Herzuma® (trastuzumab-pkrb) – New biosimilar approval

- On December 14, 2018, Teva and Celltrion announced the FDA approval of Herzuma (trastuzumab-pkrb), a biosimilar to Genentech's Herceptin® (trastuzumab).
    - Herzuma is the second FDA-approved biosimilar to Herceptin.
    - Mylan's Ogivri® (trastuzumab-dkst) is the first biosimilar to Herceptin and was approved on December 1, 2017. Mylan signed a settlement agreement with Genentech that will delay the launch of Ogivri until the second half of 2019 or later.

- Herzuma, Ogivri and Herceptin share the following indications:
    - **Adjuvant breast cancer:** adjuvant treatment of HER2 overexpressing node positive or node negative (ER/PR negative or with one high risk feature breast cancer as part of a treatment regimen consisting of doxorubicin**,** cyclophosphamide**,** and either paclitaxel or docetaxel**;** or as part of a treatment regimen with docetaxel and carboplatin
    - **Metastatic breast cancer:** in combination with paclitaxel for first-line treatment of HER2-overexpressing metastatic breast cancer; or as a single agent for treatment of HER2 overexpressing breast cancer in patients who have received ≥ 1 chemotherapy regimens for metastatic disease
    - Patients should be selected for therapy based on an FDA-approved companion diagnostic for a trastuzumab product.

- Ogivri and Herceptin are also indicated as a single agent following multi-modality anthracycline based therapy for the treatment of adjuvant breast cancer and in combination with cisplatin and capecitabine or 5-fluorouracil, for the treatment of patients with HER2-overexpressing metastatic gastric or gastroesophageal junction adenocarcinoma who have not received prior treatment for metastatic disease.
- A biosimilar product is a biological agent that is considered highly similar to an already-approved biological drug, known as the reference product. Biological products are generally derived from a living organism and can come from many sources, including humans, animals, microorganisms or yeast.
    - A biosimilar product must show no clinically meaningful differences in terms of safety and effectiveness from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products.
    - In addition, a biosimilar product may only be approved for the indication(s) and condition(s) that have been FDA approved for the reference product, and must have the same mechanism(s) of action, route(s) of administration, dosage form(s) and strength(s) as the reference product.
- Herzuma has been approved as a biosimilar, ***not*** as an interchangeable product.
- The approval of Herzuma was based on review of a comprehensive data package inclusive of foundational analytical similarity data, nonclinical data, clinical pharmacology, immunogenicity, clinical efficacy and safety data.
    - The results of the clinical development program for Herzuma demonstrated that there were no clinically meaningful differences in purity, potency and safety between Herzuma and Herceptin for the treatment of HER2-overexpressing breast cancer for the approved indications.

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- Like Herceptin, Herzuma carries a boxed warning regarding the risk of cardiomyopathy, infusion reactions, embryo-fetal toxicity, and pulmonary toxicity.

- Another warning and precaution of Herzuma includes exacerbation of chemotherapy-induced neutropenia.
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- The most common adverse reactions vary by indication.

  — In adjuvant breast cancer, the most common adverse reactions (≥ 5%) with trastuzumab use were headache, diarrhea, nausea, and chills.
  — In metastatic breast cancer, the most common adverse reactions (≥ 10%) with trastuzumab use were fever, chills, headache, infection, congestive heart failure, insomnia, cough, and rash.
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- The recommended dosage of Herzuma varies by indication as follows:

Indication	Recommended Dosage
Adjuvant breast cancer (during and following paclitaxel, docetaxel, or docetaxel/carboplatin)	· Initial dose of 4 mg/kg as an intravenous (IV) infusion, then 2 mg/kg IV weekly during chemotherapy for the first 12 weeks (paclitaxel or docetaxel) or 18 weeks (docetaxel/carboplatin). · One week following the last weekly dose of Herzuma, administer Herzuma 6 mg/kg IV every three weeks.
Metastatic breast cancer	Alone or in combination with paclitaxel, at an initial dose of 4 mg/kg IV followed by subsequent once weekly doses of 2 mg/kg IV until disease progression.

  — Do not substitute Herzuma with Kadcyla® (ado-trastuzumab emtansine).
  — For additional dosing information, refer to the Herzuma drug label.

- Teva and Celltrion's launch plans are pending due to ongoing litigation. Herzuma will be available as a 420 mg lyophilized powder in a multi-dose vial for reconstitution.