Clinical Policy Title:	pertuzumab
Policy Number:	RxA.249
Drug(s) Applied:	Perjeta®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Pertuzumab is a human epidermal growth factor receptor 2 protein (HER2)/neu receptor antagonist indicated for:

- Use in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.
- Use in combination with trastuzumab and chemotherapy as:
  - neoadjuvant treatment of patients with HER2-positive, locally advanced, inflammatory, or early-stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer;
  - adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pertuzumab (Perjeta®)	Breast cancer	The initial dose is 840 mg administered as a 60-minute intravenous infusion, followed every 3 weeks thereafter by 420 mg administered as a 30-to-60-minute intravenous infusion. MBC: Administer pertuzumab, trastuzumab or trastuzumab hyaluronidase-oysk, and docetaxel every 3 weeks. For neoadjuvant treatment: Administer pertuzumab, trastuzumab or trastuzumab hyaluronidase-oysk, and chemotherapy preoperatively every 3 weeks for 3 to 6 cycles. For adjuvant treatment: Administer pertuzumab, trastuzumab or trastuzumab hyaluronidase-oysk, and chemotherapy postoperatively every 3 weeks for a total of 1 year (up to 18 cycles).	840 mg IV initially, then 420 mg IV every 3 weeks.

Dosage Forms

- Single-dose vial for injection: 420 mg/14 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Breast Cancer (must meet all):

1. Diagnosis of HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Prescribed as combination therapy (*see Appendix B);*
5. Request meets one of the following (a or b):
   a. Initial dose: 840 mg, followed by maintenance dose: 420 mg every 3 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Colon Cancer (off label) (must meet all):

1. Diagnosis of HER2-amplified and RAS and BRAF wild-type colon cancer;
2. Request is for one of the following (a or b):
   a. Pertuzumab therapy is prescribed in combination with trastuzumab in patients (HER2-amplified and RAS and BRAF wild-type) who are not appropriate for intensive therapy, if no previous treatment with a HER2 inhibitor and meets one of the following (i, ii, iii, iv, v, or vi):
      i. as primary treatment for locally unresectable or medically inoperable disease;
      ii. for unresectable synchronous liver and/or lung metastases that remain unresectable after primary systemic therapy;
      iii. as primary treatment for synchronous abdominal/peritoneal metastases that are non-obstructing, or following local therapy for patients with existing or imminent obstruction;
      iv. for synchronous unresectable metastases of other sites;
      v. as primary treatment for unresectable metachronous metastases in patients who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy;
      vi. for unresectable metachronous metastases that remain unresectable after primary treatment;
   b. Pertuzumab is prescribed as a subsequent therapy in combination with trastuzumab for progression of advanced or metastatic disease (HER2-amplified and RAS and BRAF wild-type) not previously treated with HER2 inhibitor, in patients previously treated and meets one of the following (i, ii, iii, iv, or v):
      i. with oxaliplatin-based therapy without irinotecan;
      ii. with irinotecan-based therapy without oxaliplatin;
      iii. with oxaliplatin and irinotecan;
      iv. without irinotecan or oxaliplatin;
      v. without irinotecan or oxaliplatin followed by FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) with or without bevacizumab;

3. Prescribed by or in consultation with an oncologist;
4. Member is 18 years of age or older;
5. Dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence)*.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Head and Neck Cancer (off label) (must meet all):
1. Diagnosis of HER2-positive recurrent, unresectable, or metastatic salivary gland tumor;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Pertuzumab is given in combination with trastuzumab, as systemic therapy for HER2-positive disease with (a or b):
   a. distant metastases in patients with a ECOG performance status (PS) of 0-3;
   b. unresectable locoregional recurrence or second primary with prior radiation therapy;
5. Dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

D. Rectal Cancer (off label) (must meet all):
E. Diagnosis of HER2-amplified and RAS and BRAF wild-type rectal cancer;
1. Request is for one of the following (a or b):
   a. Pertuzumab therapy is prescribed in combination with trastuzumab in patients who are not appropriate for intensive therapy, if no previous treatment with a HER2 inhibitor and meets one of the following (i, ii, iii, iv, v, vi, vii, or viii):
      i. as primary treatment for T3, N Any; T1-2, N1-2; T4, N Any; or locally unresectable or medically inoperable disease if resection is contraindicated following neoadjuvant or total neoadjuvant therapy;
      ii. for synchronous liver only and/or lung only metastases that are unresectable or medically inoperable and remain unresectable (with no progression of primary tumor) after primary systemic therapy;
      iii. following palliative radiation therapy (RT) or chemo/RT for synchronous liver only and/or lung only metastases that are unresectable or medically inoperable and remain unresectable (with progression of primary tumor) after primary systemic therapy;
      iv. as primary treatment for synchronous abdominal/peritoneal metastases that are nonobstructing, or following local therapy for patients with existing or imminent obstruction;
      v. as primary treatment for synchronous unresectable metastases of other sites;
      vi. as primary treatment for unresectable isolated pelvic/anastomotic recurrence;
      vii. as primary treatment for unresectable metachronous metastases in patients who have not received previous adjuvant FOLFOX or CapeOX within the past 12 months, who have received previous fluorouracil/leucovorin (5-FU/LV) or capecitabine therapy, or who have not received any previous chemotherapy;
      viii. for unresectable metachronous metastases that remain unresectable after primary treatment;
   b. Pertuzumab is prescribed as a subsequent therapy in combination with trastuzumab for progression of advanced or metastatic disease not previously treated with HER2 inhibitor, in patients previously

