UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable – HER2 Antagonist) – Perjeta Utilization Management Medical Policy
- Perjeta® (pertuzumab intravenous infusion –Genentech)

REVIEW DATE: 08/06/2025

OVERVIEW

Perjeta, a human epidermal growth factor receptor 2 (HER2) antagonist, is indicated for the treatment of **HER2-positive breast cancer** for the following uses:[1]

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

Dosing

An initial one-time dose of Perjeta 840 mg administered intravenously and then Perjeta 420 mg administered not more frequently than once every 3 weeks is recommended for the approved uses.[1] This dosing was also used in a clinical study for salivary gland tumors and biliary tract cancers.[2,3]

Guidelines

Perjeta is discussed in the guidelines from the National Comprehensive Cancer Network (NCCN):

- **Breast Cancer**: NCCN guidelines (version 4.2025 – April 17, 2025) recommend Perjeta in the preoperative/adjuvant and metastatic setting.[4,5] For preoperative (neoadjuvant)/adjuvant therapy in HER2-positive disease, docetaxel + carboplatin + trastuzumab + Perjeta is a "Preferred Regimen" (category 2A); doxorubicin + cyclophosphamide followed by paclitaxel + trastuzumab and Perjeta is recommended as "Useful in Certain Circumstances" (category 2A). Under "Other Recommended Regimens", doxorubicin + cyclophosphamide followed by docetaxel + trastuzumab + Perjeta is also listed (category 2A). In the neoadjuvant/adjuvant setting, the chemotherapy agents in combination with trastuzumab + Perjeta are administered for approximately four cycles, followed by trastuzumab ± Perjeta to complete 1 year of therapy. If there is no residual disease after preoperative therapy or no preoperative therapy, the guidelines recommend completing up to one year of HER2 targeted therapy with trastuzumab ± Perjeta after completing planned chemotherapy regimen course. In the metastatic setting, the "Preferred Regimens" are Perjeta + trastuzumab + docetaxel (category 1) or Perjeta + trastuzumab + paclitaxel (category 2A). In this setting, chemotherapy + trastuzumab + Perjeta are continued until disease progression or unmanageable toxicity. It is noted in a footnote that maintenance trastuzumab/Perjeta after response can be given, with concurrent endocrine therapy if estrogen receptor-positive and HER2+ metastatic disease. Under additional considerations, it is noted that patients previously treated with chemotherapy + trastuzumab, in the absence of Perjeta, may be considered for one line of therapy. This therapy may include both trastuzumab + Perjeta in combination with or without cytotoxic chemotherapy.
- **Colon Cancer/Rectal Cancer**: NCCN guidelines (version 4.2025 – June 27, 2025) for colon cancer and rectal cancer (version 2.2025 – March 31, 2025) recommend use of Perjeta +

trastuzumab in patients with HER2-amplified, *RAS* and *BRAF* wild-type, colon and rectal cancer.[5-7] Anti-HER2 therapy with signal transduction inhibition is indicated for patients with HER2 immunohistochemistry (IHC) 3+, IHC2+/in situ hybridization (ISH)+, or next generation sequencing (NGS) amplified cancer that is *RAS* and *BRAF* wild-type. Perjeta + trastuzumab is recommended for use in a variety of therapy settings (e.g., adjuvant therapy, primary treatment, subsequent therapy), in patients who are not appropriate for intensive therapy and with no previous treatment with a HER2 inhibitor. It is a category 2A recommendation for primary and subsequent therapy settings; category 2B recommendation for adjuvant therapy.

- **Head and Neck Cancers:** NCCN guidelines (version 4.2025 – June 20, 2025) recommend Perjeta + trastuzumab as a systemic therapy option for recurrent, unresectable, or metastatic salivary gland tumors under "Useful in Certain Circumstances" for HER2 positive tumors (category 2A).[5,8]
- **Biliary Tract Cancers:** NCCN guidelines (version 2.2025 – July 2, 2025) recommend Perjeta + trastuzumab as subsequent treatment for biliary tract cancers for progression on or after systemic treatment for unresectable or metastatic disease that is HER2-positive as "Useful in Certain Circumstances" (category 2A).[9]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Perjeta. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Perjeta, as well as the monitoring required for adverse events and long-term efficacy, approval requires Perjeta to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Perjeta is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Breast Cancer – Neoadjuvant or Adjuvant Therapy. Approve for 1 year (total) if the patient meets ALL of the following (A, B, C, D, and E):

A) Patient is ≥ 18 years of age; AND
B) Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
C) Patient meets ONE of the following (i or ii):
  i. The medication will be used in combination with chemotherapy; OR
  Note: Examples of chemotherapy include doxorubicin, cyclophosphamide, docetaxel, paclitaxel, carboplatin.
  ii. The medication is continued after chemotherapy to complete 1 year of neoadjuvant or adjuvant therapy; AND
D) The medication will be used in combination with a trastuzumab product; AND
E) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve BOTH of the following (A and B):
A) An initial one-time dose of 840 mg administered intravenously; AND
B) Perjeta 420 mg administered not more frequently than once every 3 weeks.

