PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Capecitabine Taro 500 mg
Film-coated tablets

Composition:
Each film-coated tablet contains: capecitabine 500 mg

Inactive ingredients and allergens: see section 2 under "Important information about some of the ingredients of the medicine" and section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine.
This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

- Keep the leaflet. You may need to read it again.
- This medicine was prescribed to treat your illness. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.
- If you have any side effects, refer to your doctor or pharmacist. This includes possible side effects that do not appear in this leaflet (see section 4 – "Side Effects").

1) WHAT IS THE MEDICINE INTENDED FOR?

The medicine, Capecitabine Taro 500 mg, belongs to a group of medicines called cytostatics, which stop the development of cancer cells. The medicine itself is not cytostatic, rather, after being absorbed in the body, it changes into an active anti-cancer medicine (more in the tumor tissue than in normal tissue).
Capecitabine Taro 500 mg is intended for the treatment of breast cancer after previous treatments, stomach cancer and colorectal cancer. In addition, Capecitabine Taro 500 mg is used to prevent recurrence of colon cancer, after complete surgical removal of the tumor.

The medicine Capecitabine Taro 500 mg can be taken alone or in combination with other medicines.

Therapeutic group: Pyrimidine analogs.

2) BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient (capecitabine) or to any of the additional ingredients contained in the medicine (see section 6 – "Further Information"). You should inform your doctor if you have a known allergy or sensitivity to this medicine.
- You have previously had severe reactions to fluoropyrimidine therapy (a group of anti-cancer medicines such as fluorouracil).
- You are pregnant or breastfeeding.
- You have very low blood levels of white blood cells or platelets (leucopenia, neutropenia or thrombocytopenia).
- You have severe liver or kidney problems.
- You know you have no activity of an enzyme called dihydropyrimidine dehydrogenase (DPD) (complete DPD deficiency).
- You are currently being treated or have been treated in the last four weeks with brivudine as part of herpes zoster (chickenpox or shingles) therapy.

Special warnings regarding use of the medicine
Before treatment with the medicine, tell the doctor if:

- You know you have a partial deficiency of activity of the dihydropyrimidine dehydrogenase (DPD) enzyme.
- Someone in your family has partial or complete deficiency of the dihydropyrimidine dehydrogenase (DPD) enzyme.
- You suffer from liver or kidney diseases.
- You have or have had heart problems (for example, an irregular heart rate or pain in the chest, jaw and back brought on by physical effort and due to problems with the blood flow to the heart).
- You have brain-related diseases (for example, cancer that has spread to the brain or peripheral nerve disease - neuropathy).
- You suffer from an imbalance in calcium levels (seen in blood tests).
- You have diabetes.
- You cannot hold down food or drink in your body because of severe nausea and vomiting.
- You have diarrhea.
- You are suffering from loss of fluids (dehydration).
- You have imbalances of ions in your blood (electrolyte imbalances, seen in blood tests).
- You have suffered in the past from eye problems; you may need extra monitoring of your eye condition.
- You have a severe skin reaction.

DPD deficiency:
DPD deficiency is a genetic condition, which normally is not associated with health issues, unless you are taking certain medicines. If you have DPD deficiency and you are taking this medicine, you are at increased risk of developing severe side effects (as listed in section 4 – "Side Effects"). It is recommended that you be tested for DPD deficiency before starting treatment. If you have no activity of the enzyme, you should not take this medicine. If you have reduced activity of the enzyme (partial deficiency), your doctor may prescribe you a lower dose. If the results of the test for DPD deficiency are negative, severe and life-threatening side effects may still occur.

Children and adolescents
This medicine is not intended for treatment of children and adolescents. Do not give the medicine to children and adolescents.

Drug interactions
If you are taking, have recently taken, or may take other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. It is very important to do so, since taking several medicines at the same time can increase or weaken the effect of the medicines.

Do not take brivudine (an anti-viral medicine to treat shingles or chickenpox) in parallel to capecitabine treatment (including during all break periods between treatments (rest periods), when you are not taking any capecitabine tablets).

If you have taken brivudine, wait at least 4 weeks after discontinuing brivudine treatment before starting to take capecitabine. See also "Do not use the medicine if" section.

