# Clinical Policy: Trastuzumab/Biosimilars, Trastuzumab-Hyaluronidase

Reference Number: PA.CP.PHAR.228
Effective Date: 01/2018
Last Review Date: 04/2024

Revision Log

**Description**

- Trastuzumab (Herceptin®) is a human epidermal growth factor receptor 2 (HER2)/neu receptor antagonist.
- Trastuzumab-dkst (Ogivri®), trastuzumab-pkrb (Herzuma®), and trastuzumab-dttb (Ontruzant®), trastuzumab-qyyp (Trazimera®), and trastuzumab-anns (Kanjinti®) are Herceptin biosimilars.
- Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta™) is a combination of trastuzumab and hyaluronidase, an endoglycosidase.

**FDA Approved Indication(s)**

| Indications* | Description | | Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti | Herceptin Hylecta |
|---|---|---|---|---|
| Adjuvant breast cancer | For adjuvant treatment of HER2-overexpressing node positive or node negative (ER/PR negative or with one high risk feature**) breast cancer: | As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel | X | X |
| | | As part of a treatment regimen with docetaxel and carboplatin | X | X |
| | | As a single agent following multi-modality anthracycline based therapy | X | X |
| Metastatic breast cancer | In combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer | | X | X |
| | As a single agent for treatment of HER2-overexpressing breast cancer in patients who have received one or more chemotherapy regimens for metastatic disease | | X | X |
| Gastric cancer | In combination with cisplatin and capecitabine or 5-fluorouracil for the | | X | – |

| Indications* | Description | Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti | Herceptin Hylecta |
|---|---|---|---|
| | treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction (esophagogastric junction; EGJ) adenocarcinoma who have not received prior treatment for metastatic disease | | |

*Select patients for therapy based on an FDA-approved companion diagnostic for trastuzumab.
** High-risk is defined as ER/PR positive with one of the following features: tumor size > 2 cm, age < 35 years, or tumor grade 2 or 3>

**Policy/Criteria**
It is the policy of PA Health & Wellness® that Herceptin/biosimilars and Herceptin Hylecta 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 or leptomeningeal metastases, **imited brain metastases, or extensive brain metastases** from HER2-positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**;
      **Prior authorization may be required*
   c. Request is for Stage IV or metastatic cancer;
5. Request meets one of the following (a, b, c, or d):
   a. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: dose does not exceed 8 mg/kg IV for adjuvant therapy or 4 mg/kg IV for treatment of metastatic disease (*see Appendix D for dose rounding guidelines*);
   b. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: intrathecal administration for leptomeningeal metastasis;

c. Herceptin Hylecta: dose does not exceed 600 mg/10,000 units SC every 3 weeks (*see Appendix D for dose rounding guidelines*);
d. Dose/product is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

**B. Gastric, Esophageal and Esophagogastric Junction Cancer** (must meet all):
1. Diagnosis of HER2-positive gastric, esophageal, or EGJ adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is advanced, recurrent, unresectable, or metastatic;
   Prescribed in combination with systemic chemotherapy;
   **Prior authorization may be required.*
5. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**:
      **Prior authorization may be required*
   c. Request is for Stage IV or metastatic cancer;
6. Request meets one of the following (a or b):
   a. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: dose does not exceed 8 mg/kg IV (*see Appendix D for dose rounding guidelines*);
   b. Dose/product is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

**C. Endometrial Carcinoma (off-label)** (must meet all):
1. Diagnosis of HER2-positive endometrial carcinoma with serous histology **or carcinosarcoma**;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is advanced (i.e., stage III/IV) or recurrent;
5. Prescribed in one of the following ways (a or b):
   a. In combination with carboplatin and paclitaxel;*
   **Prior authorization may be required.*
   b. As a single agent for maintenance therapy;
6. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):

a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
   i. Kanjinti, Ogivri, Trazimera;
   ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
   **Prior authorization may be required*
b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**:
   **Prior authorization may be required*
c. Request is for Stage IV or metastatic cancer;

7. 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*).

**Approval duration: 6 months**

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

1. Diagnosis of **unresectable or medically inoperable,** advanced, or metastatic colorectal cancer and disease is all of the following (a, b, and c):
   a. HER2 positive;
   b. Wild-type *RAS* (defined as wild-type in both KRAS and NRAS [i.e., KRAS and NRAS mutation-negative] as determined by an FDA-approved test for this use);
   c. Wild-type *BRAF (i.e.*, BRAF mutation-negative);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
      **Prior authorization may be required*
   b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**;
      **Prior authorization may be required*
   c. Request is for Stage IV or metastatic cancer;
5. Prescribed in combination with Perjeta (pertuzumab), Tukysa (tucatinib) or Tykerb (lapatinib);*
   **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*).

