PIVIKTO®

Presentation: Film-coated tablets (FCT) containing 50 mg, 150mg and 200mg of alpelisib.

Indications: Alpelisib is a kinase inhibitor indicated in combination with fulvestrant for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, PIK3CA-mutated, advanced or metastatic breast cancer following progression on or after an endocrine-based regimen.

Dosage and administration:

Adults: The recommended dose of alpelisib is 300 mg taken orally, once daily on a continuous basis. Alpelisib should be taken immediately following food, at approximately the same time each day. If a dose of alpelisib is missed, it can be taken up to 9 hours after the time it is normally administered. After more than 9 hours, the dose should be skipped for that day. On the next day, alpelisib should be taken at its usual time. If patient vomits after taking the alpelisib dose, the patient should not take an additional dose on that day, and should resume the usual dosing schedule the next day, at the usual time.

Special populations: ♦*Renal impairment:* Mild or moderate: No dose adjustment is necessary.

Severe: Caution is recommended. ♦*Hepatic impairment:* Mild, moderate or severe: No dose adjustment is necessary. ♦*Geriatrics (≥65 years):* No dose adjustment is required. ♦*Pediatrics (<18 years):* Safety and efficacy have not been established.

Contraindications: ♦Patients with hypersensitivity to the active substance or to any of the excipients.

Warnings and precautions:

Hypersensitivity (including anaphylactic reaction): Serious hypersensitivity reactions (including anaphylactic reaction and anaphylactic shock), manifested by symptoms including, but not limited to, dyspnea, flushing, rash, fever or tachycardia were reported in patients treated with alpelisib in clinical studies. Angioedema has been reported in the post marketing setting in patients treated with Alpelisib. Alpelisib should be permanently discontinued and should not be re-introduced in patients with serious hypersensitivity reactions. Appropriate treatment should be promptly initiated. ♦**Severe cutaneous reactions:** Cases of severe cutaneous reactions, including Stevens-Johnson syndrome (SJS), erythema multiforme (EM) and drug reaction with eosinophilia and systemic symptoms (DRESS) were reported in patients treated with alpelisib. Alpelisib treatment should not be initiated in patients with history of severe cutaneous reactions. Patients should be advised of the signs and symptoms of severe cutaneous reactions. If symptoms or signs of severe cutaneous reactions are present, alpelisib should be interrupted until the etiology of the reaction has been determined. A consultation with dermatologist is recommended. If a severe cutaneous reaction is confirmed, alpelisib should be permanently discontinued. Alpelisib should not be reintroduced in patients who have experienced previous severe cutaneous reactions. ♦**Hyperglycemia:**.Severe hyperglycemia, in some cases associated with hyperglycemic hyperosmolar nonketotic syndrome (HHNKS) or ketoacidosis, has been observed in patients treated with Piqray. Some cases of ketoacidosis with fatal outcome have been reported in the post marketing setting Patients with poor glycemic control may be at a higher risk of developing severe hyperglycemia and associated complications (e.g. ketoacidosis). Patients with risk factors for

hyperglycemia such as obesity (BMI ≥30), elevated FPG, HbA1c at or above the upper limit of normal, or age ≥75 are at a higher risk of developing severe hyperglycemia. Those patients should be monitored for fasting glucose more frequently for the first few weeks of treatment. Patients should be advised of the signs and symptoms of hyperglycemia. Based on the severity of the hyperglycaemia, alpelisib may require treatment interruption, dose reduction, or treatment discontinuation.

Pneumonitis: Pneumonitis including serious cases of pneumonitis/acute interstitial lung disease have been reported in alpelisib treated patients in clinical studies. Patients should be advised to promptly report any new or worsening respiratory symptoms. In patients who have new or worsening respiratory symptoms or are suspected to have developed pneumonitis, alpelisib treatment should be interrupted immediately and the patient should be evaluated for pneumonitis. A diagnosis of non-infectious pneumonitis should be considered. Alpelisib should be permanently discontinued in all patients with confirmed pneumonitis. ♦**Diarrhea or colitis:** Severe diarrhea and clinical consequences, such as dehydration and acute kidney injury, have been reported during treatment with Piqray in clinical studies. Colitis has been reported in the post marketing setting. Patients should be monitored for diarrhea and additional symptoms of colitis, such as abdominal pain and mucus or blood in stool. In case of colitis, additional treatment such as steroids may be considered. Based on the severity of the diarrhea or colitis, Piqray may require dose interruption, reduction, or discontinuation. Patients should be advised to notify their healthcare provider if diarrhea or colitis occurs while taking Alpelisib.

Pregnancy, lactation, females and males of reproductive potential:

Pregnancy: It is possible that alpelisib can cause fetal harm when administered to a pregnant woman. Alpelisib should not be used during pregnancy unless the benefits to the mother outweigh the risk to the fetus. If alpelisib is used during pregnancy, the patient should be advised of the potential risk to the fetus.

