

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

The medicine is dispensed with a doctor’s prescription only

# Capecitabine Inovamed 500 mg

## Film-coated tablets

**Composition:**

Each film-coated tablet contains:

Capecitabine 500 mg

For the list of inactive and allergenic ingredients, see section 2 – “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 has been prescribed for the treatment of your ailment. 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 belongs to a group of medicines called “cytostatic medicines”, which stop the development of cancerous cells. The medicine itself is not a cytostatic medicine, rather, only after being absorbed in the body, it changes into an active anti-cancer medicine (more in the tumor tissue than in normal tissue).

The medicine is used for the treatment of breast cancer after previous treatments, gastric cancer and colon and rectal cancer. In addition, the medicine is used to prevent recurrence of colon cancer, after complete removal of the tumor by surgery. The medicine 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”). Inform your doctor if you know you have an 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 being treated now 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 Capecitabine Inovamed, tell the doctor if:**

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

**DPD deficiency:**

DPD deficiency is a genetic condition that is not usually associated with health problems unless you receive certain medicines. If you have DPD deficiency and take Capecitabine Inovamed 500 mg, you are at an increased risk of severe side effects (listed under section 4 “Side effects”). It is recommended to test you for DPD deficiency before start of treatment. If you have no activity of the enzyme you should not take Capecitabine Inovamed. If you have a reduced enzyme activity (partial deficiency) your doctor might prescribe a reduced dose. If you have negative test results for DPD deficiency, 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 Capecitabine Inovamed 500 mg 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 concomitantly can increase or weaken the effect of the medicines.**

**Do not take brivudine (an anti-viral medicine to treat shingles or chickenpox) in conjunction with Capecitabine treatment (including during all break periods between treatments (rest periods), when you aren’t taking any Capecitabine tablets). If you took brivudine, wait at least 4 weeks after discontinuing brivudine treatment before starting to take Capecitabine. Also see “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 and drink**

Take the medicine no more than 30 minutes after a meal.

**Pregnancy and breastfeeding**

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 should not take Capecitabine Inovamed if you are pregnant or think you are pregnant.

You should not breastfeed during treatment with Capecitabine Inovamed 500 mg and for two weeks after taking the last dose.

If you are a woman of child-bearing potential, use effective contraceptives during treatment with Capecitabine Inovamed 500 mg and for 6 months after taking the last dose.

If you are a male patient and your female partner is of child-bearing potential, use effective contraceptives during treatment with Capecitabine Inovamed 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, Capecitabine Inovamed 500 mg may impair your ability to drive a car or operate machinery.

**Important information about some of the ingredients of the medicine**

The medicine Capecitabine Inovamed 500 mg contains lactose (anhydrous lactose). If you have been told by the doctor that you have an intolerance to certain sugars, contact the attending doctor before taking the medicine.

This medicine contains less than 23 mg of 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 preparation dosage and treatment regimen.

Only a doctor specializing in treatment with anti-cancer medicines (an oncologist) can prescribe the medicine Capecitabine Inovamed 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 right for **you**.

Determination of the dosage of the medicine is based on an index called body surface area. Your body surface area is calculated from your weight and height. The recommended dosage for adults is generally 1,250 mg of the active ingredient capecitabine per square meter of body surface area, twice daily (morning and evening).

**Two examples are provided here for clarification:**

- A person weighing 57 kg, whose height is 1.62 meters, and who has a body surface area of 1.6 m², will take 4 tablets of Capecitabine Inovamed 500 mg, twice daily.
- A person weighing 80 kg, whose height is 1.80 meters, and who has a body surface area of 2.0 m², will take 5 tablets of Capecitabine Inovamed 500 mg, twice daily.

**Instructions for use**

- Take the tablets, **in the morning and evening**, as prescribed for you by the doctor.
- Take the tablets **within 30 minutes after the end of a meal** (breakfast and dinner) **and swallow them whole, with water**.
- It is very important that you take all your medicines as recommended by the attending doctor.
- Do not crush, halve or chew the tablets. Exposure of the caregiver or patient to a crushed or halved Capecitabine Inovamed 500 mg tablet may cause side effects. If you cannot swallow whole Capecitabine Inovamed 500 mg tablets, tell the attending doctor.

