BlueCross BlueShield Federal Employee Program

PHESGO
(pertuzumab, trastuzumab, and hyaluronidase-zzxf)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Phesgo is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase. Pertuzumab blocks ligand-dependent heterodimerization of HER2 with other HER family members, including EGFR, HER3, and HER4. Trastuzumab inhibits HER2 mediated cell proliferation and PI3K signaling pathway in human cells that overexpress HER2. Both pertuzumab and trastuzumab-mediated antibody-dependent cell-mediated cytotoxicity have been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan (1).

Regulatory Status

FDA-approved indications: Phesgo is indicated for: (1)

1. Use in combination with chemotherapy as:
    a. Neoadjuvant treatment of 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
    b. Adjuvant treatment of patients with HER2-positive early breast cancer at high risk of recurrence
2. Use in combination with docetaxel for treatment of patients with HER2-positive metastatic breast cancer (MBC) who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease

Phesgo has a boxed warning regarding cardiomyopathy. Phesgo administration can result in subclinical and clinical cardiac failure manifesting as congestive heart failure (CHF), and decreased left ventricular ejection fraction (LVEF). The incidence and severity was highest in patients receiving Phesgo with anthracycline-containing chemotherapy regimens. Cardiac function should be evaluated prior to and during treatment with Phesgo. Phesgo has not been studied in patients with a pretreatment LVEF value of < 55% in early breast cancer and < 50% in metastatic breast cancer (1).

Phesgo should be completed for a total of 1 year (up to 18 cycles) or until disease recurrence or unmanageable toxicity, whichever occurs first, as part of a complete regimen for early breast

cancer. In the treatment of metastatic breast cancer, Phesgo should be administered until disease progression or unmanageable toxicity (1).

Phesgo also carries a boxed warning for embryo-fetal toxicity. Exposure to Phesgo can result in embryo-fetal death and birth defects. Females of reproductive potential should be advised to use effective contraception during treatment and for 7 months following the last dose of Phesgo (1).

Phesgo has a third boxed warning about pulmonary toxicity. Phesgo administration can result in serious and fatal pulmonary toxicity. Phesgo should be discontinued for anaphylaxis, interstitial pneumonitis, or acute respiratory distress syndrome. Patients should be monitored until symptoms completely resolve (1).

The safety and effectiveness of Phesgo in pediatric patients have not been established (1).

Summary

Phesgo is a combination of pertuzumab and trastuzumab, HER2/neu receptor antagonists, and hyaluronidase, an endoglycosidase. Pertuzumab blocks ligand-dependent heterodimerization of HER2 with other HER family members, including EGFR, HER3, and HER4. Trastuzumab inhibits HER2 mediated cell proliferation and PI3K signaling pathway in human cells that overexpress HER2. Both pertuzumab and trastuzumab-mediated antibody-dependent cell-mediated cytotoxicity have been shown to be preferentially exerted on HER2 overexpressing cancer cells compared with cancer cells that do not overexpress HER2. Hyaluronidase increases permeability of the subcutaneous tissue by depolymerizing hyaluronan. The safety and effectiveness of Phesgo in pediatric patients have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Phesgo while maintaining optimal therapeutic outcomes.

References

1. Phesgo [package insert]. South San Francisco, CA: Genentech, Inc.; November 2024.
2. NCCN Drugs & Biologics Compendium® Pertuzumab, trastuzumab, and hyaluronidase-zzxf 2025. National Comprehensive Cancer Network, Inc. Accessed on January 8, 2025.