

<b>SUBJECT: PEPTIDE RECEPTOR RADIONUCLIDE THERAPY (PRRT)</b>	<b>EFFECTIVE DATE: 06/21/07</b> <b>REVISED DATE: 05/14/08, 04/16/09, 03/18/10, 03/17/11, 03/15/12, 02/21/13, 02/20/14</b>
<b>POLICY NUMBER: 7.01.78</b> <b>CATEGORY: Technology Assessment</b>	<b>PAGE: 1 OF: 5</b>

**• If the member's subscriber contract excludes coverage for a specific service it is not covered under that contract. In such cases, medical policy criteria are not applied.**

**• Medical policies apply to commercial and Medicaid products only when a contract benefit for the specific service exists.**

**• Medical policies only apply to Medicare products when a contract benefit exists and where there are no National or Local Medicare coverage decisions for the specific service.**

## **POLICY STATEMENT:**

Based upon our criteria and assessment of peer-reviewed literature, peptide receptor radionuclide therapy has not been proven to medically effective and is considered **investigational** for the treatment of somatostatin-receptor positive tumors, including, but not limited to neuroendocrine tumors.

*Refer to Corporate Medical Policy # 7.01.69 regarding Selective Internal Radiation Therapy (SIRT).*

*Refer to Corporate Medical Policy # 11.01.03 regarding Experimental and Investigational Services.*

*Refer to Corporate Medical Policy # 11.01.10 regarding Clinical Trials.*

## **DESCRIPTION:**

Somatostatin is a peptide hormone that regulates the endocrine system and affects neurotransmission and cell proliferation via an interaction with G-protein-coupled somatostatin receptors and inhibition of the release of numerous secondary hormones. Five somatostatin receptors have been identified and characterized with each of the receptors activating distinct signaling mechanisms within cells. Analogs of somatostatin have been synthesized that are smaller, more potent, longer-lasting and more specific in their biologic effects than natural somatostatin. Examples of these analogs include octreotide, lanreotide and vaptoreotide. Some of these analogs have become useful as medications for the treatment of acromegaly, or the treatment of diarrhea and flushing episodes associated with carcinoid syndrome.

Many types of neuroendocrine tumors express somatostatin receptors including, but not limited to, pancreatic islet cell tumors (e.g., gastrinomas, glucagonomas, GHRHomas, and nonfunctioning islet cell tumors), VIPomas, carcinoids, insulinomas, and some adrenal cortical and differentiated thyroid tumors. Somatostatin receptor (SSTR) scintigraphy has become an important image modality in patients with SSTR-positive tumors. SSTR scintigraphy involves the administration of a radiolabeled peptide tracer, which is targeted at the somatostatin receptor. A more intensified, targeted radiotherapy, known as peptide receptor radionuclide therapy (PRRT), has been proposed and investigated for those patients with inoperable or metastasized neuroendocrine tumors who suffer from debilitating symptoms, such as carcinoid syndrome.

Several radiolabeled somatostatin analogs are currently being investigated in the treatment of patients with SSTR-positive metastasized neuroendocrine tumors. These conjugates all consist of a somatostatin analog, such as octreotide or octreotide, a complexing moiety (or chelator) and a radionuclide. The chelator, which is attached to the somatostatin analog, allows a stable connection between the analog and the radionuclide. The basic principle of tumor-targeting after systemic administration of the conjugate involves binding to SSTRs, which are expressed on the cell surface of the tumor cell, followed by effective internalization of the radionuclide-peptide complex. The emitted radiation can damage the DNA, which may subsequently lead to the induction of cell death. Different combinations of radionuclides and somatostatin analogues are used to target the specific SSTR-positive tumor. These analogues differ from each other in their affinity for the various five SSTR subtypes. This variable affinity is important because it can have great influence on the clinical effectiveness of the radiolabeled somatostatin analog. Indium (111In), yttrium (90Y) and lutetium (177Lu) have been the most frequently used radionuclides for targeted radiotherapy in the various clinical trials thus far.

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#### RATIONALE:

Currently, there are no radiolabeled somatostatin analog conjugates that are FDA approved specifically for use in PRRT. Clinical studies investigating neuroendocrine tumors, in particular, those treated with 90Y- and 177Lu-labelled somatostatin analogues, are very encouraging in terms of tumor shrinkage and palliation of symptoms. However, complete responses are unusual and there have been no demonstrated improvements in survival. Differences in treatment protocols, such as administered doses, dosing schemes, the tumor response criteria, and the heterogeneity of the patient sample population in the various studies have made it impossible to come to any definitive conclusions regarding the overall health benefit of this therapy. Therefore, trials with better defined protocols and patient populations are necessary to determine the optimal PRRT and treatment scheme.

#### CODES: Number Description

*Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*

**CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.**

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

**\* No specific codes exist for PRRT, but the following codes could be billed:**

<b>CPT:</b>	78800 Radiopharmaceutical localization of tumor, or distribution of radiopharmaceutical agent(s); limited area 78801 multiple areas 78802 whole body, single day imaging 78803 tomographic (SPECT) 78804 whole body, requiring two or more days imaging
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<b>HCPCS:</b>	A4641 Radiopharmaceutical, diagnostic, not otherwise classified A9543 Yttrium Y-90 ibritumomab tiuxetan, therapeutic, per treatment dose, up to 40 millicuries A9699 Radiopharmaceutical, therapeutic, not otherwise classified J2354 Injection, octreotide, nondepot form for subcutaneous or intravenous injection, 25 mcg
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**ICD9:** Multiple diagnosis codes

**ICD10:** Multiple diagnosis codes

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\* key article

#### **KEY WORDS:**

Peptide receptor radionuclide therapy, PRRT, PRRNT, Receptor-mediated radiotherapy, Radiolabeled nuclide therapy, somatostatin analog, <sup>90</sup>Y-DOTATOC, 177Lu-DOTA0,Tyr3, 90Y-DOTA0,Tyr3

## **CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS**

Based on our review, peptide receptor radionuclide therapy is not specifically mentioned in any National or Regional Medicare coverage determinations or policies.