Drug Policy:

Trastuzumab Products, Pertuzumab, and Phesgo

POLICY NUMBER UM ONC_1134	**SUBJECT** Trastuzumab Products: Herceptin (trastuzumab), Herceptin Hylecta (trastuzumab hyaluronidase), Ogivri (trastuzumab-dkst), Herzuma (trastuzumab-pkrb), Ontruzant (trastuzumab-dttb), Kanjinti (trastuzumab-anns), Trazimera (trastuzumab-qyyp)], , Pertuzumab™ (pertuzumab), and Phesgo™ (pertuzumab, trastuzumab, and hyaluronidase-zzxf)	**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 5**
DATES COMMITTEE REVIEWED 07/22/11, 06/12/13, 07/23/14, 04/13/16, 07/26/16, 11/08/16, 09/13/17, 12/13/17, 11/14/18, 01/09/19, 03/13/19, 07/10/19, 09/11/19, 12/11/19, 01/08/20, 02/12/20, 03/11/20, 04/08/20, 06/10/20, 07/08/20, 08/27/20, 01/13/21, 03/10/21, 04/14/21, 11/15/21, 12/08/21, 01/12/22, 04/13/22, 05/11/22, 06/08/22, 07/13/22, 11/09/22, 03/08/23, 04/12/23, 09/13/23	**APPROVAL DATE** September 13, 2023	**EFFECTIVE DATE** September 29, 2023	**COMMITTEE APPROVAL DATES** 07/22/11, 06/12/13, 07/23/14, 04/13/16, 07/26/16, 11/08/16, 09/13/17, 12/13/17, 11/14/18, 01/09/19, 03/13/19, 07/10/19, 09/11/19, 12/11/19, 01/08/20, 02/12/20, 03/11/20, 04/08/20, 06/10/20, 07/08/20, 08/27/20, 01/13/21, 03/10/21, 04/14/21, 11/15/21, 12/08/21, 01/12/22, 04/13/22, 05/11/22, 06/08/22, 07/13/22 11/09/22, 03/08/23, 04/12/23, 09/13/23
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee	
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**	**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Trastuzumab products [Herceptin (trastuzumab), Herceptin Hylecta (trastuzumab hyaluronidase), Ogivri (trastuzumab-dkst), Herzuma (trastuzumab-pkrb), Ontruzant (trastuzumab-dttb), Kanjinti (trastuzumab-anns), Trazimera (trastuzumab-qyyp)], Pertuzumab (pertuzumab), and Phesgo (pertuzumab, trastuzumab, and hyaluronidase-zzxf) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this NCH policy provided:

1. The requested medication was used within the last year, AND
2. The member has not experienced disease progression and/or no intolerance to the requested medication, AND
3. Additional medication(s) are not being added to the continuation request.

B. HER-2 Positive Breast Cancer

1. The member has node positive and/or tumor stage T2 or greater HER-2 positive breast cancer AND trastuzumab/trastuzumab biosimilar +/- Perjeta (pertuzumab) may be used as neoadjuvant treatment OR as adjuvant treatment in members who did not receive neoadjuvant therapy The following chemotherapy regimens are acceptable for use with trastuzumab/trastuzumab biosimilar +/- Perjeta (pertuzumab) combination therapy as neoadjuvant or adjuvant treatment:
    a. Trastuzumab/trastuzumab biosimilar +/- Perjeta (pertuzumab) with paclitaxel following AC (doxorubicin + cyclophosphamide)
    b. Trastuzumab/trastuzumab biosimilar +/- Perjeta (pertuzumab) with docetaxel following AC (doxorubicin + cyclophosphamide)
    c. Trastuzumab/trastuzumab biosimilar +/- Perjeta(pertuzumab) with docetaxel/paclitaxel
    d. TCH (docetaxel, carboplatin, and trastuzumab/trastuzumab biosimilar) +/- Perjeta (pertuzumab)
    e. Trastuzumab/trastuzumab biosimilar with docetaxel and cyclophosphamide.

    OR
2. Trastuzumab/trastuzumab biosimilar +/- Perjeta (pertuzumab) may be used as continuation neoadjuvant/adjuvant therapy following neoadjuvant/adjuvant trastuzumab/trastuzumab biosimilar +/- Perjeta (pertuzumab) + Chemotherapy OR
3. Trastuzumab/trastuzumab biosimilar may be used as first line or subsequent line therapy, with or without Perjeta (pertuzumab) for recurrent or metastatic HER-2 positive breast cancer:
    a. In combination with Novaldex (tamoxifen), Faslodex (fulvestrant), or an aromatase inhibitor for a member whose disease is also ER/PR positive OR
    b. In combination with pertuzumab and a Taxane [Taxotere (docetaxel) or Taxol (paclitaxel)] regardless of the ER/PR status OR
    c. In combination with other single agent chemotherapy agents e.g., vinorelbine.

    OR
4. In combination with Tukysa (tucatinib) + Xeloda (capecitabine) for members with metastatic HER-2 positive breast cancer and brain metastases OR in members without brain metastases if there is disease progression on one or more prior lines of anti-HER-2 therapy in the metastatic setting.

C. HER-2 Positive Gastric/Esophageal and Esophagogastric Junction Cancers

1. The member has a diagnosis of recurrent/metastatic gastric or esophageal or esophagogastric junction cancer and the cancer is HER-2 positive (defined as IHC 3+ or FISH/ISH positive) AND

2. Trastuzumab/trastuzumab biosimilar is being used in combination with cisplatin or oxaliplatin and 5-fluorouracil (or capecitabine), with or without Keytruda (pembrolizumab) as first line therapy.

III. EXCLUSION CRITERIA

A. Trastuzumab/trastuzumab biosimilar + Perjeta (pertuzumab) containing therapy is being used in members with tumor stage T1N0 breast cancer either in the adjuvant setting or in the neoadjuvant setting.

B. Herceptin (trastuzumab)/ trastuzumab biosimilar use in gastric or gastroesophageal junction cancer after disease progression with first line therapy containing trastuzumab.

C. Continuation of trastuzumab/trastuzumab biosimilar product after disease progression on trastuzumab-based therapy in HER-2 positive esophageal, gastroesophageal, and gastric adenocarcinomas.

D. Dosing exceeds single dose limit of trastuzumab 8 mg/kg for the loading dose, 6mg/kg for subsequent doses when given every 3 weeks; 4 mg/kg for the loading dose and 2 mg/kg for the subsequent doses, when trastuzumab is being given weekly.

E. Dosing exceeds single dose limit of Phesgo (pertuzumab, trastuzumab, and hyaluronidase-zzxf) 1,200 mg (initial dose) and 600 mg (subsequent dose).

F. Dosing exceeds single dose limit of Perjeta (pertuzumab) 840 mg initially then 420 mg every 3 weeks.

G. Total treatment duration exceeds a maximum 52 weeks or 1 year (the equivalent of 17 three-week cycles) in non-metastatic HER-2 positive breast cancer. The above duration does not include any necessary therapy interruption, e.g., due to breast surgery and post-operative recovery.

H. Investigational use of Trastuzumab products/Pertuzumab/Phesgo with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

   1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
   2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
   3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
   4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
   5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.

6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Murthy RK, et al. Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer. N Engl J Med. 2020 Feb 13;382(7):597-609.

B. Gianni L et. al, 5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial. Lancet Oncol. 2016 Jun;17(6):791-800.

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