Mass General Brigham
Health Plan

Breast Cancer Therapies
Enhertu (fam-trastuzumab deruxtecan-nxki)
Faslodex (fulvestrant)
Halaven (eribulin)
Kadcyla (ado-trastuzumab)
Margenza (margetuximab-cmkb)
Perjeta (pertuzumab)
Phesgo (pertuzumab/trastuzumab/hyaluronidase-zzxf)
Trodelvy (sacituzumab govitecan-hziy)
Effective 01/06/2025

Plan	☒ MassHealth ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☐ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	N/A		
Contact Information	**Medical and Specialty Medications** All Plans | Phone: 877-519-1908 | Fax: 855-540-3693 **Non-Specialty Medications** All Plans | Phone: 800-711-4555 | Fax: 844-403-1029		
Notes	Additional agents from this class are available through the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria.		

Overview

Enhertu (fam-trastuzumab deruxtecan-nxki) is a HER2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of:

- Adult members with unresectable or metastatic HER2-positive breast cancer who have received a prior anti-HER2-based regimen either:
  - in the metastatic setting, or
  - in the neoadjuvant or adjuvant setting and have developed disease recurrence during or within six months of completing therapy
- Adult members with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based regimen .
- Adult members with unresectable or metastatic HER2-low (IHC 1+ or IHC 2+/ISH-) breast cancer who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy.
- Adult members with unresectable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating human epidermal growth factor receptor 2 HER2 (ERBB2) mutations, as detected by an FDA-approved test, and who have received a prior systemic therapy.

Faslodex (fulvestrant) is Food and Drug Administration (FDA)-approved for the treatment of:

- Hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2) negative advanced breast cancer in postmenopausal women not previously treated with endocrine therapy.

- HR-positive advanced breast cancer in postmenopausal women with disease progression following endocrine therapy.
- HR-positive, HER2-negative advanced or mBC in postmenopausal women in combination with ribociclib, as initial endocrine-based therapy or following disease progression on endocrine therapy.
- HR-positive, HER2-negative advanced or mBC in combination with palbociclib or abemaciclib in women with disease progression after endocrine therapy.

Halaven (eribulin) is classified as a non-taxane microtubule inhibitor and is believed to work by inhibiting cancer cell growth. It is indicated for:

- the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease.
- the treatment of patients with unresectable or metastatic liposarcoma who have received a prior anthracycline-containing regimen.

Kadcyla (ado-trastuzumab emtansine), also known as T-DM1, is FDA-approved as single agent therapy for the treatment of patients with HER2-positive mBC who previously received trastuzumab and a taxane, separately or in combination.

Margenza (margetuximab-cmkb) is indicated, in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

Perjeta (pertuzumab) is a HER2/neu receptor antagonist that is FDA-approved for use in combination with trastuzumab and docetaxel for the treatment of patients with HER2-positive mBC who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease.

Phesgo (pertuzumab, trastuzumab, and hyaluronidase-zzxf) is indicated for use in combination with chemotherapy as neoadjuvant treatment of adult patients with HER2-positive, locally advanced, inflammatory, or early stage breast cancer (either greater than 2 cm in diameter or node positive) as part of a complete treatment regimen for early breast cancer (EBC) and adjuvant treatment of adult patients with HER2-positive EBC at high risk of recurrence.

Trodelvy (sacituzumab govitecan-hziy) is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior therapies, at least one of them for metastatic disease.

Coverage Guidelines

Authorization may be reviewed on a case by case basis for members new to the plan who are currently receiving treatment with the requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted for members when **ALL** the following criteria are met, and documentation is provided:

Enhertu (fam-trastuzumab deruxtecan-nxki)

ONE of the following:

1. Diagnosis of unresectable or metastatic HER2-positive breast cancer

a. Prescriber is an oncologist
b. Appropriate dosing (weight required)
c. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** anti-HER2-based regimen (e.g., Herceptin®(trastuzumab), Kadcyla®(ado-trastuzumab emtansine), and Perjeta®(pertuzumab), agents that are used in combination would count as one regimen)