**Duration of treatment**

Generally, the tablets are taken for 14 days, followed by a 7-day break (during which the medicine is not taken). This period of 21 days is defined as one treatment cycle.

When combining Capecitabine Inovamed 500 mg with other medicines, the recommended dosage for adults can be lower than 1,250 mg/m² surface body area, and you may have to take the tablets for different durations of time (e.g., every day, without a break).

**The 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.**

Your doctor can recommend a combination of Capecitabine Inovamed 500 mg with other strengths of Capecitabine tablets.

**If you accidentally took a higher dosage**, contact your doctor as soon as possible before taking the next dose.

If you took a much higher dosage of Capecitabine than you should have, you may have the following side effects: nausea or vomiting, diarrhea, inflammation or ulcers in the digestive system or mouth, pain or bleeding from the intestine or stomach or bone marrow depression (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 package of the medicine with you.

**If you forgot to take the medicine** at the designated time, do not take the missed 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**

There are no side effects caused by stopping treatment with capecitabine. In case you are using coumarin anticoagulants (containing e.g., phenprocoumon), stopping Capecitabine Inovamed

500 mg might require that your doctor adjusts your anticoagulant dose.

**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 Inovamed 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 Capecitabine Inovamed 500 mg immediately and refer to a doctor if any of the following symptoms occur:

- Diarrhea:** if the number of your bowel movements per day increases by 4 or more compared to usual or if you have diarrhea during the night.
- Vomiting:** if you vomit more than once in 24 hours.
- Nausea:** if you have loss of appetite, and considerable reduction in the amount of food you consume 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 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 pains in the center of the chest, especially if they occur during exertion.
- Stevens-Johnson syndrome:** if you have a red or purplish, painful, widespread rash, and blisters and/or other lesions that begin to appear in the mucosal tissues (e.g., mouth and lips), especially if you have had prior light sensitivity, respiratory tract infections (e.g., bronchitis) and/or fever.
- Angioedema:** seek medical attention immediately if you notice any of the following symptoms – you may need urgent medical treatment: swelling mainly of the face, lips, tongue or throat which makes it difficult to swallow or breathe, itching and rash. These could be signs of angioedema.

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 continue, however, refer to the attending doctor immediately. The doctor may instruct you to resume treatment at a lower dosage.

If severe stomatitis (sores in your mouth and/or throat), mucosal inflammation, diarrhoea, neutropenia (increased risk for infections), or neurotoxicity occurs during the first cycle of treatment, a DPD deficiency may be involved (see section 2 – “Before using the medicine”).

Skin reaction on the hands and feet may cause loss of fingerprint, which may affect your identification via a biometric reader.

In addition, when Capecitabine Inovamed 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 may worsen; therefore, it is important to **always refer to the attending doctor immediately** upon onset of a side effect. The attending doctor may instruct you to decrease the dosage and/or temporarily discontinue treatment with Capecitabine Inovamed, to reduce the likelihood that the side effect continues or worsens.

**Additional side effects:**

- Common side effects – effects that occur in up to one user in 10:**
  - Decreased number of white or red blood cells (seen in blood tests)
  - Dehydration, weight loss
  - 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 in the digestive system, constipation, pain in the upper abdomen, indigestion, excess wind, dry mouth
  - Skin rash, hair loss (alopecia), redness of the skin, dry skin, itchy skin, skin discoloration, skin loss, skin inflammation, nail problems
  - Pains in the joints or limbs, chest pains, back pains
  - Fever, swelling in the limbs, feeling ill
  - Problems with liver function (seen in blood tests) and an increased level of bilirubin (secreted by the liver) in the blood

