Herceptin Hylecta™ (trastuzumab/hyaluronidase-oysk) – New formulation approval

- On February 28, 2019, Genentech announced the FDA approval of Herceptin Hylecta (trastuzumab/hyaluronidase-oysk) subcutaneous (SC) injection, in adults for the treatment of HER2-overexpressing breast cancer as follows:
    - Adjuvant treatment of 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; as part of a treatment regimen with docetaxel and carboplatin; or as a single agent following multi-modality anthracycline based therapy
    - In combination with paclitaxel for first-line treatment of metastatic breast cancer (MBC)
    - As a single agent for treatment of patients who have received one or more chemotherapy regimens for metastatic disease
    - Select patients for therapy based on an FDA-approved companion diagnostic for trastuzumab.

- Herceptin Hylecta includes the same monoclonal antibody as intravenous Herceptin® (trastuzumab) in combination with recombinant human hyaluronidase PH20, an enzyme that helps to deliver trastuzumab under the skin.
    - Herceptin carries the same indications as Herceptin Hylecta and is also indicated 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 approval of Herceptin Hylecta is based on three clinical studies. The first study (HannaH) was an open-label, non-inferiority study in 596 patients with HER2-positive operable or locally advanced breast cancer, including inflammatory breast cancer. Patients were randomized to Herceptin Hylecta or intravenous (IV) trastuzumab plus chemotherapy for a total of 18 cycles. The second study (SafeHER) was an open-label study designed to assess the overall safety and tolerability of 18 cycles of Herceptin Hylecta with chemotherapy in 1,864 patients with HER2-positive breast cancer. The third study (PrefHER) was a cross-over trial conducted in 240 patients with HER2-positive breast cancer undergoing neoadjuvant or adjuvant treatment.
    - In HannaH, non-inferior clinical efficacy was demonstrated for Herceptin Hylecta by the pathological complete response of 45.4% for Herceptin Hylecta vs. 40.7% for IV trastuzumab (difference = 4.70; 95% CI: -4.0; 13.4). In addition, the pharmacokinetic results (C_{trough} pre-dose cycle 8) showed non-inferiority of Herceptin Hylecta (78.7 mcg/mL) vs. IV trastuzumab (57.8 mcg/mL) (geometric mean ratio = 1.3; 90% CI: 1.2, 1.4).
    - In SafeHER, safety and tolerability results were consistent with the known safety profile for Herceptin Hylecta and IV trastuzumab.
    - In PrefHER, after cycle 8, 86% of patients preferred SC administration of Herceptin Hylecta vs. IV trastuzumab; the most common reason cited was administration required less time in the clinic. A total of 13% reported preferring IV trastuzumab vs. Herceptin Hylecta; the most common reason was fewer local injection reactions. A total of 1% of patients had no preference, and 3.8% withdrew from treatment prior to cycle 8.

- Herceptin Hylecta carries a boxed warning for cardiomyopathy, embryo-fetal toxicity, and pulmonary toxicity.

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- Warnings and precautions of Herceptin Hylecta include exacerbation of chemotherapy-induced neutropenia, and hypersensitivity and administration-related reactions.

- The most common adverse reactions (≥ 10%) with Herceptin Hylecta use in adjuvant breast cancer were fatigue, arthralgia, diarrhea, injection site reaction, upper respiratory tract infection, rash, myalgia, nausea, headache, edema, flushing, pyrexia, cough, and pain in extremity.

- The most common adverse reactions (≥ 10%) in MBC (based on intravenous trastuzumab) were fever, chills, headache, infection, congestive heart failure, insomnia, cough, and rash.

- The recommended dose for Herceptin Hylecta is 600 mg/10,000 units (600 mg trastuzumab and 10,000 units hyaluronidase) administered SC over approximately 2 - 5 minutes once every three weeks.

    — Patients with adjuvant breast cancer should be treated with Herceptin Hylecta for 52 weeks or until disease recurrence, whichever occurs first; extending treatment in adjuvant breast cancer beyond one year is not recommended.
    — Patients with MBC should be treated with Herceptin Hylecta until progression of disease.
    — Herceptin Hylecta should be administered by a healthcare professional.
    — Herceptin Hylecta is for SC use only. Herceptin Hylecta has different dosage and administration instructions than IV trastuzumab products. Do not administer IV.
    — Do not substitute Herceptin Hylecta for or with Kadcyla® (ado-trastuzumab emtansine).

- Genentech's launch plans for Herceptin Hylecta are pending. Herceptin Hylecta will be available as 600 mg trastuzumab and 10,000 units hyaluronidase per 5 mL (120 mg/2,000 units per mL) solution in a single-dose vial.

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