Note: If the time between two sequential infusions is 6 weeks or greater, the initial Perjeta dose of 840 mg is re-administered.

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2. Breast Cancer – Metastatic Disease. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D)
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
- **C)** The medication will be used in combination with trastuzumab; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve BOTH of the following (A and B):
- **A)** An initial one-time dose of 840 mg administered intravenously; AND
- **B)** Perjeta 420 mg administered intravenously not more frequently than once every 3 weeks.
  Note: If the time between two sequential infusions is 6 weeks or greater, the initial Perjeta dose of 840 mg is re-administered.

Other Uses with Supportive Evidence

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3. Biliary Tract Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
- **C)** Patient has tried at least one systemic chemotherapy regimen; AND
  Note: Examples of a systemic chemotherapy regimen include: gemcitabine and cisplatin; Imfinzi (durvalumab intravenous infusion) and gemcitabine, 5-flourouracil and oxaliplatin, capecitabine and oxaliplatin, gemcitabine and cisplatin.
- **D)** The medication will be used in combination with a trastuzumab product; AND
- **E)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve BOTH of the following (A and B):
- **A)** An initial one-time dose of 840 mg administered intravenously; AND
- **B)** Perjeta 420 mg administered not more frequently than once every 3 weeks.
  Note: If the time between two sequential infusions is 6 weeks or greater, the initial Perjeta dose of 840 mg is re-administered.

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4. Colon or Rectal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has human epidermal growth factor receptor 2 (HER2)-amplified disease; AND
  Note: HER2 amplified disease is HER2 immunohistochemistry (IHC) 3+, IHC 2+/in situ hybridization (ISH)+, or next-generation sequencing (NGS) amplified cancer.
- **C)** The tumor is *RAS* and *BRAF* wild-type; AND
- **D)** The medication is used in combination with trastuzumab; AND
- **E)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve BOTH of the following (A and B):
- **A)** An initial one-time dose of 840 mg administered intravenously; AND
- **B)** Perjeta 420 mg administered intravenously not more frequently than once every 3 weeks.

Note: If the time between two sequential infusions is 6 weeks or greater, the initial Perjeta dose of 840 mg is re-administered.

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5. Salivary Gland Tumor. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, and E):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has recurrent, unresectable, or metastatic disease; AND
- **C)** Patient has human epidermal growth factor receptor 2 (HER2)-positive disease; AND
- **D)** The medication is used in combination with trastuzumab; AND
- **E)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve BOTH of the following (A and B):
- **A)** An initial one-time dose of 840 mg administered intravenously; AND
- **B)** Perjeta 420 mg administered intravenously not more frequently than once every 3 weeks.
  Note: If the time between two sequential infusions is 6 weeks or greater, the initial Perjeta dose of 840 mg is re-administered.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Perjeta is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Perjeta® intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; February 2021.
2. Kurzorck R, Bowles DW, Kang H, et al. Targeted therapy for advanced salivary gland carcinoma based on molecular profiling: results from MyPathway, a phase IIa multiple basket study. *Ann Oncol.* 2020; 31:412-421.
3. Javle, M, Borad MJ, Azad NS, et al. Pertuzumab and trastuzumab for HER2-positive metastatic biliary tract cancer (MyPathway): a multicentre, open-label, phase 2a, multiple basket study. *Lancet Oncol.* 2021; 22(9):1290-1300.
4. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – April 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed August 4, 2025.
5. The NCCN Drugs & Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 30, 2025. Search term: pertuzumab.
6. The NCCN Colon Cancer Clinical Practice Guidelines in Oncology (version 4.2025 – June 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 30, 2025.
7. The NCCN Rectal Cancer Clinical Practice Guidelines in Oncology (version 2.2025 – March 31, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed July 30, 2025.
8. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (version 4.2025 – June 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 30, 2025.
9. The NCCN Biliary Tract Cancers Clinical Practice Guidelines in Oncology (version 2.2025 – July 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 30, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes	07/19/2023
Annual Revision	**Breast Cancer – Metastatic Disease:** Deleted the following criteria based on guideline recommendation: "Patient has not been previously treated with anti-HER2 therapy or chemotherapy for metastatic disease." Deleted the words "and chemotherapy" along with the examples of chemotherapy in the Note, for the criterion "The medication will be used in combination with trastuzumab and chemotherapy."	08/07/2024
Annual Revision	The policy name was changed from "Oncology (Injectable) – Perjeta UM Medical Policy" to "Oncology (Injectable - HER2 Antagonist) - Perjeta UM Medical Policy. **Colon or Rectal Cancer:** Changed qualifier from HER2-positive to HER2-"amplified" disease. Added Note defining HER2 amplified disease. Added a new requirement that the tumor is *RAS* and *BRAF* wild-type.	08/06/2025