Lutetium Lu 177 Dotatate (Lutathera) and Lutetium Lu 177 Vipivotide Tetraxetan (Pluvicto)

Policy Number: **M20180626056**

Effective Date: **8/1/2018**

Sponsoring Department: **Health Care Services**

Impacted Department(s): **Health Care Services**

Type of Policy: ☒ Internal ☒ External

Data Classification: ☐Confidential ☐Restricted ☒Public

Applies to (Line of Business):

☐ Corporate (All)
☒ State Products, if yes which plan(s): ☒MediSource; ☒ MediSource Connect; ☒Child Health Plus ☒Essential Plan
☒ Medicare, if yes, which plan(s): ☒MAPD; ☐PDP; ☒ISNP; ☒CSNP
☒ Commercial, if yes, which type: ☒Large Group; ☒Small Group; ☒Individual
☒ Self-Funded Services *(Refer to specific Summary Plan Descriptions (SPDs) to determine any pre-authorization or pre-certification requirements and coverage limitations. In the event of any conflict between this policy and the SPD of a Self-Funded Plan, the SPD shall supersede the policy.)*

Excluded Products within the Selected Lines of Business (LOB)

Applicable to Vendors? Yes ☐ No☒

Purpose and Applicability:

To set forth Independent Health's medical necessity criteria and coverage guidelines for **Lutathera (lutetium Lu 177 dotatate)** for **gastroenteropancreatic neuroendocrine tumors (GEP-NETs)** and **Pluvicto (lutetium Lu 177 vipivotide tetraxetan)** for **castration resistant prostate cancer.**

Policy:

Commercial, Self-Funded, Medicare Advantage, MediSource, MediSource Connect, Child Health Plus and Essential Plan

Lutathera:
Lutathera is considered medically necessary for the treatment of adult patients with somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs) when the following criteria are met:

- The patient is at least 18 years of age and not pregnant or breastfeeding; AND
- The patient has unresectable, locally advanced or metastatic disease confirmed by NetSpot (68-Ga DOTATATE PET/CT) or Octreoscan (111-In pentetreotide); AND
- The patient has had disease progression despite somatostatin analog therapy or molecular targeted therapy (e.g., everolimus), AND
- An appropriate imaging study has been performed to document over-expression of somatostatin receptors by the target lesions, AND
- The tumor is well-differentiated with a **Ki-67** index of 20% or less, as documented in a pathology report.

Dosing for adults with gastroenteropancreatic neuroendocrine tumors: IV: 7.4 GBq (200 mCi) every 8 weeks (±1 week) for a total of 4 doses.

Note: Coverage will be provided for 1 year (4 doses) and may NOT be renewed.

Pluvicto:
Pluvicto is considered medically necessary for treatment (up to 6 total doses) of prostate cancer when all of the following criteria are met:

- The patient is at least 18 years of age; AND
- The patient has metastatic castration-resistant prostate cancer; AND
- Patient has prostate-specific membrane antigen (PSMA)-positive disease defined as having at least one tumor lesion with gallium Ga-68 gozetotide uptake greater than normal liver;
- The patient has been treated with androgen receptor (AR) pathway inhibition (e.g., abiraterone) and taxane-based chemotherapy (e.g., docetaxel); AND
- The disease is prostate-specific membrane antigen (PSMA)-positive.

Renewal of Therapy:

- Patient continues to meet the indication-specific relevant criteria requirements AND
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include myelosuppression (e.g., anemia, thrombocytopenia, leukopenia, neutropenia), severe renal toxicity, etc.; AND
- Disease response with treatment as defined by stabilization of disease or at least a partial response; AND
- Patient has not received more than 6 doses total.

Dosing for adults with metastatic, castration resistant (PSMA-positive) prostate cancer: IV: 7.4 GBq (200 mCi) every 6 weeks for up to 6 doses, or until disease progression or unacceptable toxicity.

Background:
Gastroenteropancreatic neuroendocrine tumors (GEP-NETS) may arise at many sites in the body from widely distributed neuroendocrine cells. GEP-NETs have traditionally been divided into foregut (esophagus, stomach, proximal duodenum, liver and pancreas), midgut (distal duodenum ileum, jejunum, ascending colon and proximal two thirds of transverse colon) and hindgut tumors (distal third of transverse colon, descending colon, sigmoid colon and rectum).

Lutathera, a radiolabeled somatostatin analog, is FDA approved for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETs), including foregut, midgut, and hindgut neuroendocrine tumors in adults. Lutathera binds to somatostatin receptors on cells, including malignant somatostatin receptor-positive tumor cells and is internalized upon binding. The beta emission from Lu 177 induces cellular damage by formation of free radicals in somatostatin receptor-positive cells and in neighboring cells. Lutathera is a radiopharmaceutical, so it must be handled with appropriate safety measures to minimize radiation exposure. It should be used by or under the control of physicians who are qualified by specific training and experience.

Castration resistant prostate cancer continues growing despite decreased testosterone levels in the body. Males with advanced prostate cancer who have evidence of disease progression (e.g., an increase in serum prostate-specific antigen (PSA), new metastases, or progression of existing metastases) while being managed with androgen deprivation therapy (ADT) and who have castrate levels of serum testosterone (<50 ng/dL) are considered to have CRPC.

Pluvicto is an FDA approved treatment for castration resistant prostate cancer. The National Comprehensive Cancer Network Panel recommends Pluvicto as a category 1, useful in certain circumstances treatment option for patients with ≥1 prostate-specific membrane antigen (PSMA) - positive lesion and/or metastatic disease that is predominately PSMA-positive and with no dominant PSMA-negative metastatic lesions who have been treated previously with androgen receptor-directed therapy and a taxane-based chemotherapy. As a radiopharmaceutical, Pluvicto should also be handled with appropriate safety measures to minimize radiation exposure. It should be used by or under the control of physicians who are qualified by specific training and experience.

