165mm

155mm

The following side effects may occur with this medicine.

Very common (may affect more than 1 in 10 people):
- diarrhoea;
- feeling sick (nausea);
- being sick (vomiting);
- mouth sores, inflammation of the mouth, mouth ulcers;
- liver problems, which may cause itching, yellowing of eyes and skin, dark urine and pain or discomfort in the upper right area of the stomach;
- rash;
- joint pain;
- weight loss;
- nosebleed

Tell your doctor or pharmacist if you notice any side effects.

Reporting of side effects
Reporting of side effects If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

How to store TUCATIN
Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the blister and carton. The expiry date refers to the last day of that month.
This medicinal product does not require any special temperature storage conditions. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment

HOW SUPPLIED
Tucatin (Tucatinib) 50 mg tablets are available in blister pack of 10's. 30's & 60's.
Tucatin (Tucatinib) 150 mg tablets are available in blister pack of 10's. 30's & 120's.

Instructions: Store at 25°C (Excursions permitted between 15°C to 30°C).
Protect from sunlight & moisture.
Keep out of the reach of children.
To be dispensed on the prescription of a registered medical practitioner only.

خوراک : ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
ہدایات : دوا کو ۲۵ ڈگری سینٹی گریڈ درجہ حرارت پر رکھیں
(درجہ حرارت کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے)۔
دھوپ اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:
Kaizen Pharmaceuticals (Pvt) Ltd.,
E-127, E-128 & E-129, North Western Industrial Zone,
Port Qasim Authority, Karachi-75020, Pakistan.

Tucatin

(Tucatinib)

50mg & 150mg Film Coated Tablets

ٹیوکاٹن

(ٹیوکاٹینب)

۵۰ ملی گرام

۱۵۰ ملی گرام

Qualitative and quantitative composition

Tucatin Tablet 50mg
Each film-coated tablet contains:
Tucatinib…….... 50mg

Tucatin Tablet 150mg
Each film-coated tablet contains:
Tucatinib…….... 150mg

What TUCATIN is and what it is used for

TUCATIN is a medicine for breast cancer. It contains the active substance tucatinib and it belongs to a group of medicines called protein kinase inhibitors which prevent the growth of some types of cancer cells in the body.

TUCATIN is used for adults who have breast cancer which:

- has a receptor (target) on the cancer cells called human epidermal growth factor receptor 2 (HER2-positive breast cancer)

- has spread beyond the original tumour or to other organs such as the brain or cannot be removed by surgery

- has previously been treated with certain other breast cancer treatments
TUCATIN is taken with two other cancer medicines, trastuzumab and capecitabine. Separate patient information leaflets are available for these medicines. Ask your doctor to tell you about them.

How TUCATIN works

TUCATIN works by blocking the HER2 receptors on cancer cells. HER2 produces signals that can help the cancer to grow, and blocking it may slow or stop cancer cells from growing or may kill them altogether.

What you need to know before you take TUCATIN

Do not take TUCATIN

- if you are allergic to Tucatinib or any of the other ingredients of this medicine

Warnings and precautions
Talk to your doctor before taking TUCATIN if you have liver problems. During your treatment, your doctor will run tests to check that your liver is working properly.

- TUCATIN can cause severe diarrhoea. Talk to your doctor right away at the first sign of diarrhoea (loose stool) and if your diarrhoea persists with nausea and/or vomiting.
- TUCATIN may cause harm to an unborn baby when taken by a pregnant woman.

Talk to your doctor before you take TUCATIN if you think you may be pregnant or are planning to have a baby.
See section on "Pregnancy and breast-feeding" below.

Children and adolescents
TUCATIN should not be used in children under the age of 18 years. The safety of TUCATIN and how
effective it is has not been studied in this age group.

