Package leaflet: Information for the user

Capecitabine 150 mg film-coated tablets
Capecitabine 500 mg film-coated tablets

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

In this leaflet:

1. What Capecitabine is and what it is used for

Capecitabine belongs to the group of medicines called "cytostatic medicine", which stop the growth of cancer cells. Capecitabine film-coated tablets contains 150 mg or 500 mg capecitabine, which itself is not a cytostatic medicine. Only after being absorbed by the body is it changed into an active anti-cancer agent (more in tumour tissue than in normal tissue).

Capecitabine is used in the treatment of colon, rectal, gastric, or breast cancers.

Furthermore, capecitabine is used to prevent new occurrence of colon cancer after complete removal of the tumour by surgery.

Capecitabine may be used either alone or in combination with other agents.

2. What you need to know before you take Capecitabine

Do not use Capecitabine:

- if you are allergic to capecitabine or any of the other ingredients of this medicine (listed in section 6). You must inform your doctor if you know that you have an allergy or over-reaction to this medicine,
- if you previously have had severe reactions to fluoropyrimidine therapy (a group of anticancer medicines such as fluorouracil),
- if you are pregnant or nursing,
- if you have severely low levels of white cells or platelets in the blood (leukopenia, neutropenia or thrombocytopenia),
- if you have severe liver or kidney problems,
- if you have a known deficiency for the enzyme dihydropyrimidine dehydrogenase (DPD) involved in the metabolism of uracil and thymine, or
- if you are being treated now or have been treated in the last 4 weeks with brivudine, sorivudine or similar classes of substance as part of *herpes zoster* (chickenpox or shingles) therapy.

Warnings and precautions

Talk to your doctor or pharmacist before taking capecitabine.

- if you have liver or kidney diseases
- if you have or had heart problems (for example an irregular heartbeat or pains to the chest jaw and back brought on by physical effort and due to problems with the blood flow to the heart)
- if you have brain diseases (for example. cancer that has spread to the brain, or nerve damage (neuropathy)
- if you have calcium imbalances (seen in blood tests)
- if you have diabetes
- if you cannot keep food or water in your body because of severe nausea and vomiting
- if you have diarrhoea
- if you are or become dehydrated
- if you have imbalances of ions in your blood (electrolyte imbalances, seen in tests)
- if you have a history of eye problems as you may need extra monitoring of your eyes
- if you have a severe skin reaction.

DPD deficiency: DPD deficiency is a rare condition present at birth that is not usually associated with health problems unless you receive certain medicines. If you have an unrecognised DPD deficiency and take capecitabine, you may experience severe forms of the side effects listed under section 4 Possible side effects. Contact your doctor immediately if you are concerned about any of the side effects or if you notice any additional side effects not listed in the leaflet (see section 4 Possible side effects).

Children and adolescents

Capecitabine is not indicated in children and adolescents. Do not give capecitabine to children and adolescents.

Other medicines and Capecitabine

Before starting treatment, tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is extremely important, as taking more than one medicine at the same time can strengthen or weaken the effect of the medicines. You need to be particularly careful if you are taking any of the following:

- gout medicines (allopurinol),
- blood-thinning medicines (coumarin, warfarin),
- certain anti-viral medicines (sorivudine and brivudine),
- medicines for seizures or tremors (phenytoin),
- interferon alpha,
- radiotherapy and certain medicines used to treat cancer (folinic acid, oxaliplatin, bevacizumab, cisplatin, irinotecan),
- medicines used to treat folic acid deficiency.

Capecitabine with food and drink

You should take capecitabine no later than 30 minutes after meals .

Pregnancy and breast-feeding

Before starting treatment, you must tell your doctor if you are pregnant, if you think you are pregnant or if you intend to become pregnant. You must not take capecitabine if you are pregnant or think you might be. You must not breast-feed if you are taking capecitabine. Ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Capecitabine may make you feel dizzy, nauseous or tired. It is therefore possible that capecitabine could affect your ability to drive a car or operate machinery.

Capecitabine contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Capecitabine

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

Capecitabine should only be prescribed by a doctor experienced in the use of anticancer medicines.