**Approval duration: 6 months**

**E. Salivary Gland Tumor (off-label)** (must meet all)**:**

1. Diagnosis of HER2-positive salivary gland tumor;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is recurrent;
5. Prescribed in one of the following manners (a, b, or c):
   a. Single agent;
   b. Combination with docetaxel;*
   c. Combination with Perjeta;*

   **Prior authorization may be required.*
6. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;

      **Prior authorization may be required*
   b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**;

      **Prior authorization may be required*
   c. Request is for Stage IV or metastatic cancer*;*
7. 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*).

**Approval duration: 6 months**

**F. Gallbladder Cancer or Cholangiocarcinoma (off-label)** (must meet all):

1. Diagnosis of HER2-positive gallbladder cancer or cholangiocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease is unresectable, resected gross residual (R2) disease or metastatic;
5. Prescribed in combination with Perjeta*or **Tukysa***;

   **Prior authorization may be required.*
6. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):

i. Kanjinti, Ogivri, Trazimera;
ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
**Prior authorization may be required*

b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**;
**Prior authorization may be required*

c. Request is for Stage IV or metastatic cancer*;*

7. 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*).
**Approval duration: 6 months**

**G. Other diagnoses/indications** (must meet all):

1. Member meets one of the following (a, b, or c):
   a. Request is for Stage IV or metastatic cancer;
   b. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
      **Prior authorization may be required*
   c. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**;
      **Prior authorization may be required*
2. Refer to the off -label use policy PA.CP.PMN.53

## II. Continued Approval

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

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Documentation of positive response to therapy;
3. For adjuvant breast cancer therapy, member has received ≤ 52 weeks of therapy total;
4. If request is for Herceptin, Herzuma, or Ontruzant, member meets one of the following (a, b, or c):
   a. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Kanjinti, Ogivri, Trazimera;
      ii. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;

**Prior authorization may be required*

b. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera **or member has failed Kanjinti, Ogivri, and Trazimera.**;
**Prior authorization may be required*

c. Request is for Stage IV or metastatic cancer;

5. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. Breast cancer (i, ii, or iii):
      i. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: new dose does not exceed 8 mg/kg IV for adjuvant therapy or 4 mg/kg IV for treatment of metastatic disease (*see Appendix D for dose rounding guidelines*);
      ii. Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: intrathecal administration for leptomeningeal metastases;
      iii. Herceptin Hylecta: new dose does not exceed 600 mg/10,000 units SC every 3 weeks (*see Appendix D for dose rounding guidelines*);
   b. Gastric, esophageal, EGJ cancer: Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti : new dose does not exceed 8 mg/kg IV(*see Appendix D for dose rounding guidelines*);
   c. New dose/product is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 12 months *(total of 52 weeks for adjuvant breast cancer therapy)***

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member meets one of the following (a, b, or c):
   a. Request is for Stage IV or metastatic cancer;
   b. If request if for Herceptin, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      iii. Kanjinti, Ogivri, Trazimera;
      iv. If member has failed Kanjinti, Ogivri, and Trazimera, then member must use Ontruzant and Herzuma;
      **Prior authorization may be required*
   c. If request is for Herzuma or Ontruzant, member must use ALL of the following, unless clinically significant adverse effects are experienced or all are contraindicated: Kanjinti, Ogivri, Trazimera;
      **Prior authorization may be required*

**Approval duration: Duration of request or 6 months (whichever is less);** or

3. Refer to the off -label use policy PA.CP.PMN.53

## III. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

BRAF: v-Raf murine sarcoma viral oncogene homolog B1

FDA: Food and Drug Administration

EGJ: esophagogastric junction

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*
Not applicable

*Appendix C: Contraindications/Boxed Warnings*
- Contraindication(s): none reported
- Boxed warning(s):
  - Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti: cardiomyopathy, infusion reactions, embryo-fetal toxicity, pulmonary toxicity
  - Herceptin Hylecta: cardiomyopathy, embryo-fetal toxicity, pulmonary toxicity

*Appendix D: Dose Rounding Guidelines*

| Weight-based Dose Range | Vial Quantity Recommendation |
|---|---|
| ≤ 157.49 mg | 1 vial of 150 mg |
| 157.5 mg to 314.99 mg | 2 vials of 150 mg |
| 315 mg to 440.99 mg | 1 vial of 420 mg |
| 441 mg to 598.49 mg | 1 vial of 150 mg and 1 vial 420 mg |
| 598.5 mg to 881.99 mg | 2 vials of 420 mg |
| 882 mg to 1,039.49 mg | 1 vial of 150 mg and 2 vials of 420 mg |
| 1,039.5 mg to 1,322.99 mg | 3 vials of 420 mg |

