# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Technescan HDP Kit for radiopharmaceutical preparation

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Oxidronate 3.0 mg
The radionuclide is not part of the kit.

Excipients:
Sodium 12 mg
For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

After radiolabelling with sodium pertechnetate ($^{99m}$Tc) solution, the agent may be used for bone scintigraphy, where it delineates areas of altered osteogenesis.

### 4.2 Posology and method of administration

Posology

*Adults*
The average activity administered by single intravenous injection is 500 MBq (300 - 740 MBq) in a 70 kg adult. Other activities may be justifiable. It should be noted that in each country physicians should follow the Diagnostic Reference Levels and the rules set out by local law.

*Elderly population*
There is no special dosage regimen for the elderly patient.

*Paediatric population*
The use in paediatric children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group. The activities to be administered to children and to adolescents were calculated according to the EANM dosage card (2008) by using the following Formula:
*A***[***MBq***]**Administered **=** *Baseline Activity* x *Multiple* (with a baseline activity of 35.0)

The resulting activities to be administered may be found in the following table:

| Weight (kg) | Activity (MBq) | Weight (kg) | Activity (MBq) | Weight (kg) | Activity (MBq) |
|---|---|---|---|---|---|
| 3 | 40 | 22 | 185 | 42 | 320 |
| 4 | 40 | 24 | 200 | 44 | 335 |
| 6 | 60 | 26 | 215 | 46 | 350 |
| 8 | 75 | 28 | 225 | 48 | 360 |
| 10 | 95 | 30 | 240 | 50 | 375 |
| 12 | 110 | 32 | 255 | 52 - 54 | 395 |
| 14 | 125 | 34 | 270 | 56 - 58 | 420 |
| 16 | 140 | 36 | 280 | 60 - 62 | 445 |
| 18 | 155 | 38 | 295 | 64 - 66 | 470 |
| 20 | 170 | 40 | 310 | 68 | 490 |

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

Method of administration

According to the followed reconstitution protocol the radiolabelled preparation is either for single use or multidose use.
This medicinal product should be reconstituted before administration to the patient.

For instructions on reconstitution of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

Image acquisition
The patient should void before scanning.
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.
Image acquisition should be performed according to clinical needs and/or current international guidelines.

## 4.3 Contraindications

Hypersensitivity to the active substance, to any of the excipients listed in section 6.1 or to any of the components of the labelled radiopharmaceutical.

## 4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment
Careful consideration of the benefit risk ratio in these patients is required since an increased radiation exposure is possible.

Generalised increased soft tissue uptake can be due to renal failure.

Paediatric population
For information on the use in paediatric population, see section 4.2.
In infants and children particular attention should be paid to the relatively higher radiation exposure of the epiphyses in growing bone. Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Patient preparation
The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the study in order to reduce radiation.

Specific warnings
Inadvertent or accidental subcutaneous administration of technetium ($^{99m}$Tc) oxidronate should be avoided as perivascular inflammation has been described.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

Precautions with respect to environmental hazard are in section 6.6.

## 4.5 Interactions with other medicinal products and other forms of interaction

An increased extraossal accumulation of the radioisotope was reported for iron-containing ingredients, administration of diphosphonates, various cytostatics (vincristine, cyclophophamide, doxorubicin, methotrexate), immunosuppressive medicinal products (e.g. cortisone), antibiotics (gentamicin, amphotericin) and aluminium-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.
In patients with hypercalcaemia soft-tissue uptake of bone-seeking radiopharmaceuticals may be observed.

## 4.6 Fertility, pregnancy and lactation

Women of childbearing potential
When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy
Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only essential investigations should be carried out during pregnancy when likely benefit exceeds the risk incurred by mother and foetus. Administration of 740 MBq technetium ($^{99m}$Tc) oxidronate to a patient results in an absorbed dose to the uterus of 4.7 mGy. Doses above 5 mGy would be regarded as a potential risk for the foetus.

Breast-feeding
$^{99m}$Tc will be excreted into breast milk.
Before administering a radioactive medicinal product to a mother who is breast-feeding consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breast-feeding and to what is the most appropriate choice of radiopharmaceutical, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breast-feeding should be interrupted for 4 hours and the expressed feeds discarded.

Fertility
The effect of the administration of technetium ($^{99m}$Tc) oxidronate on pregnant women and fertility is unknown.

## 4.7 Effects on ability to drive and use machines

Technescan HDP has no or negligible influence on the ability to drive and use machines.

## 4.8 Undesirable effects

| |
|---|
| Very common (≥1/10) |
| Common (≥1/100 to <1/10) |
| Uncommon (≥1/1,000 to <1/100) |
| Rare (≥1/10,000 to <1/1,000) |
| Very rare (<1/10,000) |
| Not known (cannot be estimated from the available data) |

Information on adverse reactions is available from spontaneous reporting. The reported reaction types are anaphylactoid reactions, vegetative reactions, as well as different kinds of injection site reactions and other general disorders. Onset of symptoms may be delayed 4 to 24 hours after administration.