2. Diagnosis of locally advanced or metastatic HER2-postive gastric or GEJ adenocarcinoma
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Paid claims or physician attestation of inadequate response or adverse reaction to a trastuzumab-based regimen
3. Diagnosis of unresectable or metastatic HER2-low (IHC 1+ or ICH2+/ISH-) breast cancer
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** prior chemotherapy regimen *(e.g. anthracyclines [doxorubicin, liposomal doxorubicin], taxanes [paclitaxel], anti-metabolites [capecitabine, gemcitabine], microtubule inhibitors [vinorelbine, eribulin])*
4. Diagnosis of unresctable or metastatic non-small cell lung cancer (NSCLC) whose tumors have activating HER2 (ERBB2) mutations
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** prior systemic therapy
5. Diagnosis of unresectable or metastatic HER2-positive (IHC 3+) solid tumor
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. ONE of the following:
        i. Inadequate response or adverse reaction to ONE prior systemic therapy (refer to latest NCCN guidelines for guidance of prior systemic therapy options)
        ii. Member has no satisfactory alternative treatment options

Faslodex (fulvestrant)
ALL of the following:

1. Diagnosis of **ONE** of the following:
    a. HR-positive advanced or metastatic breast cancer
    b. Advanced or metastatic breast cancer with past trials of antiestrogen therapy *(e.g., tamoxifen, anastrazole, letrozole, exemestaine)*
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Member is HER2-negative and **ONE** of the following:
        i. Requested agent will be used as monotherapy
        ii. Requested agent will be used in combination with a CDK inhibitor *(e.g. abemaciclib, palbociclib or ribociclib)*
        iii. Concomitant therapy with anastrazole or letrozole
    b. Member is HER2-positive and **ONE** of the following:
        i. Requested agent will be used as monotherapy
        ii. Requested agent will be used in combination with trastuzumab

5. If request is for Brand Name Faslodex®, prescriber must also provide medical records documenting an inadequate response or adverse reaction to generic fulvestrant (as per the Brand Name and Non-Preferred Generic Drugs guideline)

Halaven (eribulin)
ONE of the following:
1. Diagnosis of metastatic or recurrent breast cancer
    a. Prescriber is an oncologist
    b. Appropriate dosing (height and weight or BSA is required)
    c. Two prior chemotherapy regimens that included a taxane and an anthracycline
    d. Paid claims or physician attestation of inadequate response, adverse reaction or contraindication to vinorelbine (may have been part of the previous chemotherapy regimens)
2. Diagnosis of unresectable or metastatic liposarcoma
    a. Prescriber is an oncologist
    b. Appropriate dosing (height and weight or BSA is required)
    c. Paid claims or physician attestation of inadequate response, adverse reaction or contraindication to an anthracycline-containing regimen

Kadcyla (ado-trastuzumab)
ALL of the following:
1. Diagnosis of HER2-positive breast cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. Member has recurrent or metastatic breast cancer AND paid claims or physician attestation of inadequate response or adverse reaction to trastuzumab and a taxane, separately or in combination
    b. Member has early breast cancer (EBC) and residual invasive disease after neoadjuvant taxane and trastuzumab-based treatment

Margenza (margetuximab-cmkb)
ALL of the following:
1. Diagnosis of HER2-positive metastatic breast cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. Requested agent will be used in combination with chemotherapy (capecitabine, eribulin, gemcitabine or vinorelbine)
6. Paid claims or physician attestation of inadequate response or adverse reaction to at least **TWO** anti-HER2-based regimens (e.g., Herceptin®(trastuzumab), Kadcyla®(ado-trastuzumab emtansine), and Perjeta®(pertuzumab), agents that are used in combination would count as one regimen)

Perjeta (pertuzumab)
ALL of the following:
1. Diagnosis of HER2-positive breast cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:

a. For recurrent or stage IV disease, requested agent will be used in combination with trastuzumab **AND** docetaxel or paclitaxel
b. For use is for adjuvant or neoadjuvant chemotherapy, requested agent will be used in combination with trastuzumab **AND** chemotherapy