In addition, be especially cautious if you are taking:

- Medicines to treat gout (allopurinol).
- Blood-thinning medicines (coumarin, warfarin).

- Medicines for convulsions or tremors (phenytoin).
- Interferon alpha.
- Radiotherapy and certain medicines to treat cancer (folinic acid, oxaliplatin, bevacizumab, cisplatin, irinotecan).
- Medicines to treat folic acid deficiency.

Use of the medicine with food
You should take the medicine no more than 30 minutes after a meal.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you are pregnant or are planning to become pregnant, consult the doctor or pharmacist before using the medicine.
You must not take the medicine if you are pregnant or think you might be pregnant.
You must not breastfeed if you are taking Capecitabine Taro 500 mg and for 2 weeks after the last dose.
If you are a woman who can become pregnant you should use effective contraception during treatment with Capecitabine Taro 500 mg and for 6 months after taking the last dose.
If you are a male patient and your female partner can become pregnant, you should use effective contraception during treatment with Capecitabine Taro 500 mg and for 3 months after taking the last dose.

Driving and operating machinery
Use of this medicine may cause dizziness, nausea or fatigue and therefore, the medicine may impair your ability to drive a vehicle or operate machinery.

Important information about some of the ingredients of the medicine
The medicine Capecitabine Taro 500 mg contains lactose. If you have been told by the doctor that you have an intolerance to certain sugars, contact your doctor before taking the medicine.
This medicine contains less than 23 mg sodium per tablet and is therefore considered sodium free.

3) HOW SHOULD YOU USE THE MEDICINE?
Always use the preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen.
Only a doctor specializing in anti-cancer medicines (an oncologist) can prescribe the medicine Capecitabine Taro 500 mg.

Recommended dosage
The dosage and treatment regimen will be determined by the doctor only. Your doctor will prescribe a dose and treatment regimen that is suitable for **you**.
Determination of the dosage is based on an index called body surface area. Your body surface area is calculated based on your weight and height. The recommended dosage for adults is generally 1,250 mg/m^2 of body surface area, twice daily (morning and evening).

The following is an example to illustrate:
A person who weighs 80 kg and whose is 1.80 m tall, has a body surface area of 2.0 m^2 and should take 5 tablets of 500 mg, twice daily.

Your doctor will tell you which dosage you should take, when you should take the tablets and for how long.

Do not exceed the recommended dose.

Instructions for use

- Take the tablets, **in the morning and evening**, as prescribed for you by the doctor.
- Take the tablets **no more than 30 minutes after the end of a meal** (breakfast and dinner) **and swallow them whole, with water**.
- Do not crush, split or chew the tablets. Exposure of either patient or caregiver to a crushed or split Capecitabine Taro 500 mg tablet may cause side effects. If you cannot swallow Capecitabine Taro 500 mg tablets whole, tell your doctor.
- It is very important that you take all of your medicines as recommended by the attending doctor.

Duration of treatment

- Generally, Capecitabine Taro 500 mg tablets are taken for 14 days, followed by a 7-day break (during which the tablets are not taken). These 21 days are called one treatment cycle.
- When combining Capecitabine Taro 500 mg with other medicines, the recommended dosage for adults can be lower than 1,250 mg/m^2 surface body area, and you may have to take the tablets for different durations of time (for example, every day, without a break period).

If you accidentally took a higher dosage, you must contact your doctor as soon as possible before taking the next dose.
If you took a much higher dosage of Capecitabine Taro 500 mg than you should have, you may have the following side effects: nausea or vomiting, diarrhea, inflammation or ulcers in the digestive tract or mouth, pain or bleeding from the intestine or stomach or bone marrow suppression (reduction in different types of blood cells). Refer to your doctor immediately if you experience one or more of these symptoms.
If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room and bring the medicine package with you.

If you forgot to take this medicine at the designated time, do not take the forgotten dose at all. Do not take a double dose to compensate for the forgotten dose. Instead, take the next dose at the usual time and consult your doctor.

