Enhertu® (fam-trastuzumab deruxtecan-nxki) – New indication

- On August 5, 2022, the FDA announced the approval of Astra Zeneca and Daiichi Sankyo's Enhertu (fam-trastuzumab deruxtecan-nxki), for the treatment of adult patients with unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-low (immunohistochemistry [IHC] 1+ or IHC 2+/ in situ hybridization [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.

- Enhertu is also approved for the treatment of adult patients 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 6 months of completing therapy; and adult patients with locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma who have received a prior trastuzumab based regimen.

- In 2022, It is estimated that 287,850 new cases of female breast cancer will be diagnosed in the U.S. About 60% of patients previously classified as having HER2-negative subtype can now be considered as HER2-low.

    - HER2 expression is currently determined by an IHC test which estimates the amount of HER2 protein on a cancer cell, and/or an ISH test, which counts the copies of the HER2 gene in cancer cells.

- The approval of Enhertu for the new indication was based on DESTINY-Breast04, a randomized, open-label study that enrolled 557 adult patients with unresectable or metastatic HER2-low breast cancer. Patients received Enhertu or physician's choice of chemotherapy. The major efficacy outcome measure was progression free survival (PFS) in patients with hormone receptor positive (HR+) breast cancer. Additional efficacy outcome measures were PFS in the overall population (all randomized HR+ and HR- patients), overall survival (OS) in HR+ patients, and OS in the overall population.

    - PFS in the HR+ cohort was 10.1 months in the Enhertu group vs. 5.4 months in the chemotherapy group (Hazard ratio [HR] 0.51; 95% CI: 0.40, 0.64; $p < 0.0001$).
    - PFS in the overall population was 9.9 months in the Enhertu group vs. 5.1 months in the chemotherapy group (HR 0.50; 95% CI: 0.40, 0.63; $p < 0.0001$).
    - OS in the HR+ cohort was 23.9 months in the Enhertu group vs. 17.5 months in the chemotherapy group (HR 0.64; 95% CI: 0.48, 0.86; $p = 0.0028$).
    - OS in the overall population was 23.4 months in the Enhertu group vs. 16.8 months in the chemotherapy group (HR 0.64; 95% CI: 0.49, 0.84; $p = 0.001$).

- Enhertu carries a boxed warning for interstitial lung disease and embryo-fetal toxicity.

- The recommended dose of Enhertu for the treatment of HER2-low breast cancer is 5.4 mg/kg given as an intravenous infusion once every 3 weeks (21-day cycle) until disease progression or unacceptable toxicity.

- Enhertu should not be substituted for or with trastuzumab (Herceptin® and biosimilars) or Kadcylca® (ado-trastuzumab emtansine).
- Information on FDA-approved tests for the detection of HER2 protein expression and HER2 gene amplification is available at: http://www.fda.gov/CcompanionDiagnostics.
- Refer to the Enhertu drug label for dosing for all its other indications.