

# Tucatinib

## TUKYSA®

Information for patients taking tucatinib

## Dear patient,

Your physician has prescribed the drug tucatinib to treat metastatic breast cancer. In this brochure, we will tell you more about this medicine and will explain to you how it works, how you need to take it, and what side effects may occur.

We hope that with this information you will understand more about the medicine and be able to take it correctly.

We hope that your treatment will be successful in the long term.

If you still have any questions after reading this brochure, please ask your treating physician.

Best regards,  
Your Seagen Team



ClimatePartner<sup>o</sup>  
wir drucken klimaneutral

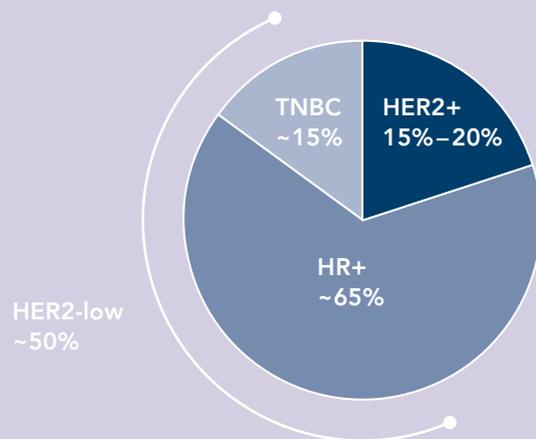
**Please note:**  
Highlighted terms are explained  
in the glossary on page 14.

## What is metastatic breast cancer?

Metastatic breast cancer is breast cancer that has spread (metastasis) to other parts of the body. Metastases can occur in the bones, the brain, the liver, and the lungs. Metastases can also affect lymph nodes that are not close to the breasts (distant lymph node metastases). Although metastatic breast cancer is not yet curable, recent research advances have resulted in people living much longer with the disease. The goal of any treatment is to reduce symptoms and improve life expectancy, while maintaining the best possible quality of life.

Breast cancer is the most common cancer in women, but there are also men who receive this diagnosis. In the long run, about 25 % of all breast cancer patients progress to an advanced stage with metastasis. About 3% of the breast cancer patients are initially diagnosed with metastasis.

### Breast Cancer Subtypes<sup>1,2</sup>



HER2, human epidermal growth factor receptor 2; HR, hormone receptor; TNBC, triple-negative breast cancer

There are different kinds of metastatic breast cancer that differ in their tumor key features. Cancer cells are differentiated by the protein structures within the cell and on their surface that are binding sites for hormones or growth factors.

Some tumor types are stimulated by the hormones estrogen and progesterone as their tumor cells have estrogen and/or progesterone receptors. This tumor type is “hormone-dependent” and called hormone-receptor positive breast cancer (HR+). These tumors are treated with anti-hormonal treatments that aim to lower the levels of estrogen and progesterone or block these hormones from getting to the cancer cell.

Other tumors have an increased number of HER2 (human epidermal growth factor receptor 2) on their cell surface and are called HER2-positive tumors (HER2+). The growth of these tumor cells is stimulated by growth factors, and the blockade of the receptor HER2 can block tumor growth.

The third tumor type has neither hormone receptors nor HER2 on the cell surface and is called “triple-negative breast cancer” (TNBC). TNBC, HR+ and HER2+ are the “classical” breast cancer subtypes.

Recently, another subtype was described, the group of so-called “HER2-low” tumors. In this new subtype, the breast cancer cells have a low protein level of HER2 (less than in the HER2+ subtype). HER2-low breast cancer cells can belong to both the TNBC and HR+ subtypes.

1. Schettini, Francesco, et al. “Clinical, pathological, and PAM50 gene expression features of HER2-low breast cancer.” *NPJ Breast Cancer* 7.1 (2021): 1–13;

2. Tarantino, Paolo, et al. “HER2-low breast cancer: pathological and clinical landscape.” *Journal of Clinical Oncology: official journal of the American Society of Clinical Oncology* 38.17 (2020): 1951–1962.

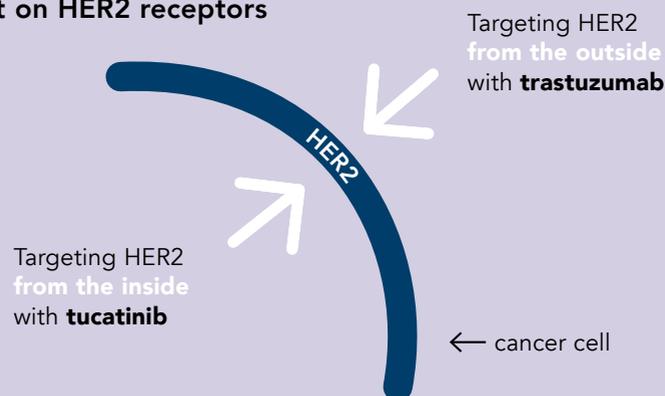
## What is tucatinib (TUKYSA®)?