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you stop taking the medicine
No side effects are caused by discontinuation of capecitabine treatment. If you are taking a coumarin anticoagulant (that contains, for example, phenprocoumon), the anticoagulant dosage may need to be adjusted by the doctor when Capecitabine Taro 500 mg treatment is discontinued.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4) SIDE EFFECTS

As with any medicine, use of Capecitabine Taro 500 mg may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Stop taking this medicine immediately and refer to a doctor if any of the following symptoms occur:

- **Diarrhea:** if there is an increase of 4 or more bowel movements per day compared to usual or if you have diarrhea during the night.
- **Vomiting:** if you vomit more than once in a 24-hour period.
- **Nausea:** if you have loss of appetite and considerable reduction in the amount of food consumed per day.
- **Inflammation of the oral mucosa (stomatitis):** if you have pain, redness, swelling or tenderness in the mouth and/or throat.
- **Skin reaction on the hands and feet:** if you have pain, swelling, redness or tingling in the hands and/or feet.
- **Fever:** if you have a fever of 38°C or above.
- **Infection:** if you have signs of an infection caused by a bacteria or virus, or other organisms.
- **Chest pain:** if you have pain in the center of the chest, especially if they occur during activity.
- **Stevens-Johnson syndrom**e:
  If you have a painful, red or purple rash that spreads, and blisters and/or other lesions that begin to appear in the mucous membranes (e.g., mouth and lips), especially if you have had sensitivity to light before, respiratory tract infections (e.g., bronchitis) and/or fever.
- **Angioedema:** Seek medical attention straight away if you notice any of the following symptoms – you may need urgent medical treatment: swelling of the face, lips, tongue or throat which makes it difficult to swallow or breathe, itching and rashes.

If these side effects are identified at an early stage, there will usually be an improvement in symptoms within 2-3 days of discontinuing treatment. If the side effects still continue, however, refer to your doctor immediately. Your doctor may instruct you to restart treatment at a lower dosage.

If severe inflammation of the oral mucosa (stomatitis - sores in your mouth and/or throat), mucosal inflammation, diarrhea, decrease in the number of neutrophils in the blood (neutropenia - increased risk for infections) or neurotoxicity occurs during the first cycle of treatment, it may be related to a DPD deficiency (see section 2 "Before using the medicine").

Skin reaction on the hands and feet may cause loss of fingerprints, which may affect your identification by fingerprint scan.

When Capecitabine Taro 500 mg is a monotherapy, very common side effects, which occur in more than one user in ten, are:

- Abdominal pain
- Rash, dry or itchy skin
- Tiredness
- Loss of appetite (anorexia)

These side effects can worsen; **therefore, it is important that you always contact your doctor immediately** upon onset of a side effect. Your doctor may instruct you to reduce the dosage and/or temporarily discontinue treatment with the medicine, to reduce the likelihood that the side effect will continue or worsen.

Additional side effects:
Common side effects – affect up to 1 in 10 users:

- Decreased number of white or red blood cells (seen in blood tests).
- Dehydration, weight loss.
- Sleeplessness (insomnia), depression.
- Headache, sleepiness, dizziness, abnormal sensation in the skin (numbness or tingling sensation), taste changes.
- Eye irritation, increased tearing, eye redness (conjunctivitis).
- Inflammation of the veins (thrombophlebitis).
- Shortness of breath, nosebleeds, cough, runny nose.
- Cold sores or other herpes infections.
- Infections in the lungs or respiratory system (e.g., pneumonia or bronchitis).
- Bleeding from the digestive tract, constipation, pain in the upper abdomen, indigestion, flatulence, dry mouth.
- Skin rash, hair loss (alopecia), skin redness, dry skin, itchy skin, skin discoloration, skin loss, skin inflammation, nail problems.
- Pain in the joints or limbs, chest pain, back pain.
- Fever, swelling in the limbs, feeling ill.
- Problems with liver function (seen in blood tests) and increased blood level of bilirubin (secreted by the liver).