Phesgo (pertuzumab/trastuzumab/ hyaluronidase-zzxf)
ALL of the following:
1. Diagnosis of HER2-positive breast cancer
2. Prescriber is an oncologist
3. Appropriate dosing
4. **ONE** of the following:
    a. For early breast cancer, requested agent will be used in combination with chemotherapy
    b. For metastatic breast cancer, requested agent will be used in combination with docetaxel as a first line treatment in a metastatic setting *(e.g., members should not have received prior anti-HER2 therapy)*

Trodelvy (sacituzumab govitecan-hziy)
ONE of the following:
1. Diagnosis of unresectable locally advanced or metastatic triple negative breast cancer
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Paid claims or physician attestation of inadequate response or adverse reaction to at least **TWO** prior systemic therapies, at least one for metastatic disease *(See Appendix for previous therapies)*
2. Diagnosis of locally advanced or metastatic urothelial cancer
    a. Prescriber is an oncologist
    b. Appropriate dosing
    c. Inadequate response or adverse reaction to a platinum containing regimen **AND** a PD-1 or PD-L1 inhibitor
3. Diagnosis of HR-positive, HER2-negative unresectable locally advanced or metastatic breast cancer
    a. Prescriber is an oncologist
    b. Appropriate dosing
    a. Inadequate response, adverse reaction to **ONE** or contraindication to **ALL** endocrine-based therapies *(See Appendix for previous therapies)*
    c. Inadequate response or adverse reaction to **TWO** prior non-endocrine-based systemic therapies in the metastatic setting *(See Appendix for previous therapies)*

Continuation of Therapy
Reauthorization will be granted when physician provides attestation of positive response to therapy.

Limitations
1. Initial approvals and reauthorizations will be granted for 12 months.

Appendix
Previous Trials for Trodelvy® (sacituzumab govitecan-hziy) in triple negative breast cancer (TNBC)
- Anthracyclines: doxorubicin, liposomal doxorubicin
- Anti-metabolites: capecitabine, gemcitabine
- Cyclophosphamide

- Epirubicin
- Ixabepilone
- Microtubule inhibitors: vinorelbine, eribulin
- Platinum: carboplatin, cisplatin
- Taxanes: paclitaxel, docetaxel, albumin-bound paclitaxel
- For germline BRCA1/BRCA2 mutations: olaparib or talazoparib
- For PD-L-1-positive TNBC: pembrolizumab + chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine and carboplatin)

The following agents are considered useful under certain circumstances per the NCCN guidelines. Each regimen should be considered as one trial.

- Carboplatin + paclitaxel or albumin-bound paclitaxel
- Cyclophosphamide/methotrexate/fluorouracil
- Docetaxel/capecitabine
- Doxorubicin/cyclophosphamide
- Epirubicin/cyclophosphamide
- Gemcitabine/carboplatin
- Gemcitabine/paclitaxel
  Gemcitabine/paclitaxel

Previous Trials for Trodelvy® (6acituzumab govitecan-hziy) (locally advanced or metastatic, HR-positive HER2-negative breast cancer

Endocrine-based therapy:

Preferred Regimens

First-line

- Aromatase inhibitor + CDK 4/6 inhibitor
  - Aromatase inhibitor + ribociclib
  - Aromatase inhibitor + abemaciclib
  - Aromatase inhibitor + palbociclib
- Fulvestrant + CDK 4/6 inhibitor
  - Fulvestrant+ ribociclib
  - Fulvestrant+ abemaciclib
  - Fulvestrant+ palbociclib

Second- and Subsequent-Line Therapy

- Fulvestrant + CDK 4/6 inhibitor (if CDK 4/6 inhibitor was not previously used)
- Everolimus + endocrine therapy (exemestane, fulvestrant, tamoxifen)

Other Recommended Regimens

- Selective ER down-regulator
  - Fulvestrant
- Selective ER down-regulator
  - Fulvestrant + anastrazole
  - Fulvestrant + letrozole
- Non-steroidal aromatase inhibitor
  - anastrozole
  - Letrozole
- Selective ER modulator
  - tamoxifen

- Steroidal aromatase inactivator
    - Exemestane

Useful in Certain Circumstances

- Megestrol
- Estradiol
- Additional targeted therapy options

Systemic Chemotherapy:

