Clinical Policy: Pertuzumab (Perjeta)

Reference Number: ERX.SPA.43
Effective Date: 07.01.16
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Pertuzumab (Perjeta®) is a human epidermal growth factor receptor 2 protein (HER2)/neu receptor antagonist.

FDA Approved Indication(s)
Perjeta is indicated for:

- Use in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease
- Use in combination with trastuzumab and chemotherapy as:
  - Neoadjuvant treatment of 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Perjeta is **medically necessary** when the following criteria are met:

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. Age ≥ 18 years;
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Colorectal Cancer (off-label) (must meet all):

1. Diagnosis of advanced or metastatic colorectal cancer and both of the following (a and b):
   a. Disease is HER2 positive;
   b. Disease is wild-type *RAS* (defined as wild-type in both KRAS and NRAS as determined by an FDA-approved test for this use);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. No previous use of a HER2 inhibitor therapy (e.g., trastuzumab, Kadcyla®, Tykerb®, Perjeta);

5. Prescribed in combination with trastuzumab;*
   **Prior authorization may be required.*
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Perjeta 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*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months (*total of 18 cycles if neoadjuvant or adjuvant therapy for breast cancer*)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
KRAS: Kirsten rat sarcoma 2 viral oncogene homologue
NRAS: neuroblastoma RAS viral oncogene homologue

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of drugs that may be used with Perjeta for breast cancer: • Chemotherapeutic agents: carboplatin, cyclophosphamide, doxocrubicin	Regimens are dependent on a variety of factors including menopausal status, treatment/progression history, clinical stage, histology, mutational, receptor status,	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• HER2-targeted agents: docetaxel (Taxotere®), paclitaxel, Herceptin® (trastuzumab) • Endocrine therapy: tamoxifen; aromatase inhibitors: anastrozole (Arimidex®), letrozole (Femara®), exemestane (Aromasin®).	treatment purpose (e.g., adjuvant and neoadjuvant treatment, treatment for metastatic disease).	

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): known hypersensitivity to pertuzumab or to any of its excipients
- Boxed warning(s): left ventricular dysfunction, embryo-fetal toxicity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Breast cancer	Initial dose of 840 mg IV, followed by maintenance dose of 420 mg IV every 3 weeks *For metastatic disease,* Perjeta should be administered as outlined above. *For neoadjuvant treatment*, Perjeta should be administered for 3-6 cycles. Following surgery, patients should continue to receive Perjeta to complete 1 year of treatment (up to 18 cycles) *For adjuvant treatment*, Perjeta should be administered for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity	See regimen

VI. Product Availability

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

VII. References

1. Perjeta Prescribing Information. South San Francisco, CA: Genentech, Inc.; December 2018. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125409s124lbl.pdf. Accessed February 10, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed February 10, 2020.
3. National Comprehensive Cancer Network Guidelines. Breast Cancer Version 2.2020. Available at www.nccn.org. Accessed February 10, 2020.
4. National Comprehensive Cancer Network Guidelines. Colon Cancer Version 1.2020. Available at www.nccn.org. Accessed February 10, 2020.
5. National Comprehensive Cancer Network Guidelines. Rectal Cancer Version 1.2020. Available at www.nccn.org. Accessed February 10, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.16	06.16
Increased approval durations from 3/6 months to 6/12 months.	04.17	05.17
2Q 2018 annual review: NCCN and FDA approved uses summarized for improved clarity; specialist involvement in care added; breast cancer FDA labels updated: neoadjuvant treatment with trastuzumab and docetaxel replaced with trastuzumab and chemotherapy; adjuvant treatment added; references reviewed and updated.	02.13.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: no significant changes; references reviewed and updated.	12.19.19	05.19
2Q 2020 annual review: added NCCN compendium-supported use of colorectal cancer; references reviewed and updated.	02.17.20	05.20

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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