**Uncommon side effects – effects that occur in up to one user in 10:**

- Blood infection, urinary tract infection, infection in the skin, infection in the nose and throat, fungal infections (including infections in the mouth), influenza, stomach and intestinal inflammation (gastroenteritis), dental abscess
- Lumps under the skin (growths of fat tissue – 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 attack, depressed mood, decreased libido
- Speaking difficulties, 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 rhythm and palpitations (arrhythmia), chest pains and heart attack
- Blood clots in deep veins, high or low blood pressure, hot flushes, cold sensation in the limbs, purple spots on the skin
- Blood clots in the veins of the lungs (pulmonary embolism), collapsed lungs, bloody cough, asthma, shortness of breath upon exertion

- Bowel obstruction, accumulation of fluid in the abdominal cavity, inflammation of the small or large intestine, inflammation in the stomach, inflammation in the esophagus, lower abdominal pain, abdominal discomfort, heartburn (regurgitation of food from the stomach), blood in the stool
- Jaundice (yellowing of the skin and eyes)
- Skin ulcers and blisters, skin reaction to sunlight, red palms, swelling or pain of the face
- Joint swelling or stiffness, bone pains, muscle weakness or stiffness
- Fluid accumulation in the kidneys, more frequent urination during the night, urinary incontinence, blood in the urine, increase in blood level of creatinine (sign of a kidney problem)
- Unusual vaginal bleeding
- Swelling (edema), chills and tremor

**Rare side effects – effects that occur in up to one user in 1,000:**

- Narrowing or blockage of the tear duct
- Liver failure
- Inflammation that causes dysfunction or obstruction in bile secretion
- Certain changes in ECG testing (prolongation of the QT interval)
- Certain types of arrhythmias (including ventricular fibrillation, torsade de pointes, slow heart rate)
- Inflammation in the eye, causing eye pain and possible vision problems
- Inflammation of the skin due to an immune system disease, causing red scaly/peeling spots
- Swelling mainly of the face, lip, tongue or throat, itching and rash (angioedema)

**Very rare side effects – effects that occur in up to one user in 10,000:**

- 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).

Some of these side effects are more common when Capecitabine Inovamed 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 – effects that occur in up to one user in 10:**

- Decrease in blood sodium, magnesium or calcium levels, increase in blood sugar level
- Nerve pain
- Ringing or buzzing in the ears (tinnitus), loss of hearing
- Vein inflammation
- Hiccups, voice changes
- Pain or altered/abnormal sensation in the mouth, pain in the jaw
- 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)

**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.**

**Reporting side effects**

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
- Store in the original package to protect from moisture
- Do not discard medicines in the waste water or waste bin. Ask the pharmacist how to dispose of medicines that are not in use. These measures will help protect the environment.

### 6. FURTHER INFORMATION

**In addition to the active ingredient, the medicine also contains:** Cellulose Microcrystalline, Hypromellose, Croscarmellose Sodium, Lactose Anhydrous, Magnesium Stearate, Talc, Titanium Dioxide (E171), Ferric Oxide Red (E172), Ferric Oxide Yellow (E172).

**What the medicine looks like and the contents of the package:** The medicine looks like a peach-colored, oblong-shaped, biconvex, film-coated tablet, debossed with “500” on one side and plain (no embossment and no writing) on the other side.

The tablets are packaged in aluminum or aluminum-plastic blisters, packaged in a carton box.

**Pack size:** The medicine is supplied in a package as follows:

- Carton packages containing tray(s)/blister(s) with 30, 60 and 120 tablets. The number of trays in each carton package may differ depending on the size of the package. The number of tablets in each pack is indicated on the carton package.
- Not all package sizes may be marketed.

**License Holder and its Address:** Inovamed Ltd., Private Co. 513988089, P.O.B. 62, Even Yehuda 40500.

**Name of Manufacturer and its Address:** Intas Pharmaceuticals, Ahmedabad, Gujarat, India.

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**Registration number of the medicine in the National Drug Registry of the Ministry of Health:** Capecitabine Inovamed 500 mg: 153.90.34426