

TEGOYES

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Abbreviated Prescribing information for TEGOYES (Tegafur, Gimeracil and Oteracil Capsules)

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES: Tegoyes is an oral fluoropyrimidine anti-cancer medicinal product. It is a fixed dose combination of three active substances, Tegafur, which after absorption is converted into the anti-cancer substance 5-FU; gimeracil, a dihydropyrimidine dehydrogenase (DPD) inhibitor to prevent degradation of 5-FU by the body; and, oteracil, an orotate phosphoribosyltransferase (OPRT) inhibitor that decreases the activity of 5-FU in normal gastrointestinal mucosa. The combination of Tegafur, gimeracil, and oteracil was set at 1:0.4:1 molar ratio as optimum in order to maintain 5-FU exposure and thus sustain anti-tumour activity while reducing toxicity associated with 5-FU alone. Tegafur is a prodrug of 5-FU with good oral bioavailability. Following oral administration, Tegafur is gradually converted to 5-FU in vivo, mainly by CYP2A6 enzyme activity in the liver. 5-FU is metabolised by the liver enzyme DPD. 5-FU is activated within cells by phosphorylation to its active metabolite, 5-fluoro-deoxyuridine-monophosphate (FdUMP). FdUMP and reduced folate are bound to thymidylate synthase leading to formation of a ternary complex which inhibits DNA synthesis. In addition, 5-fluorouridine-triphosphate (FUTP) is incorporated into RNA causing disruption of RNA functions. Gimeracil inhibits the metabolism of 5-FU by reversibly and selectively inhibiting DPD, the primary metabolic enzyme for 5-FU, so that higher plasma concentrations of 5-FU are achieved with the administration of a lower dose of Tegafur. After oral administration, oteracil was distributed at high concentrations in normal gastrointestinal tract tissues while considerably lower concentrations were seen in blood and tumour tissue in animal studies.

INDICATION: It is indicated in adults for the treatment of advanced gastric cancer when given in combination with cisplatin.

DOSAGE AND ADMINISTRATION: The capsules should be taken by mouth with water at least 1 hour before or 1 hour after a meal.

CONTRAINDICATION: hypersensitivity to the active substance (Tegafur, gimeracil, and oteracil) or to any of the excipients of this medication, History of severe and unexpected reactions to fluoropyrimidine therapy. with myopathy, Known complete dihydropyrimidine dehydrogenase (DPD) deficiency, Pregnancy and breast-feeding, Severe bone marrow suppression (severe leukopaenia, neutropaenia, or thrombocytopaenia., End stage renal disease patients requiring dialysis, Co-administration of other fluoropyrimidines with Tegoyes., Recent or concomitant treatment with brivudine and Contraindications for cisplatin.

WARNINGS & PRECAUTIONS: Talk to your doctor or pharmacist before taking TEGOYES. Warning with blood disorders, kidney disease, stomach and/or bowel problems such as pain, diarrhoea, vomiting and dehydration, eye disorders, such as “dry eye” or increased tearing, a current or previous infection of the liver with the hepatitis B virus, since your doctor may want to monitor you more closely, a partial deficiency in the activity of the enzyme dihydropyrimidine dehydrogenase (DPD) and a family member who has partial or complete deficiency of the enzyme dihydropyrimidine dehydrogenase (DPD).

DRUG INTERACTIONS: You must not take brivudine (an anti-viral medicine for the treatment of shingles or chickenpox) at the same time as Tegoyes treatment (including during any rest periods when you are not taking any Tegoyes capsules). If you have taken brivudine you must wait for at least 4 weeks after stopping brivudine before starting to take Tegoyes. See also section “Do not take Tegoyes”. Also, you need to be particularly careful if you are taking any of the following: other fluoropyrimidine based medicines such as the anti-fungal flucytosine. Tegoyes cannot be substituted for other oral fluoropyrimidine medicine, inhibitors of the enzyme CYP2A6

which activates Tegoyes such as tranlycypromine and methoxsalen, folic acid (often used in chemotherapy with methotrexate), blood-thinning medicines: coumarin-derivative anticoagulants such as warfarin, medicines for the treatment of seizures or tremors such as phenytoin and medicines that treat gout such as allopurinol.

ADVERSE REACTIONS: *Very common side effects (may affect more than 1 in 10 people) include:* Diarrhoea, nausea, vomiting, constipation, diarrhoea, avoid high-fibre, fatty and spicy foods, nausea and vomit a dose of medication, If you vomit more than two times in 24 hours, stop taking Tegoyes and contact your doctor immediately, Low red blood cell count leading to anaemia, Low white blood cell count, Low platelet count, Loss of appetite (anorexia), Nerve disorder and Weakness and fatigue. *Common side effects (may affect 1 to 10 in 100 people) include:* Nerve: headache, dizziness, sleeplessness, changes in taste, eye problems, increased or decreased tearing discomfort, vision problems, serious illness with blistering of the eyes, wearing away of the surface “skin” of the eye (corneal erosion), hearing problems, yellow eyes and skin, changes in blood tests which show the way the liver is working, hair loss, itchiness, rash or dermatitis, skin reaction, dry skin, hand-and-foot reaction (pain, swelling and redness of hands and/or feet), pigmented skin patches, decreased urine volume, changes in blood tests which show the way the kidney is working, kidney impairment and failure, chills, weight decrease, swelling in specific areas and muscle bone pain. *Uncommon side effects (may affect 1 to 10 in 1,000 people) include:* seeing and hearing some things that are not there, personality change, unable to sit still, confusion, feeling of nervousness, depression, sexual dysfunction, voice disorder, inability to speak and understand words, memory problem, unsteady gait, balance problems, one sided body weakness, sleepiness, nerve inflammation, distorted sense of smell, brain dysfunction, fainting, loss of consciousness, stroke, seizures, itchy and red eyes, allergic reactions in eyes, drooping upper eyelid, vertigo, ear clogging, ear discomfort, irregular or fast heart beat, chest pain, accumulation of excess fluid around the heart, heart attack, heart failure, inflammation of a vein, hot flush, runny nose, voice disorder, nasal clogging, pharyngeal erythema, hay fever, fluid in the abdomen, gastroesophageal reflux disease, increased salivary secretion, excessive burping and belching, lip inflammation, gastrointestinal disorder, oral pain, abnormal contractions of muscles of the oesophagus, blockage in the stomach and intestine, stomach ulcer, retroperitoneal fibrosis, teeth that crack or break easily, swallowing difficulty, disorder of the salivary gland, haemorrhoids. loss of skin colour, peeling skin, excessive body hair, nail shrinkage, excessive sweating, general condition worsening, weight increase, redness and swelling at the injection site, cancer pain and bleeding, multiple organ failure. Frequent urination, blood in urine, neck pain, back pain, breast pain, muscle tightness or cramps, joint swelling, limb discomfort, muscle weakness, arthritis inflammation and pain. *Rare side effects (may affect 1 to 10 in 10,000 people) and very rare side effects (may affect less than 1 in 10,000 people) include:* acute liver failure, pancreas infection, muscle breakdown, loss of sense of smell, sun allergy, widespread blood clotting and bleeding, disease affecting the white matter of the brain and serious illness with blistering of the skin, mouth and genitals.

MARKETED BY:



TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,

Ahmedabad-380 009, INDIA

IN/ TEGOYES 15 and 20 mg/ FEB-22/01/AbPI

(Additional information is available on request)