TUKYSA® is a drug that contains the medicine tucatinib. It is a small molecule and belongs to the group of protein kinase inhibitors. More precisely, it is a tyrosine kinase inhibitor that can prevent the growth of certain types of cancer cell. It is administered in combination with two other medicines (trastuzumab and capecitabine) to treat HER2+ metastatic breast cancer.

## How does tucatinib work?

HER2 positive tumors have a high amount of HER2 receptors on the cell surface that promote the growth of the tumor cells. Tucatinib inhibits the activity of the receptors, which can lead to cancer cell death and slow down further growth. The medicine trastuzumab acts on HER2 from the outside, whereas tucatinib acts on the receptor from inside the cell.

### Effect on HER2 receptors



Trastuzumab is an antibody which is a large molecule. It binds to the HER2 receptor and affects the tumor cell from the outside. Tucatinib is a small molecule, which enters the tumor cell and binds to the HER2 receptor from the inside. Together, the two medicines can inhibit cancer cell growth more effectively.

## How can tucatinib help you?

This combined targeting of the receptor from inside and outside of the cell may increase the effectiveness of the therapy. The third medicine that is used together with tucatinib and trastuzumab is capecitabine. Capecitabine works differently to tucatinib and trastuzumab and it also blocks the ability of the cancer to grow.

The efficacy of tucatinib in combination with trastuzumab and capecitabine was investigated in an international, randomized, placebo-controlled, double-blind study (HER2CLIMB). A total of 612 patients with metastatic HER2-positive breast cancer participated in the study, 48 % of whom had metastases in the brain. 410 patients were randomized to receive tucatinib in combination with trastuzumab and capecitabine, while 202 patients were randomized to receive trastuzumab and capecitabine combined with a placebo (a dummy treatment; control group). The tucatinib combination has shown to improve the length of time patients with HER2-positive metastatic breast cancer live without their disease getting worse, and it also prolonged the time patients lived. Nearly all patients in the tucatinib group showed some response to the treatment as the tumor growth could be at least stopped. Similar results were seen in the subgroup of patients whose cancer had spread to the brain.

## Approval

TUKYSA® was approved by the European Medicines Agency (EMA) in February 2021. It is indicated for use in combination with trastuzumab and capecitabine for the treatment of adult patients with locally advanced or metastatic HER2-positive breast cancer, who have received at least two prior anti-HER2 treatments.

## How is tucatinib taken?

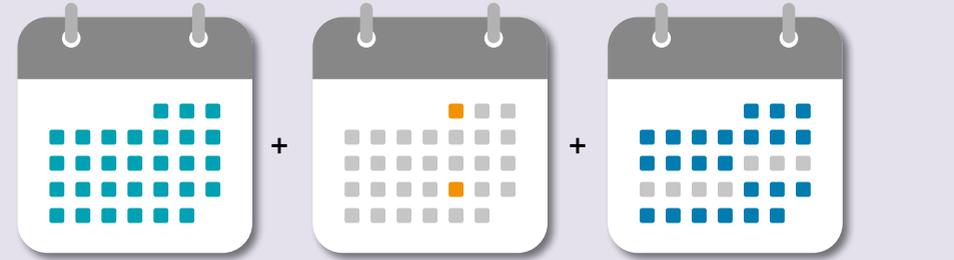
Please make sure you always take tucatinib exactly as instructed by your physician, and ask for guidance if you are uncertain about how to take it. You can also ask your pharmacist about this.

The recommended dose is 300 mg twice daily, with a 12-hour interval between doses. Each tablet contains 150 mg; so, swallow 2 tablets **one after the other** (with or without a meal), and always at the same time, if possible.

- Swallow the tablets as a whole, with water at the same time every day. Do not chew, cut, crush, or dissolve the tablets.
- Do not take damaged tablets.
- Please **do not take an additional dose** if you vomit after taking the tablets; please continue according to the treatment schedule. The same applies if you forget to take a dose.
- Please do not stop taking this medicine without consulting your physician first.
- Inform your physician **immediately** in the event of an overdose.

A 50 mg dose option is also available, if your physician recommends a different dosage due to any side effects that you may experience. The dosage can also be adjusted by changing the number of tablets you take.

## Administration schedule



### Tucatinib

take it 2x every day

- The recommended dose of tucatinib is 300 mg (2 tablets of 150 mg each) to be taken twice a day, 12 hours apart, with or without a meal. The total daily dose is 600 mg.

### Trastuzumab

once every 3 weeks

- Trastuzumab is given by infusion or injection on day 1 of tucatinib administration and then every 21 days or according to your physician's advice.

### Capecitabine

2x every day with 7 day break

- Administration of capecitabine tablets starts on day 1 of tucatinib administration.
- Please take the dose prescribed by your physician within 30 minutes after eating a meal.
- Tucatinib and capecitabine can be taken simultaneously.
- Capecitabine is taken for 14 days followed by a 7-day break, after which the cycle starts again.

