PEMOMAB

Pembrolizumab INN

Composition: Each 4 ml sterile solution contains Pembrolizumab INN 100mg.

Pharmacology:
Mechanism of Action
Binding of the PD-1 ligands, PD-L1 and PD-L2, to the PD-1 receptor found on T cells, inhibits T cell proliferation and cytokine production. Upregulation of PD-1 ligands occurs in some tumors and signaling through this pathway can contribute to inhibition of active T-cell immune surveillance of tumors. Pembrolizumab is a monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.

Indication:
Pembrolizumab is a programmed death receptor-1 (PD-1)-blocking antibody indicated:

Melanoma: for the treatment of patients with unresectable or metastatic melanoma.

Non-Small Cell Lung Cancer (NSCLC):
as a single agent for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥1%] as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, as a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Pembrolizumab.

Head and Neck Squamous Cell Cancer (HNSCC):
in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
as a single agent for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1] as determined by an FDA-approved test.

Classical Hodgkin Lymphoma (cHL): for the treatment of adult patients with relapsed or refractory cHL.
Urothelial Carcinoma: as a single agent for the treatment of patients with locally advanced or metastatic urothelial carcinoma who: o are not eligible for any platinum-containing chemotherapy.

Microsatellite Instability-High or Mismatch Repair Deficient Cancer: for the treatment of adult and pediatric patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, as determined by an FDA-approved test
for the treatment of patients with unresectable or metastatic MSI-H or dMMR colorectal cancer (CRC) as determined by an FDA-approved test.
Gastric Cancer: in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

Esophageal Cancer: for the treatment of patients with locally advanced or metastatic esophageal or gastroesophageal junction (GEJ) (tumors with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either: in combination with platinum- and fluoropyrimidine-based chemotherapy, or as a single agent after one or more prior lines of systemic therapy for patients with tumors of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

Cervical Cancer: in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

Hepatocellular Carcinoma (HCC): for the treatment of patients with HCC who have been previously treated with sorafenib.
Renal Cell Carcinoma (RCC): in combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.

Endometrial Carcinoma: in combination with lenvatinib, for the treatment of patients with advanced endometrial carcinoma that is mismatch repair proficient (pMMR) as determined by an FDA-approved test or not MSI-H

Triple-Negative Breast Cancer (TNBC):
for the treatment of patients with high-risk early-stage TNBC in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery. in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10) as determined by an FDA approved test.

Dosage and Administration
Adult patients with unresectable or metastatic melanoma: 200 mg every 3 weeks or 400 mg every 6 weeks Adjuvant treatment of adult patients with melanoma, NSCLC, or RCC: 200 mg every 3 weeks or 400 mg every 6 weeks Adult patients with NSCLC, HNSCC, cHL, PMBCL, locally advanced or metastatic Urothelial Carcinoma, MSI-H or dMMR Cancer, MSI-H or dMMR CRC, MSI-H or dMMR Endometrial Carcinoma, Esophageal Cancer, Cervical Cancer, HCC, MCC, TMB-H Cancer, or cSCC: 200 mg every 3 weeks or 400 mg every 6 weeks Administer pembrolizumab as a diluted solution intravenously over 30 minutes through an intravenous line.

Contraindications: None

Warnings and Precautions: Immune-Mediated Pneumonitis: Pembrolizumab can cause immune-mediated pneumonitis. The incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.4% (94/2799) of patients receiving Pembrolizumab

Immune-Mediated Colitis: Pembrolizumab can cause immune-mediated colitis, which may present with diarrhea. Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis. In cases of corticosteroid-refractory colitis, consider repeating infectious workup to exclude alternative etiologies.

Hepatotoxicity and Immune-Mediated Hepatitis: Pembrolizumab can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 0.7% (19/2799) of patients receiving Pembrolizumab, including Grade 4 (<0.1%), Grade 3 (0.4%), and Grade 2 (0.1%) adverse reactions.

Immune-Mediated Endocrinopathies:
Hypophysitis: Pembrolizumab can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism.

