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Drug Interactions:

"7 DRUG INTERACTIONS MEKINIST is indicated for use in combination with dabrafenib. Refer to the dabrafenib prescribing information for additional risk information that applies to combination use treatment."

Precautions:
No information available

Description:

"11 DESCRIPTION Trametinib dimethyl sulfoxide is a kinase inhibitor. The chemical name is acetamide, N-3-3-cyclopropyl-5-(2-fluoro-4- iodophenyl)amino-3,4,6,7-tetrahydro-6,8-dimethyl- 2,4,7-trioxopyrido4,3-dpyrimidin-1(2H)-ylphenyl-, compound with 1,1'-sulfinylbismethane (1:1). It has a molecular formula C 26 H 23 FIN 5 O 4 •C 2 H 6 OS with a molecular mass of 693.53 g/mol. Trametinib dimethyl sulfoxide has the following chemical structure: Trametinib dimethyl sulfoxide is a white to almost white powder. It is practically insoluble in the pH range of 2 to 8 in aqueous media. MEKINIST (trametinib) tablets for oral use are supplied as 0.5 mg and 2 mg tablets for oral administration. Each 0.5 mg tablet contains 0.5635 mg trametinib dimethyl sulfoxide equivalent to 0.5 mg of trametinib non-solvated parent. Each 2 mg tablet contains 2.254 mg trametinib dimethyl sulfoxide equivalent to 2 mg of trametinib non-solvated parent. The inactive ingredients of MEKINIST tablets are: Tablet Core: colloidal silicon dioxide, croscarmellose sodium, hypromellose, magnesium stearate (vegetable source), mannitol, microcrystalline cellulose, and sodium lauryl sulfate. Coating: hypromellose, iron oxide red (2 mg tablets), iron oxide yellow (0.5 mg tablets), polyethylene glycol, polysorbate 80 (2 mg tablets), and titanium dioxide. MEKINIST (trametinib) for oral solution is a white or almost white powder which produces a clear colorless solution when reconstituted with water. Each bottle contains 4.7 mg of trametinib equivalent to 5.3 mg trametinib dimethyl sulfoxide. Each mL of reconstituted trametinib solution contains 0.05 mg of trametinib non-solvated parent. The inactive ingredients of MEKINIST for oral solution are betadex sulfobutyl ether sodium, citric acid monohydrate, dibasic sodium phosphate, methylparaben, potassium sorbate, sucralose, and strawberry flavor. Trametinib Structure-01"

Indications and Usage:

"1 INDICATIONS AND USAGE MEKINIST is a kinase inhibitor indicated as a single agent for the treatment of BRAF-inhibitor treatment-naïve patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. (1.1 , 2.1) MEKINIST is indicated, in combination with dabrafenib, for: the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test. (1.1 , 2.1) the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection. (1.2 , 2.1) the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test. (1.3 , 2.1) the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options. (1.4 , 2.1) the treatment of adult and pediatric patients 1 year of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1.5 , 2.1) the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy. (1.6 , 2.1) Limitations of Use : MEKINIST is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition. (1.7 , 12.1) 1.1 BRAF V600E or V600K Mutation-Positive Unresectable or Metastatic Melanoma MEKINIST ® is indicated, as a single agent in BRAF-inhibitor treatment-naïve patients or in combination with dabrafenib, for the treatment of patients with unresectable or metastatic melanoma with BRAF V600E or V600K mutations, as detected by an FDA-approved test see Dosage and Administration (2.1) . 1.2 Adjuvant Treatment of BRAF V600E or V600K Mutation-Positive Melanoma MEKINIST is indicated, in combination with dabrafenib, for the adjuvant treatment of patients with melanoma with BRAF V600E or V600K mutations as detected by an FDA-approved test, and involvement of lymph node(s), following complete resection see Dosage and Administration (2.1). 1.3 BRAF V600E Mutation-Positive Metastatic NSCLC MEKINIST is indicated, in combination with dabrafenib, for the treatment of patients with metastatic non-small cell lung cancer (NSCLC) with BRAF V600E mutation as detected by an FDA-approved test see Dosage and Administration (2.1) . 1.4 BRAF V600E Mutation-Positive Locally Advanced or Metastatic Anaplastic Thyroid Cancer MEKINIST is indicated, in combination with dabrafenib, for the treatment of patients with locally advanced or metastatic anaplastic thyroid cancer (ATC) with BRAF V600E mutation and with no satisfactory locoregional treatment options see

Dosage and Administration (2.1) . 1.5 BRAF V600E Mutation-Positive Unresectable or Metastatic Solid Tumors MEKINIST is indicated, in combination with dabrafenib, for the treatment of adult and pediatric patients 1 year of age and older with unresectable or metastatic solid tumors with BRAF V600E mutation who have progressed following prior treatment and have no satisfactory alternative treatment options see Dosage and Administration (2.1) . This indication is approved under accelerated approval based on overall response rate and duration of response see Clinical Studies (14.6) . Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). 1.6 BRAF V600E Mutation-Positive Low-Grade Glioma MEKINIST is indicated, in combination with dabrafenib, for the treatment of pediatric patients 1 year of age and older with low-grade glioma (LGG) with a BRAF V600E mutation who require systemic therapy see Dosage and Administration (2.1) . 1.7 Limitations of Use MEKINIST is not indicated for treatment of patients with colorectal cancer because of known intrinsic resistance to BRAF inhibition see Indications and Usage (1.5), Clinical Pharmacology (12.1) ."

Warnings:
No information available

Pregnancy:

"8.1 Pregnancy Risk Summary Based on its mechanism of action see Clinical Pharmacology (12.1) and findings from animal reproduction studies, MEKINIST can cause fetal harm when administered to a pregnant woman. There is insufficient data in pregnant women exposed to MEKINIST to assess the risks. Trametinib was embryotoxic and abortifacient in rabbits at doses greater than or equal to those resulting in exposures approximately 0.3 times the human exposure at the recommended adult clinical dose (see Data) . Advise pregnant women of the potential risk to a fetus. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. Data Animal Data In reproductive toxicity studies, administration of trametinib to rats during the period of organogenesis resulted in decreased fetal weights at doses greater than or equal to 0.031 mg/kg/day approximately 0.3 times the human exposure at the recommended adult dose based on area under the curve (AUC). In rats, at a dose resulting in exposures 1.8-fold higher than the human exposure at the recommended adult dose, there was maternal toxicity and an increase in post-implantation loss. In pregnant rabbits, administration of trametinib during the period of organogenesis resulted in decreased fetal body weight and increased incidence of variations in ossification at doses greater than or equal to 0.039 mg/kg/day (approximately 0.08 times the human

exposure at the recommended adult dose based on AUC). In rabbits administered trametinib at 0.15 mg/kg/day (approximately 0.3 times the human exposure at the recommended adult dose based on AUC) there was an increase in post-implantation loss, including total loss of pregnancy, compared with control animals."

Overdosage:

"10 OVERDOSAGE The highest doses of MEKINIST evaluated in clinical trials were 4 mg orally once daily and 10 mg administered orally once daily on 2 consecutive days followed by 3 mg once daily. In seven patients treated on one of these two schedules, there were two cases of RPEDs for an incidence of 28%. Since trametinib is highly bound to plasma proteins, hemodialysis is likely to be ineffective in the treatment of overdose with MEKINIST."