*Appendix E: General Information*
- Residual Tumor (R) Classification:

| | | |
|---|---|---|
| R0 | no residual tumor | resected, negative margin |
| R1 | microscopic residual tumor | resected, positive margin |
| R2 | macroscopic residual tumor | resected, gross residual disease |

## IV. Dosage and Administration

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| Trastuzumab (Herceptin), Trastuzumab-dkst (Ogivri), Trastuzumab-dttb (Ontruzant), Trastuzumab-pkrb (Herzuma), | Adjuvant treatment, breast cancer | Administer according to one of the following doses and schedules for a total of 52 weeks:<br>***Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:***<br>During and following paclitaxel, docetaxel, or docetaxel/carboplatin:<br>• Initial dose of 4 mg/kg as an IV infusion over 90 minutes then at 2 mg/kg as an IV infusion over 30 minutes weekly during chemotherapy for the first 12 weeks | 8 mg/kg |

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| Trastuzumab-qyyp (Trazimera), Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta), Trastuzumab-anns (Kanjinti) | | (paclitaxel or docetaxel) or 18 weeks (docetaxel/carboplatin).<br>• One week following the last weekly dose of the trastuzumab product, administer trastuzumab product at 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks.<br>***Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:***<br>As a single agent within 3 weeks following completion of multi-modality, anthracycline based chemotherapy regimens:<br>• Initial dose: 8 mg/kg as an IV infusion over 90 minutes.<br>• Subsequent doses: 6 mg/kg as an IV infusion over 30 to 90 minutes every 3 weeks | |
| | | ***Herceptin Hylecta (subcutaneous product):***<br>As part of a treatment regimen consisting of doxorubicin, cyclophosphamide, and either paclitaxel or docetaxel; as part of a treatment regimen with docetaxel and carboplatin; as a single agent following multi-modality anthracycline based therapy: 600 mg trastuzumab and 10,000 units hyaluronidase administered subcutaneously over approximately 2-5 minutes once every 3 weeks | 600 mg/10,000 units every 3 weeks |
| Trastuzumab (Herceptin), Trastuzumab-dkst (Ogivri), Trastuzumab-dttb (Ontruzant), Trastuzumab-pkrb (Herzuma), Trastuzumab-qyyp (Trazimera), Trastuzumab-hyaluronidase | Metastatic treatment, breast cancer | ***Herceptin, Ogivri, Herzuma, Ontruzant, Trazimera, Kanjinti:***<br>As a single agent, or in combination with paclitaxel, at an initial dose of 4 mg/kg as a 90-minute intravenous infusion followed by subsequent once weekly doses of 2 mg/kg as 30-minute intravenous infusions until disease progression. | 4 mg/kg |
| | | ***Herceptin Hylecta (subcutaneous product):***<br>As a single agent or in combination with paclitaxel: 600 mg trastuzumab and 10,000 units hyaluronidase administered subcutaneously over approximately 2-5 minutes once every 3 weeks. | 600 mg/10,000 units every 3 weeks |

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| -oysk (Herceptin Hylecta), Trastuzumab-anns (Kanjinti) | | | |
| Trastuzumab (Herceptin), Trastuzumab-dkst (Ogivri), Trastuzumab-dttb (Ontruzant), Trastuzumab-qyyp (Trazimera), Trastuzumab-anns (Kanjinti) | Metastatic gastric cancer | ***Herceptin, Herzuma, Ogivri, Ontruzant, Trazimera, Kanjinti:***<br>Administer at an initial dose of 8 mg/kg as a 90 minute intravenous infusion followed by subsequent doses of 6 mg/kg as an intravenous infusion over 30 to 90 minutes every three weeks until disease progression. | 8 mg/kg |

## V. Product Availability

| Drug Name | Availability* |
|---|---|
| Trastuzumab (Herceptin) | Single-dose vial: 150 mg |
| Trastuzumab-dkst (Ogivri) | Single-dose vial: 150 mg<br>Multi-dose vial: 420 mg** |
| Trastuzumab-pkrb (Herzuma) | Single-dose vial: 150 mg<br>Multi-dose vial: 420 mg |
| Trastuzumab-dttb (Ontruzant) | Single-dose vial: 150 mg<br>Multi-dose vial: 420 mg |
| Trastuzumab-qyyp (Trazimera) | Single-dose vial: 150 mg<br>Multi-dose vial: 420 mg |
| Trastuzumab-hyaluronidase-oysk (Herceptin Hylecta) | Single-dose vial: 600 mg (trastuzumab)/10,000 units (hyaluronidase)/5 mL |
| Trastuzumab-anns (Kanjinti) | Single-dose vial: 150 mg<br>Multi-dose vial: 420 mg |

**All products are supplied as a powder for reconstitution with the exception of Herceptin Hylecta which is supplied as a solution.*
*** Product available with or without diluent provided*

