Tegafur-Gimeracil-Oteracil Potassium-Leucovorin Calcium Oral Formulation

National Cancer Institute

Source

National Cancer Institute. Tegafur-Gimeracil-Oteracil Potassium-Leucovorin Calcium Oral Formulation. NCI Thesaurus. Code C120099.

An orally bioavailable granular formulation composed of the fluoropyrimidine antagonist tegafur combined with two modulators of 5-fluorouracil (5-FU) activity, gimeracil and oteracil potassium, and the folic acid derivative leucovorin calcium, with potential antineoplastic activity. Tegafur is a prodrug of 5-fluorouracil (5-FU), an antimetabolite that is further metabolized to 5-fluoro-2'-deoxyuridine monophosphate (FdUMP) and 5-fluorouridine triphosphate (FUTP). FdUMP inhibits thymidylate synthase, DNA synthesis and cell division; FUTP competes with uridine triphosphate (UTP), thus inhibiting RNA and protein synthesis. Gimeracil is a reversible inhibitor of dihydropyrimidine dehydrogenase (DPD), the liver enzyme responsible for rapid catabolism of 5-FU into inactive metabolites. Oteracil potassium preferentially localizes in the gut and inhibits the enzyme orotate phosphoribosyl-transferase (OPRT), which converts tegafur to 5-FU. This decreases the amount of 5-FU in the gut and prevents activated 5-FU-related gastrointestinal (GI) toxicity. Leucovorin calcium, an active metabolite of folic acid, counteracts the toxic effects of 5-FU, thereby 'rescuing' the patient while permitting the antitumor activity of 5-FU.