Lactation: Women should not breast-feed during treatment and for at least 4 days after the last dose of alpelisib.

Females and males of reproductive potential: ♦*Pregnancy testing:* For female patients of reproductive potential, the pregnancy status should be verified, prior to initiating treatment with alpelisib. ♦*Contraception:* Sexually active females of reproductive potential (ORP) should use effective contraception and male patients with female partners ORP should use condoms during treatment with alpelisib and for 4 days after stopping treatment with alpelisib.

Infertility: Based on animal studies, alpelisib may impair fertility in females and males of reproductive potential.

Adverse drug reactions:

Very common (≥10%): Anaemia, diarrhoea, nausea, vomiting, stomatitis, abdominal pain, dyspepsia, fatigue, mucosal inflammation, oedema peripheral, pyrexia, mucosal dryness, urinary tract infection, weight decreased, blood creatinine increased, hyperglycaemia, decreased appetite, headache, dysgeusia, rash, alopecia, pruritus, dry skin, activated partial thromboplastin time increased, hemoglobin decreased, lymphocyte count decreased, platelet count decreased, alanine aminotransferase increased, albumin decreased, calcium corrected decreased, gamma-glutamyl transferase increased, glucose plasma increased, glucose plasma decreased, lipase increased.

Common (≥1 to <10%): Lymphopenia, thrombocytopenia, vision blurred, dry eye, toothache, cheilitis, gingival pain, gingivitis, oedema, hypersensitivity, glycosylated haemoglobin increased, hypokalemia, hypocalcaemia, dehydration, muscle spasms, myalgia, osteonecrosis of jaw, insomnia, acute kidney injury, pneumonitis, erythema, dermatitis, palmar-plantar erythrodysaesthesia syndrome, erythema multiforme, hypertension, lymphoedema, potassium decreased, magnesium decreased.

Uncommon (≥0.1 to <1%): Pancreatitis, ketoacidosis, Stevens-Johnson syndrome (SJS).

Adverse drug reactions from post-marketing experience (frequency not known): colitis, hyperglycaemic hyperosmolar nonketotic syndrome (HHNKS), angioedema, drug reaction with eosinophilia and systemic symptoms (DRESS).

Description of select ADRs and treatment recommendations, where applicable: ♦Rash: Topical corticosteroid treatment should be initiated at the first signs of rash and oral corticosteroids should be considered for more moderate to severe rashes. Additionally, antihistamines are recommended to manage symptoms of rash. Oral antihistamines may be initiated prophylactically, at the time of initiation of treatment with alpelisib. ♦Gastrointestinal (**GI) toxicity (nausea, diarrhoea, vomiting):** Severe diarrhoea and clinical consequences, such as dehydration and acute kidney injury have been reported during treatment with alpelisib and resolved with appropriate intervention. Patients should be managed according to local standard of care medical management, including electrolyte monitoring, administration of anti-emetics and antidiarrhoeal medications and/or fluid replacement and electrolyte supplements, as clinically indicated.

Interactions: ♦BCRP (breast cancer resistance protein) inhibitors: Caution is advised when co-administering alpelisib with a BCRP inhibitor (e.g. eltrombopag, lapatininb, pantoprazole), as inhibition of BCRP may lead to an increase in systemic exposure of alpelisib.

CYP3A4 inducers: Co-administration of alpelisib with strong CYP3A4 inducers (e.g., apalutamide, carbamazepine, enzalutamide, mitotane, phenytoin, rifampin, St. John's wort) should be avoided and selection of an alternative concomitant medicinal product, with no or minimal potential to induce CYP3A4, should be considered. **♦CYP3A4 substrates**: Caution is recommended when alpelisib is used in combination with CYP3A4 substrates that also possess an additional time-dependent inhibition and induction potential on CYP3A4 that affects their own metabolism (e.g. rifampicin, ribociclib, encorafenib). **♦CYP2C9 substrates with narrow therapeutic index**: No dose adjustment of alpelisib is required. However, in the absence of clinical data, caution is recommended when Alpelisib is co-administered with drugs that are CYP2C9 substrates with narrow therapeutic index (e.g.warfarin). **♦CYP2B6 sensitive substrates with narrow therapeutic index**: Sensitive CYP2B6 substrates (e.g. bupropion) or CYP2B6 substrates with a narrow therapeutic window should be used with caution in combination with alpelisib, as alpelisib may reduce the clinical activity of such drugs.

Hormonal contraceptives: It is currently unknown whether alpelisib may reduce the effectiveness of systemically acting hormonal contraceptives.

Before prescribing, please consult full prescribing information available from Novartis Healthcare Pvt Ltd Inspire BKC, 7th floor, Bandra Kurla Complex, Bandra (East) Mumbai 400051, Maharashtra, India India. Tel +91 22 50243335/36, Fax +91 22 50243005.

For the use of only Oncologist.

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