Thyroid Disorders: Pembrolizumab can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement for hypothyroidism or institute medical management of hyperthyroidism as clinically indicated.

Immune-Mediated Nephritis with Renal Dysfunction: Pembrolizumab can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.3% (9/2799) of patients receiving Pembrolizumab, including Grade 4 (<0.1%), Grade 3 (0.1%), and Grade 2 (0.1%) adverse reactions.
Immune-Mediated Dermatologic Adverse Reactions: Pembrolizumab can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens Johnson Syndrome, DRESS, and toxic epidermal necrolysis (TEN), has occurred with PD-1/PD-L1 blocking antibodies. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold or permanently discontinue Pembrolizumab depending on severity.

Other Immune-Mediated Adverse Reactions:

Cardiac/Vascular: Myocarditis, pericarditis, vasculitis

Nervous System: Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, autoimmune neuropathy

Ocular: Uveitis, iritis and other ocular inflammatory toxicities can occur. Some cases can be associated with retinal detachment.

Gastrointestinal: Pancreatitis, to include increases in serum amylase and lipase levels, gastritis, duodenitis

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Infusion-Related Reactions: Pembrolizumab can cause severe or life-threatening infusion-related reactions, including hypersensitivity and anaphylaxis, which have been reported in 0.2% of 2799 patients receiving Pembrolizumab. Monitor patients for signs and symptoms of infusion-related reactions including rigors, chills, wheezing, pruritus, flushing, rash, hypotension, hypoxemia, and fever.

Complications of Allogeneic HSCT: Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1 blocking antibody.

Increased Mortality in Patients with Multiple Myeloma when Pembrolizumab: Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled trials.

Embryo-Fetal Toxicity: Based on its mechanism of action, Pembrolizumab can cause fetal harm when administered to a pregnant woman. Based on its mechanism of action, Pembrolizumab can cause fetal harm when administered to a pregnant woman.

Adverse Reactions
The following clinically significant adverse reactions are described in greater details in other section of the insert (see WARNINGS AND PRECAUTIONS)
- Immune-Mediated Pneumonitis:
- Immune-Mediated Colitis:
- Hepatotoxicity and Immune-Mediated Hepatitis
- Immune-Mediated Endocrinopathies
- Immune-Mediated Nephritis with Renal Dysfunction
- Immune-Mediated Dermatologic Adverse Reactions
- Other Immune-Mediated Adverse Reactions
- Infusion-Related Reactions
- Complications of Allogeneic HSCT
- Embryo-Fetal Toxicity
- Immune-Mediated Dermatologic Adverse Reactions
- Other Immune-Mediated Adverse Reactions
- Infusion-Related Reactions
- Complications of Allogeneic HSCT
- Embryo-Fetal Toxicity

Use in Specific Populations
Pregnancy: Based on its mechanism of action, Pembrolizumab can cause fetal harm when administered to a pregnant woman. There are no available human data informing the risk of embryo-fetal toxicity. In the general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Lactation: There are no data on the presence of pembrolizumab in either animal or human milk or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with Pembrolizumab and for 4 months after the last dose.

Pediatric Use: The safety and effectiveness of Pembrolizumab as a single agent have been established in pediatric patients with melanoma, cHL, PMBCL, MCC, MSI-H or dMMR cancer, and TMB-H cancer. Use of Pembrolizumab in pediatric patients for these indications is supported by evidence from adequate and well-controlled studies in adults with additional pharmacokinetic and safety data in pediatric patients

Geriatric Use: Of 3781 patients with melanoma, NSCLC, HNSCC, or urothelial carcinoma who were treated with Pembrolizumab in clinical studies, 48% were 65 years and over and 17% were 75 years and over. No overall differences in safety or effectiveness were observed between elderly patients and younger patients.

Overdose: There is no information on overdose with pembrolizumab.

Storage: Store vials under refrigeration at 2°C- 8°C (36° F- 46°F) in original carton to protect from light. Do not freeze. Do not shake.

Packaging: Pemomab Injection : Each box contains 1 vial of Pemomab injection containing Pembrolizumab INN 100mg/ 4ml.

Manufactured by:
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh

Version: 00

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