Capecitabine tablets should be **swallowed whole with water and within 30 minutes of a meal.**

Your doctor will prescribe a dose and treatment regimen that is right for *you*. The dose of capecitabine is based on your body surface area. This is calculated from your height and weight. The usual dose for adults is 1250 mg/m^2 of body surface area taken two times daily (morning and evening). Two examples are provided here: A person whose body weight is 64 kg and height is 1.64 m has a body surface area of 1.7 m^2 and should take 4 tablets of 500 mg and 1 tablet of 150 mg two times daily. A person whose body weight is 80 kg and height is 1.80 m has a body surface area of 2.00 m^2 and should take 5 tablets of 500 mg two times daily.

Capecitabine tablets are usually taken for 14 days followed by a 7 day rest period (when no tablets are taken). This 21 day period is one treatment cycle.

In combination with other medicine the usual dose for adults may be less than 1250 mg/ m^2 of body surface area, and you may need to take the tablets over a different time period (e.g. every day, with no rest period).

Your doctor will tell you what dose you need to take, when to take it and for how long you need to take it.

Your doctor may want you to take a combination of *150 mg* and *500 mg* tablets for each dose.

- Take the tablets **morning and evening** as prescribed by your doctor.
- Take the tablets within **30 minutes after the end of a meal** (breakfast and dinner).
- It is important that you take all your medicine as prescribed by your doctor.

If you take more Capecitabine than you should

If you take more capecitabine than you should, contact your doctor as soon as possible before taking the next dose.

You might get the following side effects if you take a lot more capecitabine than you should: feeling or being sick, diarrhoea, inflammation or ulceration of the gut or mouth, pain or bleeding from the intestine or stomach, or bone marrow depression (reduction in certain kinds of blood cells). Tell your doctor immediately if you experience any of these symptoms.

If you forget to take Capecitabine

Do not take the missed dose at all and do not double the next one. Instead, continue your regular dosing schedule and check with your doctor.

If you stop taking Capecitabine

There are no side effects caused by stopping treatment with capecitabine. In case you are using coumarin anticoagulants (containing e.g. phenprocoumon), stopping capecitabine might require that your doctor adjusts your anticoagulant dose.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

STOP taking capecitabine immediately and contact your doctor if any of these symptoms occur:

- ***Diarrhoea***: if you have an increase of 4 or more bowel movements compared to your normal bowel movements each day or any diarrhoea at night.
- ***Vomiting***: if you vomit more than once in a 24-hour time period.
- ***Nausea:*** if you lose your appetite, and the amount of food you eat each day is much less than usual.
- ***Stomatitis***: if you have pain, redness, swelling or sores in your mouth and/or throat.
- ***Hand-and-foot skin-reaction:*** if you have pain, swelling, redness or tingling of hands and/or feet.
- ***Fever:*** if you have a temperature of 38°C or greater.
- ***Infection:*** if you experience signs of infection caused by bacteria or virus, or other organisms.
- ***Chest pain:*** if you experience pain localised to the centre of the chest, especially if it occurs during exercise.
- ***Steven-Johnson syndrome:*** if you experience painful red or purplish rash that spreads and blisters and/or other lesions begin to appear in the mucous membrane (e.g. mouth and lips), in particular if you had before light sensitivity, infections of the respiratory system (e.g. bronchitis) and/or fever.

If caught early, these side effects usually improve within 2 to 3 days after treatment discontinuation. If these side effects continue, however, contact your doctor immediately. Your doctor may instruct you to restart treatment at a lower dose.

In addition to the above, when capecitabine is used alone, very common side effects, which may affect more than 1 person in 10 are:

- abdominal pain
- rash, dry or itchy skin
- tiredness
- loss of appetite (anorexia)

These side effects can become severe; therefore, it is important that you **always contact your doctor immediately** when you start to experience a side effect. Your doctor may instruct you to decrease the dose and/or temporarily discontinue treatment with capecitabine. This will help reduce the likelihood that the side effect continues or becomes severe.

Other side effects are:

Common side effects (may affect up to 1 in 10 people) include:

- decreases in the number of white blood cells or red blood cells (seen in tests),
- dehydration, weight loss,
- sleeplessness (insomnia), depression,
- headache, sleepiness, dizziness, abnormal sensation in the skin (numbness or tingling sensation), taste changes,
- eye irritation, increased tears, eye redness (conjunctivitis),
- inflammation of the veins (thrombophlebitis),
- shortness of breath, nose bleeds, cough, runny nose,
- cold sores or other herpes infections,
- infections of the lungs or respiratory system (e.g. pneumonia or bronchitis),
- bleeding from the gut, constipation, pain in upper abdomen, indigestion, excess wind, dry mouth,
- skin rash, hair loss (alopecia), skin reddening, dry skin, itching (pruritus), skin discolouration, skin loss, skin inflammation, nail disorder,
- pain in the joints, or in the limbs (extremities), chest or back,
- fever, swelling in the limbs, feeling ill,
- problems with liver function (seen in blood tests) and increased blood bilirubin (excreted by the liver),

