Radiopharmaceuticals are eligible for separate reimbursement under the Medicare program in the physician office/freestanding imaging setting. Check with the local Medicare contractor for additional information.

In the hospital outpatient setting, under the Medicare program, generally, the cost of a diagnostic radiopharmaceutical is considered and then included into the payment rate for the procedure under the Medicare Hospital Outpatient APC program. Per CMS transmittal 2386¹ (item #5a page 5, 1/13/2012):

“Hospitals are strongly encouraged to report charges for all drugs, biologicals, and radiopharmaceuticals, regardless of whether the items are paid separately or packaged, using the correct HCPCS codes for the items used. It is also of great importance that hospitals billing for these products make certain that the reported units of service of the reported HCPCS codes are consistent with the quantity of a drug, biological, or radiopharmaceutical that was used in the care of the patient. More complete data from hospitals on the drugs and biologicals provided during an encounter would help improve payment accuracy for separately payable drugs and biologicals in the future. CMS strongly encourages hospitals to report HCPCS codes for all drugs and biologicals furnished, if specific codes are available. CMS realizes that this may require hospitals to change longstanding reporting practices. Precise billing of drug and biological HCPCS codes and units, especially in the case of packaged drugs and biologicals for which the hospital receives no separate payment, is critical to the accuracy of the OPPS payment rates for drugs and biologicals each year.”

Non-Medicare and Private Payer policies regarding radiopharmaceutical reimbursement vary. Check with the local insurer for more information.

Neuroendocrine Tumor Imaging

Codes Most Frequently Associated with Somatostatin Bearing Neuroendocrine Tumor Imaging

<table>
<thead>
<tr>
<th>Procedure Code*</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>78800</td>
<td>Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent, limited area</td>
</tr>
<tr>
<td>78801</td>
<td>Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent, multiple areas</td>
</tr>
<tr>
<td>78802</td>
<td>Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent, whole body, single day</td>
</tr>
<tr>
<td>78803</td>
<td>Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent, tomographic SPECT</td>
</tr>
<tr>
<td>78804</td>
<td>Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent, whole body, requiring two or more days</td>
</tr>
</tbody>
</table>

Radiopharmaceuticals (Coverage and Payment for Radiopharmaceuticals may vary based on payer type)

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description Published Verbatim From Medicare's Internet Site¹</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>A9572</td>
<td>Indium In-111 Pentetreotide Diagnostic, per study dose up to 6 mCi</td>
<td>Octreoscan¹⁰⁴⁰⁰</td>
</tr>
</tbody>
</table>


INDICATIONS

Indium In-111 pentetreotide is an agent for the scintigraphic localization of primary and metastatic neuroendocrine tumors bearing somatostatin receptors.

IMPORTANT RISK INFORMATION

Octreoscan¹⁰⁴⁰⁰ should not be administered in total parenteral nutrition (TPN) admixtures or injected into TPN IV lines. Therapy with a compound similar to pentetreotide produced severe hypoglycemia in patients with insulinomas. An IV solution of glucose should be administered in these patients just before and during administration of Octreoscan. As it is eliminated primarily by renal excretion, the use of Octreoscan in patients with impaired renal function should be carefully considered. The sensitivity of scintigraphy with Octreoscan may be reduced in patients receiving therapeutic doses of octreotide acetate. Adverse events seen in Octreoscan clinical trials in less than 1% of 538 patients were: dizziness, fever, flush, headache, hypotension, changes in liver enzymes, joint pain, nausea, sweating and weakness. These adverse events were transient. One case of bradycardia and one case of deceased hematocrit and hemoglobin were also seen.

For Full Prescribing Information on Octreoscan¹⁰⁴⁰⁰, see attached package insert.

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The material referenced and provided is based upon research of current Medicare reference sources. The final decision of billing for any product or procedure must be made by the provider of care considering the medical necessity of the services and supplies provided, the regulations of insurance carriers and any local, state or federal laws that apply to the supplies and services rendered. We are providing you this information in an educational capacity with the understanding that we are not engaged in rendering legal, accounting or other professional services.

