

Tukysa[™] (tucatinib) – New orphan drug approval

- On April 17, 2020, the [FDA announced](#) the approval of [Seattle Genetics' Tukysa \(tucatinib\)](#), in combination with [trastuzumab](#) and [capecitabine](#), for treatment of adult patients with advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-positive breast cancer, including patients with brain metastases, who have received one or more prior anti-HER2-based regimens in the metastatic setting.
- Patients with HER2-positive breast cancer have tumors with high levels of HER2, which promotes the growth of cancer cells.
 - In the U.S., 279,100 new cases of breast cancer will be diagnosed in 2020. Approximately one-fifth of breast cancers are HER2-positive, and more than 25% of women with metastatic HER2-positive breast cancer will develop brain metastases.
- Tukysa is a HER2 inhibitor. It is designed to inhibit the HER2 protein, which results in the inhibition of cell growth of HER2-expressing tumor cells.
- The efficacy of Tukysa was established in a double-blind, placebo-controlled study in 612 patients who had HER2-positive advanced unresectable or metastatic breast cancer and had prior treatment with trastuzumab, [Perjeta[®] \(pertuzumab\)](#), and [Kadcyla[®] \(ado-trastuzumab emtansine\)](#). All patients received baseline trastuzumab and capecitabine and were randomized to receive either Tukysa 300 mg or placebo orally twice daily. The primary endpoint was progression-free survival (PFS). Key secondary endpoints included overall survival (OS) and PFS in patients with brain metastases at baseline.
 - Median PFS was 7.8 months in the Tukysa arm vs. 5.6 months in the control arm (hazard ratio [HR] 0.54; 95% CI: 0.42, 0.71; $p < 0.00001$).
 - Median OS was 21.9 months in the Tukysa arm vs. 17.4 months in the control arm (HR 0.66; 95% CI: 0.50, 0.87; $p = 0.0048$).
 - For patients with brain metastases, median PFS was 7.6 months in the Tukysa arm vs. 5.4 months in the control arm (HR 0.48; 95% CI: 0.34, 0.69; $p < 0.00001$).
- Warnings and precautions for Tukysa include diarrhea, hepatotoxicity, and embryo-fetal toxicity.
- The most common adverse reactions ($\geq 20\%$) with Tukysa use were diarrhea, palmar-plantar erythrodysesthesia, nausea, fatigue, hepatotoxicity, vomiting, stomatitis, decreased appetite, abdominal pain, headache, anemia, and rash.
- The recommended dose of Tukysa is 300 mg taken orally twice daily in combination with trastuzumab and capecitabine until disease progression or unacceptable toxicity.
 - When given in combination with Tukysa, the recommended dosage of capecitabine is 1000 mg/m² orally twice daily taken within 30 minutes after a meal. Tukysa and capecitabine can be taken at the same time.
 - Refer to the drug labels for trastuzumab and capecitabine for additional dosing information.

- Seattle Genetics plans to launch Tukysa within a week of approval. Tukysa will be available as 50 mg and 150 mg tablets.



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