## VI. References

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10. National Comprehensive Cancer Network. Breast Cancer Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed February 5, 2024.
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13. National Comprehensive Cancer Network. Biliary Tract Cancers 3.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed February 5, 2024.
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16. National Comprehensive Cancer Network. Head and Neck Cancers 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed February 5, 2024.
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**Coding Implications**
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J9355 | Injection, trastuzumab, excludes biosimilar, 10 mg |
| J9356 | Injection, trastuzumab, 10 mg and hyaluronidase-oysk |
| Q5112 | Injection, trastuzumab-dttb, biosimilar, (Ontruzant), 10 mg |
| Q5113 | Injection, trastuzumab-pkrb, biosimilar, (Herzuma), 10 mg |
| Q5114 | Injection, trastuzumab-dkst, biosimilar, (Ogivri), 10 mg |
| Q5116 | Injection, trastuzumab-qyyp, biosimilar, (Trazimera), 10 mg |
| Q5117 | Injection, trastuzumab-anns, biosimilar, (Kanjinti), 10 mg |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| 1Q2018 annual review.<br>Ogivri added.Age, specialist and dosing added.Breast cancer criteria sets combined; criteria limited to a diagnosis of HER2+ breast cancer.CNS breast cancer metastatic disease off-label criteria limited to diagnosis.<br>Off-label uses removed from gastric cancer criteria - FDA indications cover through NCCN category 2A.HER2-positive lung cancer removed as an off-label indication per NCCN.<br>References reviewed and updated. | 01/2018 |
| 2Q 2019 annual review: Herceptin biosimilars and Herceptin combination product added (biosimilars - Herzuma, Ontruzant; combination product - Herceptin Hylecta); intrathecal treatment for breast cancer related CNS metastasis is moved to the breast cancer criteria set; NCCN recommended use for endometrial carcinoma are added; references reviewed and updated. | 04/2019 |
| 2Q 2020 annual review: added new Ogivri formulation: 150 mg single-dose vial; added Herceptin biosimilar, Kanjinti; Herceptin product availability for multi-dose vial corrected from 420 mg to 440 mg; references updated; newly FDA-approved indication for gastric cancer and new 150 mg vial formulation for Herzuma added; references updated.added NCCN compendium-supported indications of colon and rectal cancer; incorporated NCCN compendium-supported indication of leptomeningeal metastases from HER2-positive breast cancer into breast cancer criteria; added appendix D: dose rounding guidelines; added reference to appendix D within criteria; references reviewed and updated. | 04/2020 |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| 2Q 2021 annual review: revised requirement of medical justification for inability to use preferred Kanjinti, Ogivri, or Trazimera to "must use" language; added choice of oxaliplatin, in addition to cisplatin, for combination treatment of gastric cancers per NCCN; updated product availability for Herceptin and Kanjinti; references reviewed and updated. | 04/2021 |
| Per NCCN support, added wild-type *BRAF* criterion for colorectal cancer and choice of oxaliplatin, in addition to cisplatin, for combination treatment of gastric cancers; updated product availability for Herceptin, Kanjinti, and Trazimera; Per August SDC and prior clinical guidance, modified biosimilar redirection requirements for Herceptin to require use of Ogivri, Trazimera, Kanjinti, Ontruzant and Herzuma in a step-wise manner; for Ontruzant and Herzuma modified redirection to require use of Ogivri, Trazimera, and Kanjinti; for salivary gland tumor indication added redirection to preferred biosimilars per NCCN Compendium; references reviewed and updated. | 10/2021 |
| 2Q 2022 annual review: added qualifiers of "advanced" and "recurrent" for gastric, esophageal, or EGJ adenocarcinoma; clarified other diagnoses section to clarify intent for biosimilar steerage; references reviewed and updated. | 04/2022 |
| 2Q 2023 annual review: added gallbladder cancer and cholangiocarcinoma as NCCN supported off-label indication; references reviewed and updated. | 04/2023 |
| 2Q 2024 annual review: for adjuvant breast cancer continued therapy, added member has received ≤ 52 weeks of therapy per PI; for gastric, esophageal, or EGJ, added option for unresectable disease, revised prescribed combination therapy to "systemic chemotherapy" as additional regimens options available per NCCN; for endometrial carcinoma added option to be prescribed as single agent for maintenance therapy per NCCN; for colorectal cancer, removed requirement for no previous use of HER2 inhibitor therapy and added tucatinib as option to be prescribed in combination with; for gallbladder cancer or cholangiocarcinoma, added option for treatment with resected gross residual (R2) disease per NCCN; residual (R) tumor classification added to Appendix F; for Ogivri, updated product availability of 420 mg multi-dose vial supplied with or without diluent; references reviewed and updated. | 04/2024 |