Preferred

- Anthracycline (doxorubicin, liposomal doxorubicin)
- Taxanes: (paclitaxel, docetaxel, albumin-bound paclitaxel)
- Anti-metabolites (capecitabine, gemcitabine)
- Microtubule inhibitors (vinorelbine, eribulin)

Other Recommended

- Cyclophosphamide
- Docetaxel
- Albumin-bound paclitaxel
- Epirubicin
- Ixabepilone

Useful in Certain Circumstances

- AC (doxorubicin/cyclophosphamide)
- EC (epirubicin/cyclophosphamide)
- CMF (cyclophosphamide/ methotrexate/fluorouracil)
- Docetaxel/capecitabine
- GT (gemcitabine/paclitaxel)
- Gemcitabine/carboplatin
- Carboplatin + paclitaxel or albumin-bound paclitaxel
- For germline BRCA1/BRCA2 mutations: olaparib or talazoparib

Components of Commonly Used Regimens for Treatment of Colorectal Cancer

Regimen Abbreviation	Drug Components
5-FU	fluorouracil
CAPEOX	capecitabine/oxaliplatin
FOLFIRI	leucovorin calcium (folinic acid)/fluorouracil/irinotecan
FOLFOX	leucovorin calcium (folinic acid)/fluorouracil/oxaliplatin
FOLFOXIRI/FOLFIRINOX	leucovorin calcium (folinic acid)/5-fluorouracil/oxaliplatin/irinotecan

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Review History

11/17/2021 – Created and Reviewed for Nov P&T. matched with MH UPPL. Effective 01/01/2022
06/22/2022 - Reviewed and updated for June P&T; matched MH UPPL. Criteria update for expanded indication of Verzenio for adjuvant treatment (with endocrine therapy: tamoxifen or an aromatase inhibitor) of adults patients with HR+, HER2-, node-positive, early breast cancer as high risk of recurrence and a Ki-67 score of 20% or higher. Criteria stating "Member is postmenopausal or has received ovarian ablation or suppression" was removed throughout guideline where appropriate. Effective 08/01/22.
01/11/2023 – Reviewed and updated for Jan P&T. Updated PA table to include Tykerb, Afinitor, Afinitor Disperz. Updated verbiage of combination therapy throughout. Listed out indications within criteria."Requests which do not clearly document postmenopausal status" appendix was removed. Effective 3/1/23.
03/15/23 - Reviewed and updated for Mar P&T. Matched MH UPPL criteria. Added criteria for the following: Enhertu, Faslodex, Halaven, Kadcyla, Margenza, Perjeta, Phesgo, Trodelvy. Added Appendix "Previous Trials for Trodelvy." Effective 4/1/23.
05/10/23 – Reviewed and updated for P&T. Orserdu (elacestrant) was added to policy for the treatment of postmenopausal women or adult men with ER-positive, HER2-negative, ESR1- mutated advanced or metastatic breast cancer (mBC) with disease progression following at least one line of endocrine therapy. Effective 6/5/23.
06/30/23 – Reviewed and updated for P&T. Admin update: Clarified that Trodelvy is available through pharmacy and medical benefits (dual). Effective 6/30/23
7/12/23 – Reviewed and updated for P&T. Added expanded indication for Tukysa in combination with trastuzumab for RAS WT, HER2-positive unresectable or metastatic colorectal cancer. Added expanded indication for Trodelvy for HR-positive, HER2-negative unresectable locally advanced or metastatic breast cancer. A MH decision was made to have Trodelvy be available under medical benefit only. Effective 7/31/23

02/14/24 – Reviewed and updated for P&T. Updated Trodelvy criteria (MB) to be more in line with FDA-labeled indications. Updated Appendix for Trodelvy acceptable previous trials. Enhertu is removed from pharmacy benefit and will only be available on Medical benefit with PA. Effective 3/4/24
12/11/24 – Reviewed and updated for P&T. Separated criteria Rx vs MB drugs. Added expanded indication for Enhertu in adults with unresectable or metastatic HER2-positive (IHC 3+) solid tumors who have received prior systemic treatment and have no satisfactory alternative treatment options. Effective 1/6/25