An evaluation of the peer-reviewed scientific literature, including but not limited to subscription materials, has provided Independent Health the basis for its medical necessity coverage outlined above.

Pre-Authorization Required? Yes ☒ No ☐

Pre-authorization is required for this service.

Definitions

Castration resistant prostate cancer (CRPC) occurs when prostate cancer (CaP) progresses under therapy-induced castrate conditions.

Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) also known as carcinoids and islet cell tumors, are tumors derived from neuroendocrine cells that can occur anywhere along the gastrointestinal tract and comprise a heterogeneous family of neoplasms with a wide and complex spectrum of clinical behavior. GEP-NETs are more prevalent than many other tumors of the gastrointestinal tract, including stomach and pancreatic carcinomas combined.

Ki67 (pKi67) is a nuclear protein which is an established prognostic and predictive indicator for the assessment of biopsies from patients with cancer. Clinically, pKi67 has been shown to correlate with metastasis and the clinical stage of tumors.

Lutathera (lutetium Lu 177 dotatate) is a radiolabeled somatostatin analog approved by the Food and Drug Administration (FDA) for the treatment of somatostatin receptor-positive gastroenteropancreatic neuroendocrine tumors (GEP-NETS) including foregut, midgut and hindgut neuroendocrine tumors in adults.

Pluvicto (lutetium Lu 177 vipivotide tetraxetan) is a therapy for patients with prostate specific membrane antigen positive (PSMA+) metastatic castrate-resistant prostate cancer (mCRPC). Regardless of the location of metastasis, this therapy works by precisely delivering radiation to PSMA+ tumor cells. The current application of Pluvicto is for use in mCRPC patients resistant to androgen receptor directed inhibition (ARDI) and taxane-based chemotherapy.

References

Related Policies, Processes and Other Documents

N/A

Non-Regulatory references

Brabander T, van der Zwan W, Teunissen J, et al. Long-term efficacy, survival, and safety of [177Lu-DOTA0, Tyr3] octreotate in patients with gastroenteropancreatic and bronchial neuroendocrine tumors. Clin Cancer Res.2017 Aug 15;23(16):4617-4624.

Chan JA, Kulke M. Metastatic well-differentiated gastrointestinal neuroendocrine (carcinoid) tumors: Systemic therapy options to control tumor growth and symptoms of hormone hypersecretion. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on August 23, 2023)

Dawson NA, Leger P. Overview of the treatment of castration-resistant prostate cancer (CRPC). In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on August 23, 2023)

Díez M, Teulé A, Salazar R. Gastroenteropancreatic neuroendocrine tumors: diagnosis and treatment. Ann Gastroenterol. 2013;26(1):29-36.

Hayes, Inc. Precision Therapy Assessment Lutetium Lu 177 Dotatate (Lutathera, Advanced Accelerator Applications USA Inc) for the Treatment of Gastroenteropancreatic Neuroendocrine Tumors. Lansdale PA; September 2019.

Li LT, Jiang G, Chen Q, Zheng JN. Ki67 is a promising molecular target in the diagnosis of cancer (review). Mol Med Rep. 2015 Mar;11(3):1566-72.

Lutetium Lu-177 dotatate: Drug information In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on November 1, 2023)

Lutetium Lu-177 vipivotide tetraxetan: Drug information In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on November 1, 2023)

National Comprehensive Cancer Network (NCCN) [web site]. Neuroendocrine and Adrenal Tumors Version 1.2023 8.2.2023 . Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf Accessed August 24, 2023.

National Comprehensive Cancer Network (NCCN) [web site]. Prostate Cancer Version 3.2023 Augusts 7, 2023 . Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf Accessed August 23, 2023.

Strosberg J, El-Haddad G, Wolin E, et al. Phase 3 trial of 177Lu-dotatate for midgut neuroendocrine tumors. N Engl J Med. 2017;376(2):125-135.

U.S. Food and Drug Administration (FDA) [web site]. Lutathera (lutetium Lu 177 dotatate). Highlights of prescribing information. January 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208700s000lbl.pdf Accessed August 23, 2023.

U.S. Food and Drug Administration (FDA) [web site]. Pluvicto (lutetium Lu 177 vipivotide tetraxetan) Highlights of prescribing information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215833s000lbl.pdf Accessed August 23, 2023.

Vellky JE, Ricke WA. Development and prevalence of castration-resistant prostate cancer subtypes. Neoplasia. 2020 Nov;22(11):566-575.

Regulatory References

New York State Department of Health, Division of Managed Care Response to Coverage Question (CovQuest). Email response 6/4/2018.

New York State Department of Health, Division of Managed Care Response to Coverage Question (CovQuest). Email response 3/20/2023.

New York State Department of Health [web site]. New York State Medicaid Program Section 4 – Radiology Version April 2023. Available at: https://www.emedny.org/ProviderManuals/Laboratory/PDFS/Laboratory_Procedure_Codes.pdf Accessed August 23, 2023.

This policy contains medical necessity criteria that apply for this service. Please note that payment for covered services is subject to eligibility criteria, contract exclusions and the limitations noted in the member's contract at the time the services are rendered.

Version Control

Signature / Approval on File? Yes ☒ No ☐

Revision Date	Owner	Notes
1/1/2024	Health Care Services	Revised
11/1/2023	Health Care Services	Revised
11/1/2022	Health Care Services	Revised
11/1/2021	Health Care Services	Reviewed
12/1/2020	Health Care Services	Reviewed
1/1/2020	Medical Management	Revised
1/1/2019	Medical Management	Revised