Trazimera™ (trastuzumab-qyyp) – New biosimilar approval

- On March 11, 2019, Pfizer announced the FDA approval of Trazimera (trastuzumab-qyyp), a biosimilar to Genentech's Herceptin® (trastuzumab).
    - Trazimera is the fourth FDA-approved biosimilar to Herceptin.
    - Mylan's Ogivri® (trastuzumab-dkst) was the first biosimilar to Herceptin and was approved in December 2017. In December 2018, Teva and Celltrion's Herceptin biosimilar, Herzuma® (trastuzumab-pkrb), was approved. Samsung Bioepis and Merck's Ontruzant® (trastuzumab-dttb) was approved in January 2019.
    - Mylan, Teva/Celltrion and Samsung Bioepis/Merck's launch plans for Ogivri, Herzuma and Ontruzant are pending.

- Trazimera, Ontruzant, 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.

- Trazimera, Ontruzant, 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.

- The efficacy and safety of Trazimera was based in part on the REFLECTIONS B327-02 double-blind study of 707 patients with HER2+ metastatic breast cancer. Patients received paclitaxel and Trazimera or trastuzumab from the European Union (EU). The primary endpoint was objective response rate (ORR) with a pre-specified risk ratio equivalence margin of 0.80 – 1.25.
    - Trazimera met the risk ratio equivalence margin. The ORR was 62.5% for the Trazimera group vs. 66.5% for the trastuzumab-EU group (risk ratio = 0.940; 95% CI: 0.842, 1.049).
    - In addition, there was no statistically significant difference between treatments for progression-free survival and overall survival.

- 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

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mechanism(s) of action, route(s) of administration, dosage form(s) and strength(s) as the reference product.

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- Trazimera has been approved as a biosimilar, ***not*** as an interchangeable product.

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

- Another warning and precaution of Trazimera is exacerbation of chemotherapy-induced neutropenia.

- 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.
  — In metastatic gastric cancer, the most common adverse reactions (≥ 10%) with trastuzumab use were neutropenia, diarrhea, fatigue, anemia, stomatitis, weight loss, upper respiratory tract infections, fever, thrombocytopenia, mucosal inflammation, nasopharyngitis, and dysgeusia.

- The recommended dosage of Trazimera 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 Trazimera, administer Trazimera 6 mg/kg IV every three weeks to complete a total of 52 weeks of therapy.
Adjuvant breast cancer (as a single agent within 3 weeks following completion of multi-modality, anthracycline based chemotherapy regimens)	• Initial dose of 8 mg/kg by IV, then subsequent doses at 6 mg/kg IV every three weeks. • Extending adjuvant treatment beyond one year is not recommended.
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.
Metastatic gastric cancer	Initial dose of 8 mg/kg IV followed by subsequent doses of 6 mg/kg IV every three weeks until disease progression.

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

- Pfizer’s launch plans are pending. Trazimera will be available as a 420 mg lyophilized powder in a multiple-dose vial for reconstitution.