Clinical Policy Title:	trastuzumab
Policy Number:	RxA.674
Drug(s) Applied:	Herceptin®, Herceptin Hylecta™, Herzuma®, Kanjinti™, Ogivri®, Ontruzant®, Trazimera™
Original Policy Date:	03/09/2021
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Trastuzumab is a HER2/neu receptor antagonist indicated for:

- The treatment of HER2-overexpressing breast cancer; and
- The treatment of HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma.

All products are approved for the approved indications except Herceptin Hylecta™, which is only approved for the treatment of HER2-overexpressing breast cancer.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
trastuzumab (Herceptin®); trastuzumab-pkrb (Herzuma®); trastuzumab-anns (Kanjinti™); trastuzumab-dkst (Ogivri®); trastuzumab-dttb (Ontruzant®); trastuzumab-qyyp (Trazimera®)	Breast cancer, adjuvant treatment	During and following paclitaxel, docetaxel or docetaxel/carboplatin: Initial dose is 4mg/kg as an IV infusion over 90 minutes, then 2mg/kg IV over 30 minutes weekly for the first 12 to 18 weeks. One week after the last weekly dose, administer 6mg/kg as an IV infusion over 30-90 minutes every 3 weeks. As a single agent within 3 weeks following multi-modality anthracycline-based chemotherapy regimen: Initial dose of 8mg/kg as an IV infusion over 90 minutes, then 6mg/kg as an IV infusion over 30-90 minutes every 3 weeks. Extending adjuvant therapy beyond one year is not recommended	8 mg/kg
	Breast cancer, metastatic	Administer alone or in combination with paclitaxel. Initial dose is 4mg/kg as an IV infusion over 90 minutes, then 2mg/kg IV over 30 minutes weekly until disease progression.	4 mg/kg
	Gastric cancer, metastatic	Initial dose of 8mg/kg as an IV infusion over 90 minutes followed by subsequent doses of 6mg/kg as an IV infusion over 30-90 minutes every 3 weeks until disease progression.	8 mg/kg

trastuzumab and hyaluronidase-oysk (Herceptin Hylecta™);	Breast cancer, adjuvant treatment	600mg/10,000 units administered SQ over approximately 2-5 minutes every 3 weeks. No loading dose or dose adjustments for body weight are required. Extending adjuvant therapy beyond one year is not recommended	600 mg/10,000 units per dose
	Breast cancer, metastatic	600 mg/10,000 units administered SQ over approximately 2-5 minutes every 3 weeks. No loading dose or dose adjustments for body weight are required. Continue therapy until disease progression.	

Dosage Forms

- Herceptin®, Herzuma®, Kanjinti™, Ogivri®, and Ontruzant®: Single-dose vial, 150 mg; multiple-dose vial, 420 mg
- Herceptin Hylecta™: Single-dose vial, 600 mg trastuzumab and 10,000 units hyaluronidase per 5 mL
- Trazimera™: multiple-dose vial, 420 mg

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.

I. Initial Approval Criteria

A. Breast Cancer (must meet all)**:**

1. Member has a diagnosis of HER2 positive breast cancer or leptomeningeal metastases from HER2 positive breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Member must meet one or more of the following (a, b, c, d, or e):
   a. As a component of neoadjuvant therapy prior to surgical treatment;
   b. As adjuvant treatment to complete a 12-month (52 week) course of trastuzumab;
   c. As treatment of metastatic breast cancer, as monotherapy or in combination with a chemotherapy regimen that is recognized by ASCO or NCCN;
   d. In combination with lapatinib as treatment of metastatic breast cancer when both of the following criteria are met (i and ii):
      i. Member has received or is receiving trastuzumab-based therapy; and
      ii. Disease has progressed on or after trastuzumab.
   e. In combination with pertuzumab when the following criteria are met (i, ii, and iii):
      i. Breast tumor is HER2 positive;
      ii. Trastuzumab is used in combination with pertuzumab and either docetaxel or paclitaxel, unless there is a contraindication; and
      iii. The combination therapy with pertuzumab will be used as a single line anti-HER2 chemotherapy for metastatic breast cancer until disease progression.
5. For requests other than Trazimera™: Member must have tried and failed Trazimera™, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed FDA prescribing guidelines or dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Gastric, Esophageal and Gastroesophageal Adenocarcinoma (must meet all)**:**
1. Member has a diagnosis of HER2 positive advanced gastric, esophageal or gastroesophageal junction adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Must be used in combination with cisplatin and either capecitabine or 5-fluorouracil;
5. For requests other than Trazimera™: Member must have tried and failed Trazimera™, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed FDA prescribing guidelines or dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Colorectal Cancer (off-label) (must meet all)**:**
1. Member has a diagnosis of HER2 positive, wild-type RAS, advanced or metastatic colorectal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Member has not been treated with previous HER2 inhibitor therapy (e.g., trastuzumab, ado-trastuzumab emtansine, lapatinib, pertuzumab);
5. Must be used in combination with pertuzumab or lapatinib;
6. For requests other than Trazimera™: Member must have tried and failed Trazimera™, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

D. Endometrial Carcinoma (off-label) (must meet all)**:**
1. Member has a diagnosis of advanced (i.e., stage III/IV) or recurrent HER2 positive endometrial carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. For requests other than Trazimera™: Member must have tried and failed Trazimera™, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

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

1. Member has a diagnosis of recurrent, unresectable or metastatic HER2 positive salivary gland carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Prescribed as monotherapy or in combination with docetaxel or pertuzumab;
5. For requests other than Trazimera™: Member must have tried and failed Trazimera™, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All indications listed in section I (must meet all):

1. Member is currently receiving the medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is positively responding to therapy (e.g., tumor regression, absence of tumor progression);
3. If request is for a dose increase, dose does not exceed FDA prescribing guidelines or dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial:
Adjuvant breast cancer: 6 months
All other diagnoses: 12 months
Medicaid:
Adjuvant breast cancer: 6 months
All other diagnoses: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ADCC: Antibody-Dependent Cellular Cytotoxicity
ASCO: American Society of Clinical Oncology
FDA: Food and Drug Administration
HER2: Human Epidermal Growth Factor Receptor 2
IV: Intravenous/intravenously
RAS: Rat sarcoma 2 viral oncogene homologue
NCCN: National Comprehensive Cancer Network
SQ: Subcutaneous/subcutaneously

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - Herceptin®, Herzuma®, Kanjinti™, Ogivri®, Ontruzant®, Trazimera™: cardiomyopathy, infusion reactions, embryo-fetal toxicity, pulmonary toxicity
  - Herceptin Hylecta™: cardiomyopathy, embryo-fetal toxicity, pulmonary toxicity

APPENDIX D: General Information

- Most common adverse reactions are cardiomyopathy, infusion reactions, embryo-fetal toxicity, pulmonary toxicity, and exacerbation of chemotherapy-induced neutropenia.
- Trastuzumab is a mediator of antibody-dependent cellular cytotoxicity (ADCC). *In vitro*, trastuzumab-mediated ADCC has been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2.

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	12/23/2020	03/09/2021