OctreoScan®
Kit for the Preparation of Indium In-111 Pentetreotide
Diagnostic - For Intravenous Use.
Rx Only.

DESCRIPTION

OctreoScan® is a kit for the preparation of Indium In-111 pentetreotide, a diagnostic radiopharmaceutical. It is a kit consisting of two components:

1) A 10-mL OctreoScan® Reaction Vial which contains a lyophilized mixture of:
   (i) 10 µg pentetreotide [N-(diethylenetriamine-N,N,N',N"-tetraacetic acid-N"-acetyl-D-phenylalanyl-L-hemicyclstyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-hemicyclstyl-L-threoninol cyclic (2→7) disulfide], (also known as octreotide DTPA),
   (ii) 2.0 mg genital acid [2, 5-dihydrouracil acid],
   (iii) 4.9 mg trisodium citrate, anhydrous,
   (iv) 0.37 mg citric acid, anhydrous, and
   (v) 10.0 mg inositol.

Pentetreotide has the following structural formula:

\[
\begin{align*}
\text{HOOCCH}_2 & \quad \text{COOH} \\
\text{HOOCCH}_2 & \quad \text{CH} \\
\text{CHCH}_2 & \quad \text{CH}_2 \text{COOH} \\
\text{HOOCCH}_2 & \quad \text{COOH} \\
\text{CHO} & \quad \text{CH} \\
\text{CHO} & \quad \text{COOH} \\
\end{align*}
\]

Prior to lyophilization, sodium hydroxide or hydrochloric acid may have been added for pH adjustment. The vial contents are sterile and nonpyrogenic. No bacteriostatic preserve is present.

2) A 10-mL vial of Indium In-111 Chloride Sterile Solution, which contains: 1.1 mL or 111 MBq/mL (3.0 mCi/mL) indium In-111 chloride in 0.02N HCl at time of calibration. The vial also contains ferric chloride at a concentration of 3.5 µg/mL (ferric ion, 1.2 µg/mL). The vial contains sterile and nonpyrogenic. No bacteriostatic preserve is present.

Indium In-111 pentetreotide is prepared by combining the two kit components (see INSTRUCTIONS FOR THE PREPARATION OF INDIUM IN-111 PENTETREOTIDE). Indium In-111 reacts with the diethylenetriaminetetraacetic acid portion of the pentetreotide molecule to form indium In-111 pentetreotide. The pH of the resultant indium In-111 pentetreotide solution is between 3.8 and 4.3. No bacteriostatic preserve is present.

The indium In-111 pentetreotide solution is suitable for intravenous administration as is, or it may be diluted to a maximum volume of 3.0 mL with 0.9% Sodium Chloride Injection, USP, immediately before intravenous administration. In either case, the labeling yield of indium In-111 pentetreotide should be determined before administration to the patient. A method recommended for determining the labeling yield is presented at the end of this package insert.

Physical Characteristics

Indium In-111 decays by electron capture to cadmium-111 (stable) and has a physical half-life of 2.805 days (67.32 hours) (see Table 2). The principal photons that are useful for detection and imaging are listed in Table 1.

<table>
<thead>
<tr>
<th>Radiation</th>
<th>Mean Percent Per Disintegration</th>
<th>Energy (kEv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma-2</td>
<td>90.2</td>
<td>171.3</td>
</tr>
<tr>
<td>Gamma-3</td>
<td>94.0</td>
<td>245.4</td>
</tr>
</tbody>
</table>

The specific gamma ray constant for In-111 is 3.21 R/hr-mCi at 1 cm. The first half-value thickness of lead (Pb) for In-111 is 0.023 cm. Selected coefficients of attenuation are listed in Table 2 as a function of lead shield thickness. For example, the use of 0.834 cm of lead will attenuate the external radiation by a factor of about 1000.

CONTRAINDICATIONS

None known.