Uncommon side effects (may affect up to 1 in 100 people) include:

- blood infection, urinary tract infection, infection of the skin, infections in the nose and throat, fungal infections (including those of the mouth), influenza, gastroenteritis, tooth abscess,
- lumps under the skin (lipoma),
- decreases in blood cells including platelets, thinning of blood (seen in tests)
- allergy
- diabetes, decrease in blood potassium, malnutrition, increased blood triglycerides,
- confusional state, panic attacks, depressed mood, decreased libido,
- difficulty speaking, impaired memory, loss of movement coordination, balance disorder, fainting, nerve damage (neuropathy) and problems with sensation
- blurred or double vision,
- vertigo, ear pain.
- irregular heartbeat and palpitations (arrhythmias), chest pain and heart attack (infarction),
- blood clots in the deep veins, high or low blood pressure, hot flushes, cold limbs (extremities), purple spots on the skin
- blood clots in the veins in the lung (pulmonary embolism), collapsed lung, coughing up blood, asthma, shortness of breath on exertion,
- bowel obstruction, collection of fluid in the abdomen, inflammation of the small or large intestine, the stomach or the oesophagus, pain in the lower abdomen, abdominal discomfort, heartburn (reflux of food from the stomach), blood in the stool,
- jaundice (yellowing of skin and eyes)
- skin ulcer and blister, reaction of the skin with sunlight, reddening of palms, swelling or pain of the face
- joint swelling or stiffness, bone pain, muscle weakness or stiffness,
- fluid collection in the kidneys, increased frequency of urination during the night, incontinence, blood in the urine, increase in blood creatinine (sign of kidney dysfunction)
- unusual bleeding from the vagina
- swelling (oedema), chills and rigors

Some of these side effects are more common when capecitabine is used with other medicines for the treatment of cancer. Other side-effects seen in this setting are the following:

Common side effects (may affect up to 1 in 10 people) include:

- decrease in blood sodium, magnesium or calcium, increase in blood sugar,
- nerve pain,
- ringing or buzzing in the ears (tinnitus), loss of hearing,
- vein inflammation,
- hiccups, change in voice,
- pain or altered/abnormal sensation in the mouth, pain in the jaw,
- sweating, night sweats,
- muscle spasm,
- difficulty in urination, blood or protein in the urine,
- bruising or reaction at the injection site (caused by medicines given by injection at the same time)

Rare side effects (may affect up to 1 in 1,000 people) include:

- narrowing or blockage of tear duct (lacrimal duct stenosis),
- liver failure,
- inflammation leading to dysfunction or obstruction in bile secretion (cholestatic hepatitis),
- specific changes in the electrocardiogram (QT prolongation),
- certain types of arrhythmia (including ventricular fibrillation, torsade de pointes, and bradycardia).
- eye inflammation causing eye pain and possibly eyesight problems
- inflammation of the skin causing red scaly patches due to an immune system illness

Very rare side effects (may affect up to 1 in 10,000 people) include:

- severe skin reaction such as skin rash, ulceration and blistering which may involve ulcers of the mouth, nose, genitalia, hands, feet and eyes (red and swollen eyes).

Reporting of side effects

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

For UK - You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

For Ireland - Via;
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Capecitabine

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 outer pack and labels after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not use this medicine if you notice any visible signs of deterioration.

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 protect the environment.

6. Contents of the pack and other information

What Capecitabine contains

- The active substance is capecitabine.

  Each film-coated tablet contains 150 mg capecitabine.

  Each film-coated tablet contains 500 mg capecitabine.
- The other ingredients are:
  - Tablet core: Lactose monohydrate , Microcrystalline cellulose (E460), Hypromellose (E464), Crosscarmellose sodium, Magnesium stearate (E572)
  - Tablet coating: Hypromellose (E464), Titanium dioxide (E171), Macrogol, Iron oxide red (E172)

What Capecitabine looks like and contents of the pack

Capecitabine 150 mg film-coated tablets

Pink coloured, capsule shaped, biconvex, film coated tablets, debossed with "150" on one side and plain on other side.

The pack contains 60 film-coated tablets (6 blisters of 10 tablets).