For more information, contact:
- Local Covidien Representative: 800-634-1515
- Customer Service: 888-744-1414
- [http://imaging.covidien.com](http://imaging.covidien.com)
OctreoScan®
Kit for the Preparation of Indium In-111 Pentetreotide
Diagnostic - For Intraoperative 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-(diethylaminoethyl)pentamethylenetetraacetic acid-N,N',N''-tetraacetic acid-N-acetyl-D-phenylalanyl-L-hemicycst-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-hemicycst-L-threono1 cyclic (2→7) disulfide], also known as octreotide DTPA,
   (ii) 2.0 mg gentisic acid [2,5-dihydroxybenzoic 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:

\[
\text{HOOCH}_2 \text{COOH} \quad \text{CH} \quad \text{CH(OH)COOH} \quad \text{CH(OH)CH}_2 \text{COOH}
\]

Prior to lyophilization, sodium hydroxide or hydrochloric acid may have been added for pH adjustment. The vial contents are sterile and nonpyrogenic. No bacteriostatic preservative 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 µCi/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 contents are sterile and nonpyrogenic. No bacteriostatic preservative 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 preservative 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 2.065 days (67.32 hours) (see Table 2). The principal photons that are useful for detection and imaging are listed in Table 1.

| Table 1. Principal Radiation Emission Data* |
|-----------------|-----------------|-----------------|
| Radiation       | Mean Percent Per Disintegration | Energy (keV)    |
| Gamma-2         | 90.2            | 171.3           |
| Gamma-3         | 72.3            | 324.4           |

The specific gamma ray constant for In-111 is 3.21 R/hr-mCi at 1 cm1. 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 0.934 cm of lead will attenuate the external radiation by a factor of about 1000.

| Table 2. Radiation Attenuation by Lead Shielding |
|-----------------|-----------------|-----------------|
| Shield Thickness (Pb) cm | Coefficient of Attenuation | |
| 0.023 | 0.5 | |
| 0.203 | 0.1 | |
| 0.513 | 0.01 | |
| 0.834 | 0.001 | |
| 1.12 | 0.0001 | |


Table 3 lists fractions remaining at selected time intervals before and after calibration. This information may be used to correct for physical decay of the radionuclide.

Table 3. Physical Decay Chart: Indium In-111, Half-life 2.065 Days (67.32 hours)

<table>
<thead>
<tr>
<th>Hours (Calibration)</th>
<th>Hours</th>
<th>Fraction Remaining</th>
</tr>
</thead>
<tbody>
<tr>
<td>-72</td>
<td>2.000</td>
<td>1.000</td>
</tr>
<tr>
<td>-60</td>
<td>1.854</td>
<td>0.970</td>
</tr>
<tr>
<td>-48</td>
<td>1.639</td>
<td>0.940</td>
</tr>
<tr>
<td>-36</td>
<td>1.418</td>
<td>0.885</td>
</tr>
<tr>
<td>-24</td>
<td>1.280</td>
<td>0.781</td>
</tr>
<tr>
<td>-12</td>
<td>1.131</td>
<td>0.690</td>
</tr>
<tr>
<td>-6</td>
<td>1.064</td>
<td>0.610</td>
</tr>
</tbody>
</table>

* Calibration time

CLINICAL PHARMACOLOGY

General
Pentetreotide is a DTPA conjugate of octreotide, which is a long-acting analog of the human hormone, somatostatin. Indium In-111 pentetreotide binds to somatostatin receptors on cell surfaces throughout the body. Within an hour of injection, most of the dose of indium In-111 pentetreotide distributes from plasma to extravascular body tissues and concentrates in tumors containing a high density of somatostatin receptors. After background clearance, visualization of somatostatin receptor-rich tissue is achieved. In addition to somatostatin receptor-rich tumors, the normal pituitary gland, thyroid gland, liver, spleen and urinary bladder also are visualized in most patients, as is the bowel, to a lesser extent. Excretion is almost exclusively via the kidneys.

Pharmacokinetics
Radioactivity leaves the plasma rapidly; one third of the radioactive injected dose remains in the blood pool at 10 minutes after administration. Plasma levels continue to decline so that by 20 hours post-injection, about 1% of the radioactive dose is found in the blood pool. The biological half-life of indium In-111 pentetreotide is 6 hours.