WARNINGS

DO NOT ADMINISTER IN TOTAL PARENTERAL NUTRITION (TPN) MIXTURES OR INJECT INTO TPN INTRAVENOUS ADMINISTRATION LINES. IN THESE SOLUTIONS. A COMPLEX GLYCOSYL COTRETIDER CONJUGATE MAY FORM.

The sensitivity of scintigraphy with indium In-111 pentetreotide may be reduced in patients concurrently receiving therapeutic doses of octreotide acetate. Consideration should be given to temporarily suspending octreotide acetate therapy before the administration of indium In-111 pentetreotide and to monitoring the patient for any signs of withdrawal.

PRECAUTIONS

1. Therapy with octreotide acetate can produce severe hypoglycemia in patients with insulinomas. Since pentetreotide is an analog of octreotide, an intravenous line is recommended in any patient suspected of having an insulinoma. An intravenous solution containing glucose should be administered just before and during administration of indium In-111 pentetreotide.

2. The contents of the two vials supplied with the kit are intended only for use in the preparation of indium In-111 pentetreotide and are NOT to be administered separately to the patient.

3. Since indium In-111, pentetreotide is eliminated primarily by renal excretion, use in patients with impaired renal function should be carefully considered.

4. To help reduce the radiation dose to the thyroid, kidneys, bladder, and other target organs, patients should be well hydrated before the administration of indium In-111 pentetreotide. They should increase fluid intake and void frequently for one day after administration of this drug. In addition, it is recommended that patients be given a mild laxative (e.g., bisacodyl or lactulose) before and after administration of indium In-111 pentetreotide (see DOSAGE AND ADMINISTRATION section).

5. Indium In-111 pentetreotide should be prepared for labeling yield of radioactivity prior to administration. The product must be used within six hours of preparation.

6. Components of the kit are sterile and nonpyrogenic. To maintain sterility, it is essential that directions are followed carefully. Aseptic technique must be used during the preparation and administration of indium In-111 pentetreotide.

7. Octreotide acetate and the natural somatostatin hormone may be associated with cholelithiasis, presumably by altering fat absorption and possibly by decreasing motility of the gallbladder. A single dose of indium In-111 pentetreotide is not expected to cause cholelithiasis.

8. As with any other radioactive material, appropriate shielding should be used to avoid unnecessary radiation exposure to the patient, occupational workers, and other persons.

9. Radiopharmaceuticals should be used only by physicians who are qualified by specific training in the safe use and handling of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Studies have not been performed with indium In-111 pentetreotide to evaluate carcinogenic potential or effects on fertility. Pentetreotide was evaluated for mutagenic potential in an in vitro
mouse lymphoma forward mutation assay and in vivo mouse micronucleus assay; evidence of mutagenicity was not found.

### Pregnancy Category C

Animal reproduction studies have not been conducted with indium In-111 pentetreotide. It is not known whether indium In-111 pentetreotide can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Therefore, indium In-111 pentetreotide should not be administered to a pregnant woman unless the potential benefit justifies the potential risk to the fetus.

### Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when indium In-111 pentetreotide is administered to a nursing woman.

### Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

### Adverse Reactions

The following adverse effects were observed in clinical trials at a frequency of less than 1% of 538 patients: dizziness, fever, flush, headache, hypotension, changes in liver enzymes, joint pain, nausea, sweating, and weakness. These adverse effects were transient. Also in clinical trials, there was one reported case of bradycardia and one case of decreased hematocrit and hemoglobin.

Pentetreotide is derived from octreotide which is used as a therapeutic agent to control symptoms from certain tumors. The usual dose for indium In-111 pentetreotide is approximately 5 to 20 times less than for octreotide and is sub-therapeutic. The following adverse reactions have been associated with octreotide in 3% to 10% of patients: nausea, injection site pain, diarrhea, abdominal pain/discomfort, loose stools, and vomiting. Hypertension and hyper- and hypoglycemia have also been reported with the use of octreotide.

