

Pfizer's TUKYSA Regimen Receives FDA Approval as Front-Line Maintenance Treatment for HER2+ Metastatic Breast Cancer

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TUKYSA in combination with trastuzumab and pertuzumab showed more than 50% improvement in median progression-free survival, supporting approval as a chemotherapy-free maintenance option

NEW YORK--(BUSINESS WIRE)-- [Pfizer Inc.](#) (NYSE: PFE) today announced that the U.S. Food and Drug Administration (FDA) has approved TUKYSA[®] (tucatinib) in combination with trastuzumab and pertuzumab for the maintenance treatment of adults with unresectable locally advanced or metastatic human epidermal growth factor 2-positive (HER2+) breast cancer following induction treatment. The approval expands the use of TUKYSA to frontline, an earlier stage of metastatic disease, offering a new chemotherapy-free maintenance treatment option that may help further delay disease progression.

"Since its first approval in 2020, TUKYSA has become an important treatment for patients with second-line HER2+ metastatic breast cancer. Today's FDA approval marks the next chapter for TUKYSA, bringing it into the front-line maintenance setting and offering patients a chemotherapy-free option that can help delay disease progression after initial treatment. This approval reflects Pfizer's commitment to advancing therapies across the breast cancer treatment journey and delivering meaningful new options for people living with metastatic breast cancer."

- Aamir Malik, Executive Vice President, Chief U.S. Commercial Officer, Pfizer

"The treatment landscape for HER2+ metastatic breast cancer has evolved dramatically over the past decade, but many patients still experience disease progression despite initial benefit from therapy. The HER2CLIMB-05 findings support TUKYSA plus trastuzumab and pertuzumab as a chemotherapy-free maintenance strategy that allows us to target HER2-positive tumors from multiple angles and can help prolong disease control."

- Erika Hamilton, M.D., principal investigator of HER2CLIMB-05 and Chief Development Officer, Late Phase & Director, Breast Cancer Research for Sarah Cannon Research Institute (SCRI)

Key Results from the HER2CLIMB-05 Phase 3 Trial

- **Prolonged Median Progression-Free Survival (PFS):** The primary endpoint analysis showed a 35.9% reduction in the risk of disease progression or death among patients treated with TUKYSA, trastuzumab, and pertuzumab compared to those treated with placebo, trastuzumab, and pertuzumab, following induction treatment, as assessed by the investigator (hazard ratio of 0.64, 95% confidence interval (CI): 0.51-0.80; 2-sided p<0.0001). Median investigator-assessed PFS for patients in the TUKYSA arm was

24.9 months (95% CI, 21.3-not reached) compared to 16.3 months (95% CI, 12.6-18.7) in the placebo arm, representing a difference of 8.6 more months that patients lived without their cancer worsening.

- **Safety Profile:** The safety and tolerability of TUKYSA was generally consistent with its known safety profile, with the exception of increased severity of hepatotoxicity. The majority of hepatotoxicity events were generally asymptomatic and reversible with dose modification and/or discontinuation. The most commonly reported adverse events (?20%) were diarrhea, musculoskeletal pain, hepatotoxicity, nausea, fatigue, rash, and vomiting. Serious adverse reactions in ?1% of patients included hepatotoxicity (3.9%), including one patient who experienced a fatal adverse reaction of drug-induced liver injury.
- **Published Previously:** Results from HER2CLIMB-05 were published in the [Journal of Clinical Oncology](#) and presented at the 2025 San Antonio Breast Cancer Symposium (SABCS).

About the Phase 3 HER2CLIMB-05 Trial

- The HER2CLIMB-05 trial is a randomized, double blind, placebo-controlled, pivotal Phase 3 study evaluating the efficacy and safety of TUKYSA compared to placebo, both in combination with trastuzumab and pertuzumab, as maintenance therapy for patients with HER2+ metastatic breast cancer (MBC) following induction therapy in the front-line setting.
- HER2 is overexpressed in up to 15-20% of breast cancers and is associated with poor prognosis, with an estimated five-year survival rate of 41% to 47%, depending on hormone receptor status.¹⁻³
- Trial participants who completed induction therapy of trastuzumab, pertuzumab, and a taxane, with no evidence of progression, were randomized to receive TUKYSA in combination with trastuzumab plus pertuzumab (n=326) or placebo in combination with trastuzumab plus pertuzumab (n=328).
- The primary endpoint is PFS as assessed by the investigator. Overall survival is a key secondary endpoint.