Anaphylactoid reactions:
Anaphylactoid reactions were reported with a wide array of symptoms ranging from mild skin reactions to anaphylactic shock, which however was only reported in isolated cases.

Vegetative reactions (nervous system and gastrointestinal disorders)
Single cases of severe vegetative reactions like circulatory collapse or syncope have been reported, however, most of the reported vegetative effects include gastrointestinal reactions like nausea or vomiting. Other reports include vasovagal reactions like headache or dizziness. Vegetative effects are rather considered to be related to the examinational setting than to technetium ($^{99m}$Tc) oxidronate, especially in anxious patients.

General disorders and administration site conditions
Injection site reactions are related to extravasation of the radioactive material during the injection, and the reported reactions rank from local swelling up to cellulitis. Extended extravasation may necessitate surgical treatment.

The following table subsumes the observed reaction types and symptoms. Due to the fact that only spontaneous reports could be analysed, no frequency indications could be provided.

Adverse Reactions sorted by System Organ Class

| |
|---|
| Immune system disorders<br>Frequency unknown*: Anaphylactic reactions (e.g. Anaphylactic shock, loss of consciousness, cardio-respiratory arrest, hypersensitivity, angioedema, tachycardia, hypertension, dyspnoea, conjunctivitis, rhinitis and nasal congestion, dermatitis, generalised pruritus, face oedema, laryngeal oedema, tongue oedema, and other types of oedema, urticaria, erythema, rash, dysgeusia, paraesthesia, sweating increased) |
| Nervous system disorders<br>Frequency unknown*: Vasovagal reactions (e.g. Syncope, circulatory collapse, dizziness, headache, tachycardia, bradycardia, hypotension, tremor, vision blurred, flushing) |
| Gastrointestinal disorders<br>Frequency unknown*: Vomiting, nausea, diarrhoea, abdominal pain |

| General disorders and administration site conditions<br>Frequency unknown*: Injection site reactions (e.g. Cellulitis, inflammation, pain, erythema, swelling), chest pain, chills |
|---|

* Adverse reactions derived from spontaneous reporting

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 4.2 mSv (70 kg individual) when the maximal recommended activity of 740 MBq is administered these adverse reactions are expected to occur with a low probability.
Higher doses may be justified in some clinical circumstances. In all cases it is necessary to ensure that the risks of the radiation are less than from the disease itself.
This product contains no excipients that have a recognised action or effect, or knowledge of which is important for safe and effective use of the product.

Paediatric population
Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via the national reporting system at Statens legemiddelverk.
Website: www.legemiddelverket.no/meldesjema

### 4.9 Overdose

In the event of 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 frequent bladder voiding. It might be helpful to estimate the effective dose that was applied.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals skeleton, ATC code: V09B A01.

At chemical concentrations of radiopharmaceuticals and excipients used for diagnostic procedures technetium ($^{99m}$Tc) oxidronate does not appear to exert any pharmacodynamic effect.

### 5.2 Pharmacokinetic properties

Distribution
Intravenously administered technetium ($^{99m}$Tc) oxidronate is rapidly distributed throughout the extracellular space.

Organ uptake
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 %.

Elimination
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.

### 5.3 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, which were treated for 14 consecutive days, long-lasting indurations at the site of injection were observed.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Stannous chloride (dihydrate)
Gentisic acid
Sodium chloride
Hydrochloric acid
Sodium hydroxide

Contents are present in a nitrogen atmosphere.

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

### 6.3 Shelf life

24 months

After reconstitution and labelling chemical and physical in-use stability has been demonstrated for 8 hours below 25°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution / dilution (etc.) has taken place in controlled and validated aseptic conditions.

### 6.4 Special precautions for storage

Lyophilised powder: Store below 25°C.
Store in the original container in order to protect from light.

For storage conditions after radiolabelling of the medicinal product, see section 6.3.
Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

### 6.5 Nature and contents of container

Colourless glass vial with grey stopper and blue crimp cap containing a grey white powder. Technescan HDP is supplied as five vials with 3.0 mg in a carton box. 10 ml glass vial (Type 1 Ph.Eur) closed with a bromobutyl rubber stopper sealed with an aluminium crimp cap.

### 6.6 Special precautions for disposal and other handling

General warning

Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.

Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

Contents of the vial are intended only for use in the preparation of technetium ($^{99m}$Tc) oxidronate injection and are not to be administered directly to the patient without first undergoing the preparative procedure.

For instructions on reconstitution of the medicinal product before administration, see sections 12.