Other medicines and TUCATIN
Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. Some medicines may affect the way TUCATIN works or TUCATIN may affect the way they work.
These medicines include some medicines in the following groups:
• St John's wort – a herbal product used to treat depression
• itraconazole, ketoconazole, voriconazole, posaconazole – used to treat fungal infections
• rifampicin – used to treat bacterial infections
• darunavir, saquinavir, tipranavir – used to treat HIV
• phenytoin, carbamazepine – used to treat epilepsy or a painful condition of the face called trigeminal neuralgia or to control serious mood disorder when other medicines do not work
• buspirone– used to treat certain mental health problems
• sirolimus, tacrolimus – used to control your body's immune response after a transplant
• digoxin – used to treat heart problems
• lomitapide, lovastatin – used to treat abnormal cholesterol levels
• alfentanil – used for pain relief
• avanafil, vardenafil – used to treat erectile dysfunction
• darifenacin – used to treat urinary incontinence
• midazolam, triazolam –used to treat seizures, anxiety disorders, panic, agitation, and insomnia
• repaglinide – used to treat type 2 diabetes
• ebastine – an antihistamine used to treat seasonal and perennial allergic rhinitis and rhino-conjunctivitis.
• everolimus, ibrutinib – used to treat certain cancers
• naloxegol – used to treat to treat constipation

TUCATIN with food and drink

TUCATIN tablets may be taken with or without food.

Pregnancy and breast-feeding

TUCATIN may cause harmful effects to an unborn baby when taken by a pregnant woman. Your doctor will do a pregnancy test before you start taking TUCATIN.
• If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine. The doctor will weigh the potential benefit to you against the risk to the unborn baby.
• Use a reliable method of contraception to avoid becoming pregnant while you are taking TUCATIN and for at least 1 week after the last dose.
• If you are male and have a female sexual partner who can become pregnant, use a reliable
• method of contraception to avoid pregnancy while you are taking TUCATIN and for at least 1 week after the last dose.
• If you become pregnant during treatment with TUCATIN, tell your doctor. The doctor will assess the potential benefit to you of continuing this medicine and the risk to the unborn baby.

It is not known whether TUCATIN passes into breast milk.
• If you are breast feeding or planning to breast feed, ask your doctor for advice before taking this medicine. You should not breastfeed during treatment with TUCATIN and for at least 1 week after the last dose. Talk to your doctor about the best way to feed your baby during treatment.
Ask your doctor or pharmacist for advice before taking TUCATIN if you have any questions.

Driving and using machines
TUCATIN is not expected to affect your ability to drive or operate machines. However, you are responsible for deciding whether you can drive a motor vehicle or perform other tasks that require increased concentration.

TUCATIN contains sodium and potassium
This medicine contains 55.3 mg sodium (main component of cooking/table salt) in each 300mg dose.
This is equivalent to 2.75% of the recommended maximum daily dietary intake of sodium for an adult.
This medicine contains 60.6 mg potassium per 300 mg dose. To be taken into consideration by patients with reduced kidney function or patients on a controlled potassium diet.

How to take TUCATIN
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Dosage
The recommended dose is 300 mg (two 150 mg tablets) by mouth twice a day.
Your doctor may change your dose of TUCATIN if you experience certain side effects. To allow for a lower dose, your doctor may prescribe 50 mg tablets.

Method of administration
TUCATIN can be taken with food or between meals.
• Swallow the tablets whole, one after the other.
• Take each dose about 12 hours apart at the same times every day.
• Do not chew or crush the tablet.
• Do not take an additional dose if you vomit after taking TUCATIN but continue with the next
scheduled dose.

If you take more TUCATIN than you should
Talk to a doctor or pharmacist straight away. If possible, show them the pack
If you forget to take TUCATIN
Do not take a double dose to make up for the forgotten dose. Just take the next dose at the scheduled time.

If you stop taking TUCATIN
TUCATIN is for long-term treatment and you should take it continuously. Do not stop taking TUCATIN without talking to your doctor

While you are taking TUCATIN
• Depending on the side effects you have, your doctor may recommend lowering your dose or temporarily stopping your treatment.
• Your doctor will also check your liver function during treatment with TUCATIN.

Possible side effects
Like all medicines, this medicine can cause side effects, although not everybody gets them:

Reference of Tucatin;

Regulatory & prescribing information

1. **Seagen Inc.** *TUKYSA® (tucatinib) tablets — Full Prescribing Information (US label),* revised Jan 2023 (and original 2020 label). Available from FDA. FDA Access Data+1
2. **U.S. Food & Drug Administration.** *FDA approval notice — TUKYSA for HER2-positive metastatic breast cancer (April 17, 2020).* U.S. Food and Drug Administration
3. **U.S. Food & Drug Administration.** *FDA announcement — accelerated approval of tucatinib + trastuzumab for RAS wild-type HER2-positive metastatic colorectal cancer (Jan 19, 2023).* U.S. Food and Drug Administration
4. **European Medicines Agency (EMA).** *Tukysa EPAR / Product Information* (EMA approval materials, Feb 2021). FDA Access Data