Continuing Pfizer's Legacy of Leadership in Breast Cancer

Pfizer has been a leader in breast cancer for over 25 years, and today we have five medicines and one biosimilar approved to treat different subtypes of the disease, reaching over 4.9 million patients worldwide.

In the U.S., TUKYSA is already a National Comprehensive Cancer Network[®] (NCCN[®]) Category 1 second-line plus treatment for HER2+ MBC patients. This approval extends the reach of TUKYSA as part of a front-line maintenance regimen, bringing patients a new option to delay disease progression without the need for continued chemotherapy and helping physicians further individualize treatment plans to best meet the needs of each unique patient.

About TUKYSA[®] (tucatinib)

TUKYSA (tucatinib) is an orally administered tyrosine kinase inhibitor of HER2. TUKYSA is approved in combination with trastuzumab and pertuzumab for the maintenance treatment of adult patients with unresectable locally advanced or metastatic HER2-positive breast cancer following induction treatment. TUKYSA has also been approved in combination with trastuzumab and capecitabine to treat adults with HER2-positive advanced unresectable or MBC, including patients with brain metastases who have received one or more prior anti-HER2 breast cancer treatments in the metastatic setting.

The full U.S. Prescribing Information for TUKYSA can be found [here](#). There may be a delay as the document is updated with the latest information. It will be available as soon as possible. Please check back for the updated full information shortly.

Related Content

- [TUKYSA Added to First-Line Maintenance Therapy Extends Median Progression-Free Survival by Over 8 Months in Patients with HER2+ Metastatic Breast Cancer | Pfizer](#)

- [TUKYSA Combination Significantly Improves Progression-Free Survival as First-Line Maintenance in HER2+ Metastatic Breast Cancer in HER2CLIMB-05 Trial | Pfizer](#)
- [HER2CLIMB-05: A Phase III Study of Tucatinib Versus Placebo in Combination With Trastuzumab and Pertuzumab as First-Line Maintenance Therapy for HER2+ Metastatic Breast Cancer | Journal of Clinical Oncology](#)

IMPORTANT SAFETY INFORMATION

BOXED WARNING: Severe Hepatotoxicity

TUKYSA can cause severe and fatal hepatotoxicity, particularly after rechallenge. Obtain liver function tests before initiation and during treatment with TUKYSA. Withhold, reduce dose, or permanently discontinue TUKYSA as recommended based on severity of hepatotoxicity.

Warnings and Precautions

Hepatotoxicity: TUKYSA can cause severe and fatal hepatotoxicity, particularly after rechallenge. Monitor ALT, AST, and bilirubin prior to starting TUKYSA, every 2 weeks for the first 2 months, then every 3 weeks during treatment, and as clinically indicated. For patients who experience AST/ALT $>3 \times$ ULN and bilirubin $> \text{ULN}$ to $? 2 \times$ ULN, repeat testing within 48-72 hours. For patients who experience AST/ALT $> 5 \times$ ULN, withhold TUKYSA and repeat testing within 48-72 hours to determine if worsening. Based on the severity of hepatotoxicity, reduce dose or permanently discontinue TUKYSA. Institute weekly liver function monitoring if TUKYSA is resumed after resolution to Grade $? 1$.

In HER2CLIMB-05, when Tukysa was given in combination with trastuzumab and pertuzumab, 18% of patients who received TUKYSA had an ALT increase $>5 \times$ ULN, 10% had an AST increase $>5 \times$ ULN, and 1.2% had a bilirubin increase $>3 \times$ ULN (Grade $?3$). There were five confirmed Hy's Law cases, including a fatal case. All occurred following rechallenge with TUKYSA. Hepatotoxicity led to dose reduction of TUKYSA in 15% of patients and discontinuation of TUKYSA in 8% of patients.