Half of the injected dose is recoverable in urine within six hours after injection, 85% is recovered in the first 24 hours, and over 90% is recovered in urine by two days. An additional 5% is excreted in the feces within three days after injection.

Metabolism
For several hours after administration, plasma radioactivity is predominantly in parent form. Ten percent of the radioactivity excreted is nonpeptide-bound.

Pharmacodynamics
Indium In-111 pentetreotide binds to cell surface receptors for somatostatin. In nonclinical pharmacologic studies, the hormonal effect of OctreoScan® in vitro is one-tenth that of octreotide. Since diagnostic imaging doses of indium In-111 pentetreotide are lower than the therapeutic doses of octreotide, indium In-111 pentetreotide is not expected to exert clinically significant somatostatin effects.

Indium In-111 pentetreotide is cleared from the body primarily by renal excretion. Indium In-111 pentetreotide elimination has not been studied in anephric patients or in those with poorly functioning kidneys. It is not known whether indium In-111 pentetreotide elimination has been determined before administration to the patient. A method recommended for determining the labeling yield is presented at the end of this package insert.

INDICATIONS AND USAGE

Indium In-111 pentetreotide is an agent for the scintigraphic localization of primary and metastatic neuroendocrine tumors bearing somatostatin receptors.

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 OCTREOTIDE CONJUGATE MAY FORM.

The sensitivity for OctreoScan® scintigraphy was 85.3%; for CT/MRI the rate was 68%. The specificity rate for OctreoScan® scintigraphy was 50%; the rate for CT/MRI was 12%. Larger studies are needed to confirm these comparisons. Overall, including all tumor types with or without the presence of somatostatin receptors, there were 3/508 false positives and 104/508 false negatives.

Of the 309 patients, 87 had received octreotide for therapeutic purposes within 72 hours of OctreoScan® administration. These patients had an overall 95% success rate. The effect of different dose levels of octreotide on success rates has not been evaluated.

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 tested 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 cholcholethiasis, 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 cholcholethiasis.

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
The estimated radiation doses\(^1\) to the average adult (70 kg) from intravenous administration of 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 pentetreotide. An OctreoScan® kit. 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.

mGy/111 MBq | rads/3 mCi | mGy/222 MBq | rads/6 mCi
--- | --- | --- | ---
Kidneys | 54.16 | 5.42 | 108.32 | 10.83
Liver | 12.15 | 1.22 | 24.31 | 2.43
Spleen | 73.86 | 7.39 | 147.73 | 14.77
Uterus | 6.34 | 0.63 | 12.76 | 1.27
Ovaries | 4.89 | 0.49 | 9.79 | 0.98
Testes | 2.90 | 0.29 | 5.80 | 0.58
Red Marrow | 3.46 | 0.35 | 6.91 | 0.69
Urinary Bladder Wall | 30.24 | 3.02 | 60.48 | 6.05
GI Tract | 5.67 | 0.57 | 11.34 | 1.13
Small Intestine | 4.78 | 0.48 | 9.56 | 0.96
Upper Large Intestine | 5.80 | 0.58 | 11.59 | 1.16
Lower Large Intestine | 7.73 | 0.77 | 15.46 | 1.55
Adrenals | 7.55 | 0.76 | 15.11 | 1.51
Thyroid | 7.43 | 0.74 | 14.86 | 1.49

Effective Dose\(^1\)

\[ \begin{array}{c|c|c|c|}
\hline
& \text{mGy/111 MBq} & \text{rem/3 mCi} & \text{mGy/222 MBq} & \text{rem/6 mCi} \\
\hline
\text{Equivalent} & 13.03 & 1.30 & 6.05 & 0.61 \\
\hline
\end{array} \]