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Pivotal randomized trial(s) — HER2CLIMB and updates

5. Murthy RK, et al. *Tucatinib, Trastuzumab, and Capecitabine for HER2-Positive Metastatic Breast Cancer.* **N Engl J Med. 2020;382:597–609.** (HER2CLIMB — pivotal randomized, double-blind trial that showed improved PFS and OS, including intracranial benefit). New England Journal of Medicine+1
6. Lin NU, et al. *Updated / subgroup analyses and longer follow-up from HER2CLIMB (intracranial outcomes/OS updates).* **JAMA Oncol. 2023;** (HER2CLIMB analyses / brain-metastasis subgroups). PubMed

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Phase I / II and early clinical studies (selected)

7. Murthy R, et al. *Tucatinib with capecitabine and trastuzumab in advanced HER2-positive metastatic breast cancer with and without brain metastases: non-randomized, open-label Phase 1b.* **Lancet Oncol. 2018;19(7):880–888.** (established dose and intracranial activity). The Lancet+1
8. Borges VF, et al. *Tucatinib combined with ado-trastuzumab emtansine (T-DM1) — Phase 1b study.* **JAMA Oncol. 2018;** (MTD, preliminary activity). ClinicalTrials.gov: **NCT01983501**. JAMA Network+1

9. Metzger Filho O, et al. *Phase I dose-escalation trial of tucatinib + trastuzumab in patients with HER2-positive brain metastases* (Annals/abstracts / full report). PubMed+1

Colorectal cancer (MOUNTAINEER) — key trial & approval

10. Strickler JH, et al. *Tucatinib + trastuzumab in chemotherapy-refractory, HER2-positive metastatic colorectal cancer.* **Lancet Oncol. 2023;** (MOUNTAINEER results supporting activity). The Lancet

11. **ClinicalTrials.gov:** *MOUNTAINEER — NCT03043313* (tucatinib ± trastuzumab; open-label studies and data supporting accelerated approval). ClinicalTrials+1

12. FDA announcement/label update granting accelerated approval for colorectal-cancer indication (Jan 2023). U.S. Food and Drug Administration

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Pharmacokinetics / Safety / Toxicity studies

13. Topletz-Erickson AR, et al. *Effect of Tucatinib on Cardiac Repolarization in Healthy Subjects* (QT study) / other PK/safety publications — see studies compiled in FDA review and PK literature. PMC+1

14. Population PK analyses and dose-modification guidance published in clinical pharmacology journals (e.g., Zhang D. population PK analysis 2024). SpringerLink

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Preclinical / mechanism of action

15. Olson D, et al. *HER2-selective and reversible tyrosine kinase inhibitor (review/preclinical profile of tucatinib).* **(Review / preclinical papers; 2023).** (Details on HER2 selectivity and minimal EGFR inhibition). PMC

16. Articles / abstracts demonstrating tucatinib potentiation of HER2-directed ADCs (mechanistic preclinical work). AACR Journals

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Important reviews, guidelines & positioning papers

17. Sirhan Z, et al. *The efficacy of tucatinib-based therapeutic approaches: review (2022).* **Mil Med Res. 2022;** (systematic review of tucatinib evidence and combinations). SpringerLink

18. Conte P, et al. *Positioning of tucatinib in the clinical scenario — consensus paper (2024).* (practical guidance on where tucatinib fits in HER2+ mBC sequence). ScienceDirect

19. ESMO / ASCO guideline citations and ESMO scorecards summarizing tucatinib's place in care. esmo.org

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Selected additional clinical/trial resources (useful NCT IDs)

- **NCT02614794** — *HER2CLIMB* (tucatinib vs placebo + trastuzumab + capecitabine). ClinicalTrials
- **NCT01983501** — tucatinib + T-DM1 (Phase 1b). ClinicalTrials
- **NCT03043313** — *MOUNTAINEER* (tucatinib combinations in HER2+ mCRC). ClinicalTrials
- **NCT03758339** — absorption/metabolism/excretion study (healthy volunteers; PK). MedPath
- Ongoing/post-approval HER2CLIMB-04 and other trials (e.g., tucatinib + T-DXd combinations): see ClinicalTrials.gov and ASCO/ESMO abstracts. ResearchGate+1