Uncommon side effects – affect up to 1 in 100 users:

- Blood infection, urinary tract infection, infection of the skin, infections in the nose and throat, fungal infections (including infections in the mouth), influenza, inflammation in the stomach and intestine (gastroenteritis), tooth abscess.
- Lumps under the skin (fatty tissue tumors – lipoma).
- Decrease in the number of blood cells including platelets, thinning of the blood (seen in blood tests).
- Allergy.
- Diabetes, decrease in blood potassium levels, malnutrition, increased blood triglyceride levels.
- Feeling confused, panic attacks, depressed mood, decreased libido.
- Difficulty speaking, impaired memory, impaired coordination and movement, impaired balance, fainting, nerve damage (neuropathy) and sensation disturbances.
- Blurred or double vision.
- Vertigo (dizziness), ear pain.
- Irregular heart rate and heartbeat (arrhythmia), chest pain and heart attack.
- Deep vein thrombosis, high or low blood pressure, hot flashes, cold sensation in the limbs, purple spots on the skin.
- Blood clots in the veins of the lung (pulmonary embolism), collapsed lungs, bloody cough, asthma, shortness of breath on exertion.
- Bowel obstruction, accumulation of fluid in the abdominal cavity, inflammation of the small or large intestine, inflammation of the stomach, inflammation of the esophagus, pain in the lower abdomen, abdominal discomfort, heartburn (reflux of food from the stomach), blood in the stool.
- Jaundice (yellowing of the skin and eyes).
- Skin ulcers and blisters, skin reaction to sunlight, redness on palms, swelling or pain of the face.
- Joint swelling or stiffness, bone pain, muscle weakness or stiffness.
- Fluid accumulation in the kidneys, more frequent urination during the night, urinary incontinence, blood in the urine, increase in blood creatinine levels (sign of a kidney problem).

- Unusual vaginal bleeding.
- Swelling (edema), chills and tremor.

Some of these side effects are more common when Capecitabine Taro 500 mg is used in combination with other medicines for the treatment of cancer.

Additional side effects that have been observed upon combined use are:
Common side effects – affect up to 1 in 10 users:
- Decrease in blood sodium, magnesium or calcium levels, increase in blood sugar level.
- Nerve pain.
- Buzzing or ringing in the ears (tinnitus), loss of hearing.
- Vein inflammation.
- Hiccups, voice changes.
- Pain or altered/abnormal sensation in the mouth, jaw pain.
- Sweating, night sweats.
- Muscle spasms.
- Difficulty in urination, blood or protein in the urine.
- Signs of injury or a reaction at the injection site (caused by medicines administered by injection at the same time).

Rare side effects – affect up to 1 in 1,000 users:
- Narrowing or blockage of the tear duct.
- Liver failure.
- Inflammation leading to dysfunction or obstruction in bile secretion.
- Certain changes in the ECG test (prolongation of the QT interval).
- Certain types of arrhythmia (including ventricular fibrillation, torsade de pointes, slow heart rate).
- Inflammation of the eye causing pain in the eye and possible vision problems.
- Inflammation of the skin causing red scaly patches due to an immune system disease.
- Swelling mainly of the face, lips, tongue or throat, itching and rash (angioedema).

Very rare side effects – affect up to 1 in 10,000 users:
- Severe skin reaction, such as skin rash, ulcers and blisters that can appear in the mouth, nose, genitals, hands, feet and eyes (red and swollen eyes).

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5) HOW SHOULD THE MEDICINE BE STORED?
- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Storage conditions: Store below 25°C.

- Do not discard the medicine into the wastewater or as household waste. Consult the pharmacist on how to dispose of this medicine (medicines no longer in use). This will help protect the environment.

6) FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Anhydrous lactose, hypromellose 2910, microcrystalline cellulose, croscarmellose sodium, talc, magnesium stearate, film coating (contains: HPMC 2910, lactose monohydrate, titanium dioxide, PEG 4000, iron oxide red, iron oxide yellow).

What the medicine looks like and the contents of the package:
An elliptic, biconvex, film-coated, peach-colored tablet, imprinted with “500” on one side and plain on the other side.
A package of Capecitabine Taro 500 mg contains 120 film-coated tablets.

License holder's name and address: Taro International Ltd., 14 Hakitor Street, Haifa Bay 2624761.

Manufacturer's name and address: SUN Pharmaceutical Industries Ltd., Sun House; Plot No. 201 B/L, Western Express Highway, Goregaon (E), Mumbai 400063, Maharashtra, India.

The leaflet was revised in April 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 157.76.34725