### Dosage and Administration

Before administration, a patient should be well hydrated. After administration, the patient must be encouraged to drink fluids liberally. Elimination of extra fluid intake will help reduce the radiation dose by flushing out unbound, labelled pentetreotide from the bowel. In a patient with diarrhea, a laxative (e.g., bisacodyl or lactulose) be given to the patient to help eliminate and the bowel-cleansing process. In a patient with an insulinoma, bowel-cleansing should be undertaken only after consultation with an endocrinologist.

The recommended intravenous dose for planar imaging is 111 MBq (3.0 mCi) of indium In-111 pentetreotide prepared from an OctreoScan® kit. The recommended intravenous dose for SPECT imaging is 222 MBq (6.0 mCi) of indium In-111 pentetreotide.

The dose should be confirmed by a suitably calibrated radioactivity ionization chamber immediately before administration.

As with all intravenously administered products, OctreoScan® should be inspected visually for particulate matter and discolarization prior to administration, whenever solution and container permit. Preparations containing particulate matter or discolarization should not be administered. They should be disposed of in a safe and approved manner. Aseptic techniques and effective shielding should be employed in withdrawing doses for administration to patients. Waterproof gloves should be worn during the administration procedure.

Do not administer OctreoScan® in TPN solutions or through the procedure.

### Radiation Dosimetry

The estimated radiation doses1 to the average adult (70 kg) from intravenous administration of 111 MBq (3 mCi) and 222 MBq (6 mCi) are presented in Table 4. These estimates were calculated by Oak Ridge Associated Universities using the data published by Krenning, et al.1

1 Values listed include a correction for a maximum of 0.1% indium In-114m radiocontaminant at calibration.


### Table 4. Estimated Absorbed Radiation Doses after Intravenous Administration of Indium In-111 Pentetreotide* to a 70 kg Patient

<table>
<thead>
<tr>
<th>Organ</th>
<th>PLANAR (mGy/111 MBq, rads/3 mCi)</th>
<th>SPECT (mGy/222 MBq, rads/6 mCi)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidneys</td>
<td>54.16</td>
<td>5.42</td>
</tr>
<tr>
<td>Liver</td>
<td>12.15</td>
<td>1.22</td>
</tr>
<tr>
<td>Spleen</td>
<td>73.86</td>
<td>7.39</td>
</tr>
<tr>
<td>Uterus</td>
<td>6.34</td>
<td>0.63</td>
</tr>
<tr>
<td>Ovaries</td>
<td>4.89</td>
<td>0.49</td>
</tr>
<tr>
<td>Testes</td>
<td>2.90</td>
<td>0.29</td>
</tr>
<tr>
<td>Red Marrow</td>
<td>3.46</td>
<td>0.35</td>
</tr>
<tr>
<td>Urinary Bladder Wall</td>
<td>30.24</td>
<td>3.02</td>
</tr>
<tr>
<td>GI Tract</td>
<td>5.67</td>
<td>0.57</td>
</tr>
<tr>
<td>Stomach Wall</td>
<td>4.78</td>
<td>0.48</td>
</tr>
<tr>
<td>Small Intestine</td>
<td>5.80</td>
<td>0.58</td>
</tr>
<tr>
<td>Upper Large Intestine</td>
<td>7.73</td>
<td>0.77</td>
</tr>
<tr>
<td>Lower Large Intestine</td>
<td>7.55</td>
<td>0.76</td>
</tr>
<tr>
<td>Adrenals</td>
<td>7.43</td>
<td>0.74</td>
</tr>
<tr>
<td>Thyroid</td>
<td>3.46</td>
<td>0.35</td>
</tr>
<tr>
<td></td>
<td>mSv/111 MBq, rem/3 mCi</td>
<td>mSv/222 MBq, rem/6 mCi</td>
</tr>
<tr>
<td>Effective Dose</td>
<td>13.03</td>
<td>1.30</td>
</tr>
</tbody>
</table>

* Assumes 4.8 hour voiding interval and International Commission on Radiological Protection (ICRP) 30 model for the gastrointestinal tract calculations.