If at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The content of the kit before extemporary preparation is not radioactive. However, after sodium pertechnetate ($^{99m}$Tc) is added, adequate shielding of the final preparation must be maintained.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomit, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7 MARKETING AUTHORISATION HOLDER

Curium Netherlands B.V.
Westerduinweg 3
1755 LE Petten
The Netherlands

## 8 MARKETING AUTHORISATION NUMBER

MT 8293

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

31 January 1995/1 February 2005

## 10 DATE OF REVISION OF THE TEXT

08.07.2021

## 11 DOSIMETRY

Technetium ($^{99m}$Tc) is produced by means of a ($^{99}$Mo/$^{99m}$Tc) generator and decays with the emission of gamma radiation with an energy of 140 keV and a half-life of 6 hours to ($^{99}$Tc) Technetium which, in view of its long half-life of 2.13 x $10^5$ years, can be regarded as quasi stable.

The dosimetry data listed below are from ICRP publication 80.

Absorbed doses: $^{99m}$Tc-labelled phosphates and phosphonates (absorbed dose per unit activity administered [mGy/MBq]):

| **Organ** | **Adult** | **15 years** | **10 years** | **5 years** | **1 year** |
|---|---|---|---|---|---|
| Adrenals | 0.0021 | 0.0027 | 0.0039 | 0.0058 | 0.011 |
| Bladder wall | 0.048 | 0.06 | 0.088 | 0.073 | 0.13 |
| Bone surface | 0.063 | 0.082 | 0.13 | 0.22 | 0.53 |
| Brain | 0.0017 | 0.0021 | 0.0028 | 0.0043 | 0.0061 |
| Breast | 0.00071 | 0.00089 | 0.0014 | 0.0022 | 0.0042 |
| Gall bladder | 0.0014 | 0.0019 | 0.0035 | 0.0042 | 0.0067 |
| Stomach wall | 0.0012 | 0.0015 | 0.0025 | 0.0035 | 0.0066 |
| Small intestine | 0.0023 | 0.0029 | 0.0044 | 0.0053 | 0.0095 |
| Colon | 0.0027 | 0.0034 | 0.0053 | 0.0061 | 0.011 |
| Upper large intestine | 0.0019 | 0.0024 | 0.0039 | 0.0051 | 0.0089 |
| Lower large intestine | 0.0038 | 0.0047 | 0.0072 | 0.0075 | 0.013 |
| Heart | 0.0012 | 0.0016 | 0.0023 | 0.0034 | 0.006 |
| Kidneys | 0.0073 | 0.0088 | 0.012 | 0.018 | 0.032 |
| Liver | 0.0012 | 0.0016 | 0.0025 | 0.0036 | 0.0066 |
| Lungs | 0.0013 | 0.0016 | 0.0024 | 0.0036 | 0.0068 |
| Muscles | 0.0019 | 0.0023 | 0.0034 | 0.0044 | 0.0079 |
| Oesophagus | 0.001 | 0.0013 | 0.0019 | 0.003 | 0.0053 |
| Ovaries | 0.0036 | 0.0046 | 0.0066 | 0.007 | 0.012 |
| Pancreas | 0.0016 | 0.002 | 0.0031 | 0.0045 | 0.0082 |
| Red marrow | 0.0092 | 0.01 | 0.017 | 0.033 | 0.067 |
| Skin | 0.001 | 0.0013 | 0.002 | 0.0029 | 0.0055 |
| Spleen | 0.0014 | 0.0018 | 0.0028 | 0.0045 | 0.0079 |
| Testes | 0.0024 | 0.0033 | 0.0055 | 0.0058 | 0.011 |
| Thymus | 0.001 | 0.0013 | 0.0019 | 0.003 | 0.0053 |
| Thyroid | 0.0013 | 0.0016 | 0.0023 | 0.0035 | 0.0056 |
| Uterus | 0.0063 | 0.0076 | 0.012 | 0.011 | 0.018 |
| Other tissue | 0.0019 | 0.0023 | 0.0034 | 0.0045 | 0.0079 |
| **Effective dose** [mSv/MBq] | **0.0057** | **0.007** | **0.011** | **0.014** | **0.027** |

The effective dose resulting from the administration of 740 MBq for an adult weighing 70 kg is 4.2 mSv. For an administered activity of 740 MBq the typical radiation dose to the target organ (bone) is 47 mGy and the typical radiation dose to the critical organ (bladder wall) is 36 mGy.

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

| Organ | Adult | 15 years | 10 years | 5 years | 1 year |
|---|---|---|---|---|---|
| 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** (mSv/MBq) | **0.0082** | **0.011** | **0.017** | **0.028** | **0.061** |

## 12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

As with any pharmaceutical product, if at any time in the preparation of this product the integrity of this vial is compromised it should not be used.

Method of preparation

*Preparation for multi-dose application*

Aseptically add the required amount of sodium pertechnetate ($^{99m}$Tc) Solution (Fission or Non-Fission) with a maximum activity of 14 GBq, in a volume of 3-10 ml to one vial Technescan HDP. 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.

*Properties after labelling*

After labelling the solution is colourless and clear to slightly opalescent.

Quality control

Examine by TLC on silica gel coated glass-fibre sheets.

1. 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.
2. 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).

Individual and the total impurities may not be more than 5 %.