In HER2CLIMB, when TUKYSA was given in combination with trastuzumab and capecitabine 8% of patients who received TUKYSA had an ALT increase $>5 \times$ ULN, 6% had an AST increase $>5 \times$ ULN, and 1.5% had a bilirubin increase $>3 \times$ ULN (Grade $?3$). Hepatotoxicity led to TUKYSA dose reductions in 8% of patients and TUKYSA discontinuation in 1.5% of patients.

Diarrhea: TUKYSA can cause severe diarrhea including dehydration, hypotension, acute kidney injury, and death. If diarrhea occurs, administer antidiarrheal treatment as clinically indicated. Perform diagnostic tests as clinically indicated to exclude other causes of diarrhea. Based on the severity of the diarrhea, interrupt dose, reduce dose or permanently discontinue TUKYSA.

In HER2CLIMB-05, 73% of patients who received TUKYSA experienced diarrhea, including 6% with Grade 3 events. The median time to onset of the first episode of diarrhea was 11 days and the median time to resolution was 2 days. Diarrhea led to dose reductions of TUKYSA in 6% of patients and discontinuation of TUKYSA in 1.5% of patients. Prophylactic use of antidiarrheal treatment was not required in HER2CLIMB-05.

In HER2CLIMB, 81% of patients who received TUKYSA experienced diarrhea, including 0.5% with Grade 4 and 12% with Grade 3. Both patients who developed Grade 4 diarrhea subsequently died, with diarrhea as a contributor to death. Median time to onset of the first episode of diarrhea was 12 days and the median time to resolution was 8 days. Diarrhea led to TUKYSA dose reductions in 6% of patients and TUKYSA discontinuation in 1% of patients. Prophylactic use of antidiarrheal treatment was not required on HER2CLIMB.

Embryo-Fetal Toxicity: TUKYSA can cause fetal harm. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential, and male patients with female partners of reproductive potential, to use effective contraception during TUKYSA treatment and for 1 week after the last dose. When TUKYSA is used in combination, advise patients to use effective contraception during treatment and for the longest post-treatment duration recommended in the Prescribing Information of any of the individual products.

Increased Serum Creatinine Without Affecting Renal Function: TUKYSA can increase serum creatinine. Across three clinical trials in 816 patients (HER2CLIMB-05, HER2CLIMB, and MOUNTAINEER), the mean increase in serum creatinine was 29%-32% within the first 21 days of treatment with TUKYSA. The serum creatinine increase persisted throughout treatment and were reversible upon treatment completion. These increases were not associated with changes in glomerular function. These increases in serum creatinine may be due to inhibition of renal tubular transport of creatinine. During TUKYSA treatment, use alternative measures that are not based on serum creatinine to assess renal function.

Adverse Reactions:

In HER2CLIMB-05, serious adverse reactions occurred in 17% of patients who received TUKYSA. Serious adverse reactions in 1% of patients included hepatotoxicity (3.9%). One patient experienced a fatal adverse reaction of drug-induced liver injury. Adverse reactions leading to permanent discontinuation occurred in 14% of patients who received TUKYSA; the most common (in 1% of patients) were hepatotoxicity (8%) and diarrhea (1.5%). Adverse reactions leading to dosage interruptions of TUKYSA occurred in 49% of patients, the most common (in 1% of patients) were hepatotoxicity (19%) and diarrhea (9%). Adverse reactions leading to dose reduction of TUKYSA occurred in 29% of patients, the most common (in 2% of patients) were hepatotoxicity (16%) and diarrhea (6%). The most common (20%) adverse reactions were diarrhea, musculoskeletal pain, hepatotoxicity, nausea, fatigue, rash, and vomiting. Other clinically relevant adverse reactions in <10% of patients who received TUKYSA in combination with trastuzumab and pertuzumab included epistaxis (3.7%).

In HER2CLIMB, serious adverse reactions occurred in 26% of patients; the most common (in 2% of patients) were diarrhea (4%), vomiting (2.5%), nausea (2%), abdominal pain (2%), and seizure (2%). Fatal adverse reactions occurred in 2% of patients who received TUKYSA including sudden death, sepsis, dehydration, and cardiogenic shock. Adverse reactions led to treatment discontinuation in 6% of patients who received TUKYSA; the most common (in 1% of patients) were hepatotoxicity (1.5%) and diarrhea (1%). Adverse reactions led to dose reduction in 21% of patients who received TUKYSA; the most common (in 2% of patients) were hepatotoxicity (8%) and diarrhea (6%). The most common adverse reactions in patients who received TUKYSA (20%) were diarrhea, palmar-plantar erythrodysesthesia, nausea, hepatotoxicity, vomiting, stomatitis, decreased appetite, anemia, and rash.

