas	0.0032	0.0040	0.0059	0.0089	0.016
Red marrow	0.018	0.023	0.037	0.072	0.14
Spleen	0.0026	0.0034	0.0051	0.0078	0.015
Testes	0.0023	0.0027	0.0039	0.0060	0.011
Thyroid	0.0024	0.0037	0.0054	0.0083	0.014
Uterus	0.0029	0.0037	0.0054	0.0082	0.015
Other tissue	0.0030	0.0036	0.0053	0.0081	0.015
Effective dose equivalent (mSv/MBq)	**0.0082**	**0.011**	**0.017**	**0.028**	**0.061**

PHARMACEUTICAL PARTICULARS

List of Excipients

After labelling the main component of Technetium (^{99m}Tc) Oxidronate Injection is pertechnetate in saline solution, obtained from a Technetium generator. Other ingredients are stannous chloride dihydrate, gentisic acid, sodium chloride, hydrochloric acid 37% and sodium hydroxide. Contents are present in a nitrogen atmosphere.

Properties of TechneScan HDP after reconstitution/labelling:
Clear to slightly opalescent, colourless, aqueous solution.
pH: 4.0 – 5.0

Incompatibilities

No known incompatibilities exist. Dilution should preferably be done with Normal Saline solution (B.P.).

Shelf life

Refer to outer carton.

Special precautions for storage

Refer to outer carton for storage condition. Storage should be in accordance with national regulations for radioactive material.

Pack size

TechneScan HDP is supplied as five vials in a carton box.

Instruction for use/handling

Instructions for labelling
Add aseptically the required amount of Sodium Pertechnetate (^{99m}Tc) Injection (Fission or Non-Fission) with a maximum activity of 14 GBq, in a volume of 3-10 ml to one vial Technescan HDP and shake for 30 seconds to dissolve the contents. The preparation is then ready for injection.

Dilution should preferably be done with Sodium Chloride 0.9 % solution.

For a single patient at most 1 mg of HDP (1/3 of a vial) may be injected.

Instructions for quality control
Examine by TLC on silica gel coated glass-fibre sheets.

a) Develop 5 to 10 µl in 13.6% sodium acetate R; technetium oxidronate complex and pertechnetate ion migrate near the solvent front, hydrolysed technetium and technetium in colloidal form remain at the start.
b) Develop 5 to 10 µl in methyl ethyl ketone R; pertechnetate ion migrates near the solvent front, technetium oxidronate complex and technetium in colloidal form remain at the start.

For particulars consult the European Pharmacopoeia (Monograph 641).

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.
Radioactive waste must be disposed of in conformity with the relevant national and international regulations for radioactive material.

PRODUCT OWNER
Manufactured and released by:
Curium Netherlands B.V.
Westerduinweg 3
1755 LE PETTEN
The Netherlands

Marketing Authorisation Holder:
QT Instruments (S) Pte Ltd
100H Pasir Panjang Road
#07-01 OC@Pasir Panjang
Singapore 118524

MARKETING AUTHORISATION NUMBER
SIN12151P

DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION
23 December 2002

DATE OF (PARTIAL) REVISION OF THE TEXT
10 July 2023