Drug Therapy Guidelines

Herceptin® (trastuzumab)

Applicable

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Effective: 6/21/17</th>
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<tbody>
<tr>
<td>Pharmacy-Formulary 1</td>
<td>Next Review: 6/18</td>
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<tr>
<td>Pharmacy-Formulary 2</td>
<td>Date of Origin: 6/09</td>
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<tr>
<td>Pharmacy-Formulary 3/Exclusive</td>
<td>Review Dates: 6/17/09, 12/09, 6/10, 12/10, 12/11, 12/12, 12/13, 12/14, 6/15, 6/16, 6/17</td>
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<td>Pharmacy-Formulary 4/AON</td>
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I. Medication Description

The HER2 (or c-erbB2) proto-oncogene encodes a transmembrane receptor protein of 185 kDa, which is structurally related to the epidermal growth factor receptor. HER2 protein overexpression is observed in 25% to 30% of primary breast cancers. HER2 protein overexpression can be determined using immunohistochemistry (IHC). The presence of HER2 overexpression may also be inferred when HER2 gene amplification is identified using fluorescence in situ hybridization (FISH) on fixed tumor blocks.

Trastuzumab has been shown, in both in vitro assays and in animals, to inhibit the proliferation of human tumor cells that overexpress HER2. 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.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for every request.

III. Policy

Coverage of Herceptin is available when the following criteria have been met:

- Member is at least 18 years of age AND
- The medication is prescribed by a hematologist/oncologist AND
- For all indications, HER2 overexpression is confirmed with documentation as follows:
  - Immunohistochemistry (IHC) assay 3+ OR
  - Fluorescence in situ hybridization (FISH) Assay ratio of at least 2.0
  - If IHC is 2+, must confirm with FISH assay ratio of at least 2.0 AND
- The requested use is supported by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (NCCN Guidelines®) and/or NCCN Drugs & Biologics Compendium (NCCN Compendium®) with a recommendation of category level 1 or 2A.

IV. Quantity Limits

Quantities will be approved to allow for FDA-approved or compendia-supported dosing.
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V. Coverage Duration

• Coverage of adjuvant breast cancer therapy is available for 12 months and may not be renewed.
• Coverage for other usages is available for 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed based upon the following criteria:

• Tumor response with stabilization of disease, lack of disease progression, decrease in size of tumor or tumor spread (unless used for metastatic breast cancer) AND
• Absence of unacceptable toxicity from the drug

VII. Billing/Coding Information

• J9355 – 1 billable unit is 10mg
• Pertinent indications
  o Breast Cancer: C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929
  o Gastric Cancer: C16.0 – C16.6, C16.8, C16.9, D37.1, Z85.00, Z85.028
  o Esophageal/Esophagogastric Junction Cancer: C15.3 – C15.5, C15.8, C15.9, C16.0, D37.8, D37.9
  o CNS leptomeningeal metastases: C79.32

VIII. Summary of Policy Changes

• 3/1/11: Addition of metastatic gastric cancer indication, addition of Warnings/Precautions section, addition of Billing/Coding information
• 6/15/12: addition of Embryo Fetal Toxicity to Black Box Warnings, extended duration of approval for adjuvant breast cancer therapy.
• 3/15/13:
  o Simplified coverage criteria to allow coverage in all NCCN-supported scenarios
  o Addition of new dosing regimen
• 6/2013: updated policy to allow FISH ratio of at least 2.0 to be considered positive
• 3/15/14: addition of breast cancer coverage for males
• 6/9/14: addition of coverage in NSCLC and CNS cancer based on current NCCN guidelines
• 3/15/15: revised coverage renewal language to allow for continuation for all metastatic disease regardless of progression.
• 7/1/15: formulary distinctions made
• 9/15/15: updated policy to correspond with current NCCN treatment guidelines
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- 7/19/16: policy updated to correspond with current NCCN treatment guidelines
- 6/21/17: coverage criteria updated to allow use as supported by current NCCN guidelines
- 6/30/17: updated quantity limit language to address all supported uses of the medication

IX. References

1. UpToDate Online, retrieved October 2010
3. Facts and Comparisons Online, retrieved November 12, 2010

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.