\(^1\) Assumes 4.8-hour voicing 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 lophophorized mixture of:
   - 10 mg pentetreotide (N-[diethylamino]amino-N,N,N’-tetraacetic acid-N-acetyl-D-phenylalanyl-L-hemicycystyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-hemicycystyl-L-threonyl cyclic (2+7) disulfide), also known as octreotide (DTPA),
   - 2.25 mg octreotide (2, 5-dihydroxybenzoic acid).
2. 3.49 mg trisodium citrate, anhydrous
3. 0.37 mg citric acid, anhydrous
4. 10.0 mg inositol

Before administration, a patient should be well hydrated. After administration, the patient must be encouraged to drink fluids liberally. Extravasation of extra fluid intake will help reduce the radiation dose by flushing out unbound, labelled pentetreotide by glomerular filtration. It is also recommended that a mild laxative (e.g., disacodyl or lactulose) be given to the patient starting the evening before the radioactive drug is administered, and continuing for 48 hours. Ample fluid uptake is necessary during this period as a support both to renal elimination 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.

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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 discoloration prior to administration, whenever solution and container permit. Preparations containing particulate matter or discoloration should not be administered. They should be disposed of in a safe manner, in compliance with applicable regulations. 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 same intravenous line.

Radiation Dosimetry

The estimated radiation doses\(^1\) 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.\(^4\)

\(^4\) Values listed include a correction for a maximum of 0.1% indium In-114m radiocontamination at calibration.

\(^1\) Estimated according to ICRP Publication 53.

Preparation of the Sep-Pak Cartridge

1. Rinse the Sep-Pak cartridge with 10 mL methanol as follows: fill a 10-mL syringe with 10 mL methanol, attach the syringe to the longer end of the Sep-Pak cartridge, and push the methanol through the cartridge. Discard the eluate in a safe and approved manner.
2. Similarly, rinse the cartridge with 10 mL water. Ensure that the cartridge is kept wet and that there is no air bubble present. If an air bubble is present, rinse the cartridge with additional 5 mL of water. Discard the eluate.

Sample Analysis

1. Using a 1-mL syringe with needle, withdraw 0.05 to 0.1 mL indium In-111 pentetreotide from the OctreoScan® Reaction Vial. Apply the preparation to the Sep-Pak cartridge through the longer end of the cartridge. Make sure that the sample is migrating onto the column of the cartridge. Note: After this step, the cartridge and all solutions eluted from it will be radioactive.
2. With a disposable 5-mL syringe, slowly (in a dropwise manner) push 5 mL water through the longer end of the cartridge, collecting the eluate in a counting vial or tube. Label this eluate as “Fraction 1.”
3. Similarly, elute the cartridge with 5 mL methanol. Be sure that this solution is pushed slowly through the longer end of the cartridge so that the elution occurs in a dropwise manner. Collect this fraction in a second culture tube or vial for counting. Label it as “Fraction 2.” Push two 5-mL portions of air through the longer end of the cartridge and collect the eluate with Fraction 2.
4. Place the Sep-Pak cartridge in a third culture tube or vial for assay.

Assay

1. Assay the activity of Fraction 1 in a suitably calibrated ionization chamber. This fraction contains the hydrophilic impurities (e.g., unbound indium In-111).
2. Assay the activity of Fraction 2. This fraction contains the indium In-111 pentetreotide.
3. Assay the activity of the Sep-Pak cartridge. This component contains the remaining non-eluatable impurities.
4. Dispose of all of the materials used in the preparation, the sample analysis, and the assay in a safe and approved manner.

Calculations

1. Percent indium In-111 pentetreotide = \( \left( \frac{\text{Fraction 2 Activity}}{\text{Total Activity}} \right) \times 100\% \)
Where Total Activity = Fraction 1 + Fraction 2 + activity remaining in Sep-Pak
2. Note: If this value is less than 90%, do not use the preparation. Discard it in a safe and approved manner.
3. Percent hydrophilic impurities = \( \left( \frac{\text{Fraction 1 Activity}}{\text{Total Activity}} \right) \times 100\% \)
4. Percent non-eluatable impurities = \( \left( \frac{\text{Activity remaining in Sep-Pak}}{\text{Total Activity}} \right) \times 100\% \)

This radiopharmaceutical is licensed by the Illinois Department of Nuclear Safety for distribution to persons licensed pursuant to 330.260(a) 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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