### How Supplied

The OctreoScan® kit (NDC 0019-9050-40) is supplied with the following components:

1. A 10-mL OctreoScan® Reaction Vial which contains a lyophilized mixture of:
   - (i) 10 µg pentetreotide [N-(diethylenetriamine-N,N,N',N"-tetraacetic acid-N-acetyl-D-phenylalanyl-L-hemicyctyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-hemicyctyl-L-threoninol cys] (2-7) disulfide), (also known as octreotide DTPA),
   - (ii) 2.0 mg gentisic acid [2, 5-dihydroxybenzoic acid],
   - (iii) 4.9 µg trisodium citrate, anhydrous,
   - (iv) 0.37 µg citric acid, anhydrous, and
   - (v) 10.0 µg inositol.

2. A 10-mL vial of Indium In-111 Chloride Sterile Solution, which contains 1.1 mL In-111 MBq/mL (3.0 mCi/mL) indium In-111 chloride in 0.02 N HCl at time of calibration. The vial also contains ferric chloride at a concentration of 3.5 µg/mL (ferric ion, 1.2 µg/mL). The vials are sterile and nonpyrogenic. No bacteriostatic preservative is present.

3. Aseptically remove the contents of the Indium In-111 Chloride Sterile Solution into the OctreoScan® Reaction Vial, (2) pressure sensitive label, and (3) a package insert.

### Procedure for the Preparation of Indium In-111 Pentetreotide

1. Place the OctreoScan® Reaction Vial in a lead dispensing shield (of minimum wall thickness 1/4 inch) fitted with a lid.
2. Swab the rubber stopper of the reaction vial with an appropriate antiseptic and allow the vial to dry.
3. Aseptically remove the contents of the Indium In-111 Chloride Sterile Solution vial using the needle provided and a shielded, sterile syringe.
4. Inject the Indium In-111 Chloride Sterile Solution into the OctreoScan® Reaction Vial.
5. Gently swirl the OctreoScan® Reaction Vial until the lyophilized pellet is completely dissolved.
6. Incubate the indium In-111 pentetreotide solution at or below 25°C (77°F) for a minimum of 30 minutes. Note: A 30 minute incubation time is required. Shorter incubation periods may result in inadequate labeling.
7. Using proper shielding, visually inspect the vials. The solution should be clear, colorless, and free of particulate matter. If not, the solution should not be used. It should be disposed of in a safe and approved manner.
8. Assay the indium In-111 pentetreotide solution using a suitably calibrated ionization chamber. Record the date, time, total activity, and patient identifier (e.g., patient name and number) on the radioassay information label and affix the label to the lead dispensing shield.
9. The labeling yield of the reconstituted solution should be checked before administration to the patient, according to the instructions given below. If the radiochemical purity is less than 90%, the product should not be used.
10. Store the reaction vial containing the indium In-111 pentetreotide solution at or below 25°C (77°F) until use. The Indium In-111 pentetreotide must be used within six hours of preparation.

### Calculations

1. Percent indium In-111 pentetreotide = \( \frac{(\text{Fraction 2 Activity} \times \text{Total Activity}) \times 100}{\text{Fraction 1 Activity} + \text{Fraction 2 Activity}} \)

2. Percent hydrophilic impurities = \( \frac{\text{Fraction 1 Activity} \times \text{Total Activity}}{\text{Fraction 2 Activity}} \times 100\% \)

3. Percent non-eligible impurities = \( \frac{\text{Activity remaining in Sep-Pak cartridge} \times \text{Total Activity}}{100\%} \)

The radiopharmaceutical is licensed by the Illinois Department of Nuclear Safety for distribution to persons licensed pursuant to 560/99 (for the radioactive material specified in 32 IL. Adm. Code 335.4010 or under equivalent licenses of the U.S. Nuclear Regulatory Commission, an Agreement State, or a Licensing State.

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