Lab Abnormalities

In HER2CLIMB-05, Grade 3 laboratory abnormalities reported in 5% of patients who received TUKYSA were increased ALT, and increased AST.

In HER2CLIMB, Grade 3 laboratory abnormalities reported in 5% of patients who received TUKYSA were decreased phosphate, increased ALT, decreased potassium, and increased AST.

Drug Interactions

- **Strong CYP3A/Moderate CYP2C8 Inducers:** Concomitant use may decrease TUKYSA activity. Avoid concomitant use of TUKYSA.
- **Strong or Moderate CYP2C8 Inhibitors:** Concomitant use of TUKYSA with a strong CYP2C8 inhibitor may increase the risk of TUKYSA toxicity; avoid concomitant use. Increase monitoring for TUKYSA toxicity with moderate CYP2C8 inhibitors.
- **CYP3A Substrates:** Concomitant use may increase the toxicity associated with a CYP3A substrate. Avoid concomitant use of TUKYSA with a CYP3A substrate, where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, decrease the CYP3A substrate dosage.
- **P-gp Substrates:** Concomitant use may increase the toxicity associated with a P-gp substrate. Consider reducing the dosage of P-gp substrates, where minimal concentration changes may lead to serious or life-threatening toxicities.

Use in Specific Populations

- **Lactation:** Advise women not to breastfeed while taking TUKYSA and for 1 week after the last dose.
- **Renal Impairment:** Use of TUKYSA in combination with capecitabine and trastuzumab is not recommended in patients with severe renal impairment (CLCr < 30 mL/min), because capecitabine is contraindicated in patients with severe renal impairment.
- **Hepatic Impairment:** Reduce the dose of TUKYSA for patients with severe (Child-Pugh C) hepatic impairment.

About Pfizer Oncology

At Pfizer Oncology, we are at the forefront of a new era in cancer care. Our industry-leading portfolio and extensive pipeline includes three core mechanisms of action to attack cancer from multiple angles, including small molecules, antibody-drug conjugates (ADCs), and multispecific antibodies, including other immune-oncology biologics. We are focused on delivering transformative therapies in some of the world's most common cancers, including breast cancer, gastrointestinal cancers, genitourinary cancers, hematology-oncology, and thoracic cancers, which includes lung cancer. Driven by science, we are committed to accelerating breakthroughs to help people with cancer live better and longer lives.

About Pfizer: Breakthroughs That Change Patients' Lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 175 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.Pfizer.com. In addition, to learn more, please visit us on www.Pfizer.com and follow us on X at [@Pfizer](https://twitter.com/Pfizer) and [@Pfizer News](https://twitter.com/PfizerNews), [LinkedIn](https://www.linkedin.com/company/pfizer), [YouTube](https://www.youtube.com/pfizer) and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

Disclosure Notice

The information contained in this release is as of October 7, 2026. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about Pfizer Oncology and TUKYSA[®] (tucatinib), including their potential benefits, results from the Phase 3 HER2CLIMB-05 trial and an approval in the U.S. for TUKYSA in combination with trastuzumab and pertuzumab for the maintenance treatment of adult patients with unresectable locally advanced or metastatic HER2-positive breast cancer following induction treatment, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of TUKYSA; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; whether the HER2CLIMB-05 trial will meet the secondary endpoint of overall survival; risks associated with initial, preliminary or interim data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when applications for TUKYSA may be filed in particular jurisdictions for any potential indications; whether and when regulatory authorities in any jurisdictions may approve any such applications that may be pending or filed for TUKYSA, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether TUKYSA for any potential indication will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety, and/or other matters that could affect the availability or commercial potential of TUKYSA; risks and uncertainties related to issued or future executive orders or other new, or changes in, laws or regulations; uncertainties regarding the impact of COVID-19 on Pfizer's business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2025, and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

References

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