## Getting the most out of your therapy

Treatment can only be effective if the medication is taken regularly and in accordance with the prescribed treatment schedule.

The following can help you remember to take your medicine:



Take your medication at the same time as another daily activity (e.g., always after brushing your teeth).



Use simple reminders (e.g., a post-it note on the bathroom mirror, reminders on your smartphone).

Please tell your physician if you are struggling with your treatment for any reason.

## What are the safety guidelines for tucatinib?

- **Please promptly contact your physician in case of:**
  - pain in the belly
  - itching, eyes and skin turning yellow, dark urine
  - fast and unexpected weight loss
  - any persisting and worsening side effect.
  
- Please inform your doctor immediately if you have taken an overdose.
  
- Tell your physician about all the medicines you take, including prescription and over-the-counter medicines, vitamins and herbal supplements (e.g., St. John's Wort or grapefruit juice). Tucatinib may affect the way your other medicines work, and other medicines may affect the way tucatinib works.
  
- Do not take TUKYSA® **if you are allergic** to its medicine, tucatinib, or to any other ingredient contained in this medicine.
  
- **Tucatinib must not be taken during pregnancy.**
  
- Tucatinib may have an impact on your fertility.
  
- Please ensure you use reliable contraception while taking tucatinib and for at least one week after taking the last dose of tucatinib. This also applies to male patients whose partner may become pregnant.
  
- **Do not breastfeed** your child **while taking tucatinib**, or for **at least one week after taking the last dose**, as it is not known whether and to what extent tucatinib is released into breast milk.

## What are the most common side effects?

Like with any other medication, treatment with tucatinib may be accompanied by side effects. These do not necessarily occur, but they may, and sometimes they go away in the course of treatment. If you notice any changes in yourself, please make sure you tell your doctor, as side effects, e.g., diarrhea and liver problems, can also have life-threatening consequences.

**Please follow the instructions your treating physician has given you on how to manage your side effects at home.**

### The most common side effects include:

- Diarrhea
- Elevated liver enzymes
- Fatigue
- Headache
- Inflammation of the mucous membrane of the oral cavity, oral ulcers
- Joint pain
- Liver problems, that can cause itching, yellowing of the skin and eyes, dark urine, or pain/discomfort in the upper right abdomen
- Low red blood cell count (anemia)
- Nausea
- Nosebleeds
- Rash
- Redness, pain, swelling, or blisters on the palms of the hands or soles of the feet
- Reduced appetite
- Vomiting
- Weight loss

These are not all of the possible side effects of tucatinib. The drugs used in combination with tucatinib may also have side effects.

If you are at all unsure or if you experience any symptoms, please consult your treating physician, who will be able to take measures to reduce the side effects, e.g., by adjusting the dosage.

Further information is provided on the product information leaflet enclosed with each packet of tablets.

### Dear patient,

We sincerely hope that you will find this information brochure helpful in managing your disease. Please keep a close eye on your body while your treatment with tucatinib is ongoing. Make sure you talk to your doctor promptly about how you are feeling, your physical condition, any changes that may have occurred, or any drug side effects that are not yet listed here, so that you can discuss the required therapy steps and adjust them if necessary. This will help to make your treatment safer and more effective.

We wish you all the best!

## Glossary of terms

### Capecitabine

Drug for the treatment of cancer

### Double-blind study

A study in which neither the investigator nor the study participants know which test group they belong to

### Enzyme

A substance that accelerates biochemical reactions

### HER2 (human epidermal growth factor receptor 2)

A receptor on the surface of cells through which growth signals are transmitted from the cell surface to the cell interior, to promote cell growth

### HER2-positive

HER2-positive breast cancer is a cancer characterized by an increased number of HER2 receptors on the surface of cancer cells

### Metastasis

The spread of cancer cells or secondary tumors (metastases) to organs or other tissue that are not in the vicinity of the initial tumor

### Placebo-controlled

With a control group receiving a placebo (dummy drug) instead of the drug under investigation

### Progression-free

Without any progression of the disease

### Protein kinases

A group of enzymes that modify proteins and influence their function

### Protein kinase inhibitors

Drugs that inhibit the activity of protein kinases

### Randomized

Allocated at random

### Receptor

Binding site for small molecules such as growth signals

### Trastuzumab

Medicine for the treatment of cancer

### Tucatinib

The medicine in TUKYSA®

### Tyrosine

An amino acid – a biochemical component in many proteins

### Tyrosine kinases

Enzymes of the family of protein kinases that play a decisive role in cell processes

### Tyrosine kinase inhibitor

A drug that inhibits the activity of tyrosine kinases

You have received this brochure to accompany your treatment with TUKYSA®.

This document is only to be given out by treating doctors to patients medicated with tucatinib.

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