Capecitabine 500 mg film-coated tablets

Pink coloured, capsule shaped, biconvex, film coated tablets, debossed with "500" on one side and plain on other side.

The pack contains 120 film-coated tablets (12 blisters of 10 tablets).

Marketing Authorisation Holder

For UK

Fresenius Kabi Oncology Plc.
Lion Court, Farnham Road, Bordon
Hampshire, GU35 0NF
United Kingdom

For IRL

Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1,
61352 Bad Homburg v.d.Höhe
Germany

Manufacturer

Fresenius Kabi Oncology Plc.
Lion Court, Farnham Road, Bordon
Hampshire, GU35 0NF
United Kingdom

Fresenius Kabi Deutschland GmbH
Pfingstweide 53
61169 Friedberg
Germany

Pharmadox Healthcare Ltd.

KW20A Kordin Industrial Park Paola PLA3000
MALTA.

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria	Capecitabin Fresenius Kabi 150 mg Filmtabletten Capecitabin Fresenius Kabi 500
Belgium	Capecitabine Fresenius Kabi 150 mg filmomhulde tabletten Capecitabine Fresenius Kabi 500 mg
Cyprus	Capecitabine Fresenius Kabi 150 mg επικαλυμένα με λεπτό υμένιο δισκία Capecitabine Fresenius Kabi 500 mg επικαλυμένα με λεπτό υμένιο δισκία
Czech Republic	Capecitabine Fresenius Kabi 150 mg potahované tablety Capecitabine Fresenius Kabi 500 mg
Denmark	Capecitabin Fresenius Kabi
Estonia	Capecitabine Fresenius Kabi 150 mg Capecitabine Fresenius Kabi
Greece	Capecitabine Fresenius Kabi 150 mg επικαλυμμένα με λεπτό υμένιο δισκία Capecitabine Fresenius Kabi 500 mg επικαλυμμένα με λεπτό υμένιο δισκία
Spain	Capecitabina Fresenius Kabi 150 mg comprimidos recubiertos con película EFG Capecitabina Fresenius Kabi 500 mg comprimidos recubiertos con película EFG
France	Capecitabine Fresenius Kabi 150 mg comprimé pelliculé Capecitabine Fresenius Kabi 500 mg
Hungary	Capecitabine Fresenius Kabi 150 mg filmtabletta Capecitabine Fresenius Kabi 500
Ireland	Capecitabine 150 mg film-coated tablet Capecitabine 500 mg film-
Iceland	Capecitabin Fresenius Kabi 150 mg filmuhúðuð tafla Capecitabin Fresenius Kabi 500 mg filmuhúðuð tafla
Italy	Capecitabina Fresenius Kabi
Latvia	Capecitabine Fresenius Kabi 150 mg apvalkotās tabletes Capecitabine Fresenius Kabi 500 mg apvalkotās tabletes
Lithuania	Capecitabine Fresenius Kabi 150 mg plėvele dengtos tabletės Capecitabine Fresenius Kabi 500 mg plėvele dengtos tabletės
Malta	Capecitabine 150 mg film-coated tablet Capecitabine 500 mg film-coated tablet
The Netherlands	Capecitabine Fresenius Kabi150 mg filmomhulde tabletten Capecitabine Fresenius Kabi500 mg filmomhulde tabletten
Norway	Capecitabin Fresenius Kabi 150 mg filmdrasjerte tabletter Capecitabin Fresenius Kabi 500 mg filmdrasjerte tabletter
Poland	Capecitabine Fresenius Kabi
Portugal	Capecitabina Fresenius Kabi 150 mg Capecitabina Fresenius Kabi 500 mg
Romania	Capecitabina Fresenius Kabi 150 mg comprimate filmate Capecitabina Fresenius Kabi500 mg comprimate filmate
Sweden	Capecitabin Fresenius Kabi 150 mg, filmdragerade tabletter Capecitabin Fresenius Kabi 500 mg, filmdragerade tabletter
Slovenia	Kapecitabin Fresenius Kabi 150 mg filmskoobloženetablete Kapecitabin Fresenius Kabi 500 mg filmskoobloženetablete
Slovak Republic	Capecitabine Fresenius Kabi 150 mg filmom obalené tablety Capecitabine Fresenius Kabi500 mg filmom obalené tablety
United Kingdom	Capecitabine 150 mg film-coated tablet Capecitabine 500 mg film-coated tablet

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