treated and meets one of the following (i, ii, iii, iv, or v):
   i. with oxaliplatin-based therapy without irinotecan;
   ii. with irinotecan-based therapy without oxaliplatin;
   iii. with oxaliplatin and irinotecan;
   iv. without irinotecan or oxaliplatin;
   v. without irinotecan or oxaliplatin followed by FOLFOX (fluorouracil, leucovorin, and oxaliplatin) or CapeOX (capecitabine and oxaliplatin) with or without bevacizumab;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy, or documentation supports that member is currently receiving pertuzumab for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 420 mg every 3 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence).*

Approval Duration
Commercial: 12 months (Total of 18 cycles if neoadjuvant or adjuvant therapy)
Medicaid: 12 months (Total of 18 cycles if neoadjuvant or adjuvant therapy)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
MBC: Metastatic Breast Cancer
FDA: Food and Drug Administration
HER2: Human Epidermal growth factor Receptor 2
LVEF: Left Ventricular Ejection Fraction
CHF: Congestive Heart Failure
ECOG: Eastern Cooperative Oncology Group

APPENDIX B: Therapeutic Alternatives

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of drugs that may be used with pertuzumab: • Chemotherapeutic agents: carboplatin, cyclophosphamide, doxorubicin • HER2-targeted agents: docetaxel (Taxotere®), paclitaxel, trastuzumab (Herceptin®) • Endocrine therapy: tamoxifen; aromatase inhibitors: anastrozole (Arimidex®), letrozole (Femara®), exemestane (Aromasin®)	Regimens are dependent on a variety of factors including menopausal status, treatment/progression history, clinical stage, histology, mutational and receptor status, treatment purpose (e.g., adjuvant and neoadjuvant treatment, treatment for metastatic disease).	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients with known hypersensitivity to pertuzumab or to any of its excipients.

- Boxed Warning(s):
  - Left ventricular dysfunction: Pertuzumab can result in subclinical and clinical cardiac failure manifesting as decreased LVEF and CHF. Evaluate cardiac function prior to and during treatment. Discontinue Perjeta® treatment for a confirmed clinically significant decrease in left ventricular function.
  - Embryo-fetal Toxicity: Exposure to pertuzumab can result in embryo-fetal death and birth defects. Advise patients of these risks and the need for effective contraception.

APPENDIX D: General Information

- Infusion-Related Reactions: Monitor for signs and symptoms. If a significant infusion-associated reaction occurs, slow or interrupt the infusion and administer appropriate medical therapies.
- Hypersensitivity Reactions/Anaphylaxis: Monitor for signs and symptoms, including angioedema. If a severe hypersensitivity reaction/anaphylaxis occurs, discontinue the infusion immediately and administer appropriate medical therapies.

References

1. Perjeta® Prescribing Information. South San Francisco, CA: Genentech, Inc.; February 2021. Available at http://www.gene.com/download/pdf/perjeta_prescribing.pdf. Accessed May 02, 2021
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed May 02, 2021.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version 4.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf . Accessed May 02, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical policy title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Continued Therapy criteria II.A.1. was rephrased to "Currently receiving medication that has been authorized by RxAdvance.." 4. Initial approval criteria approval duration was updated to include Commercial, Medicaid and HIM approval duration as 6 months. 5. Continued therapy approval duration was updated to include Commercial, Medicaid and HIM approval duration as 12 months. 6. References were reviewed and updated.	07/08/2020	09/14/2020
Policy was reviewed: 1. Policy title was updated. 2. Dosing information was updated. 3. Clinical policy - Verbiage added: ''The provision of provider samples does not guarantee coverage under the provisions of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage" after "Provider must submit…" 4. Initial approval criteria were updated with off label indication. 5. Appendix A and C were updated. 6. Appendix D was added. 7. References were updated.	05/02/2021	06/10/2021