NEW

PEMREST

Pembrolizumab INN

Everest

COMPOSITION

PEMREST Injection: Each single dose vial contains Pembrolizumab INN 100 mg in 4 mL solution (25 mg/ mL).

PHARMACOLOGY

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. 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.

INDICATION

Pembrolizumab is indicated in:

- Unresectable or metastatic melanoma, and for adjuvant treatment of adults and pediatric patients (≥12 years) with Stage IIB, IIC, or III melanoma following complete resection.
- Non-small cell lung cancer
  1. In combination with Pemetrexed and platinum chemotherapy, for the first-line treatment of patients with metastatic nonsquamous non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
  2. In combination with Carboplatin and either Paclitaxel or Paclitaxel protein-bound, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.
  3. As a single agent, for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumor Proportion Score (TPS) ≥1%] with no EGFR or ALK genomic tumor aberrations, and is either Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.
  4. As a single agent, for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) with disease progression 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 Pembrolozumab.
  5. Resectable NSCLC (tumors ≥4 cm or node-positive) when used with platinum-containing chemotherapy as neoadjuvant therapy, followed by continuation as a single-agent adjuvant treatment after surgery.
  6. As a single agent, is indicated as adjuvant treatment following resection and platinum-based chemotherapy for adult patients with Stage IB (T2a ≥4 cm), II, or IIIA NSCLC.
- Unresectable advanced or metastatic malignant pleural mesothelioma in combination with Pemetrexed and platinum chemotherapy for the first-line treatment.
- Head and Neck Squamous Cell Cancer (HNSCC)
  1. Resectable locally advanced HNSCC whose tumors express PD-L1 [Combined Positive Score (CPS) ≥1 as a single agent as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy (RT) with or without Cisplatin and then as a single agent.
  2. In combination with platinum and Fluorouracil (FU), for the first-line treatment of patients with metastatic or with unresectable, recurrent head and neck squamous cell carcinoma (HNSCC).
  3. As a single agent for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumors express PD-L1.
  4. As a single agent for the recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.
  5. Adults with relapsed or refractory classical Hodgkin lymphoma and for pediatric patients with refractory cHL or cHL relapsed after two or more prior therapies. (not recommended for PMBCL patients who require urgent cytoreductive therapy)
- Urothelial Cancer
  1. In combination with Enfortumab Vedotin is indicated for adults with locally advanced or metastatic urothelial cancer.
  2. As monotherapy is indicated for locally advanced or metastatic urothelial carcinoma in patients:
     –not eligible for any platinum-containing chemotherapy, or
     –with disease progression during or after platinum-containing chemotherapy, or within 12 months of neoadjuvant/adjuvant platinum-based treatment.
  3. With Enfortumab Vedotin as neoadjuvant therapy, continued as adjuvant therapy after cystectomy, is indicated for adults with muscle invasive bladder cancer (MIBC) who are ineligible for Cisplatin-containing chemotherapy.
  4. As monotherapy for BCG-unresponsive, high-risk non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (with or without papillary tumors) in patients ineligible for or declining cystectomy.

- Unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) solid tumors, that have progressed following prior treatment and who have no satisfactory alternative treatment options.
- Unresectable or metastatic Microsatellite Instability-High or Mismatch Repair Deficient Colorectal Cancer.

- Gastric Cancer
  1. In combination with Trastuzumab, Fluoropyrimidine- and Platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥1).
  2. In combination with Fluoropyrimidine- and Platinum-containing chemotherapy, for the first-line treatment of adults with locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction (GEJ) adenocarcinoma whose tumors express PD-L1 (CPS ≥ 1).
  3. 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 for patients with tumors that express PD-L1 (CPS ≥ 1).
     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).

- Cervical Cancer
  1. In combination with chemoradiotherapy (CRT), for locally advanced cervical cancer involving the lower third of the vagina, with or without extension to pelvic sidewall, or hydronephrosis/non-functioning kidney, or spread to adjacent pelvic organs (FIGO 2014 Stage III-IVA).
  2. In combination with chemotherapy, with or without Bevacizumab, for persistent, recurrent, or metastatic cervical cancer whose tumors express PD-L1 (CPS ≥ 1).
  3. As a single agent for recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumors express PD-L1 (CPS ≥ 1).

- Hepatocellular carcinoma (HCC) secondary to hepatitis B who have received prior systemic therapy other than a PD-1/PD-L1-containing regimen.
- Locally advanced unresectable or metastatic biliary tract cancer (BTC) in combination with Gemcitabine and Cisplatin.
- Recurrent locally advanced or metastatic Merkel cell carcinoma (MCC).
- Renal Cell Carcinoma
  1. In combination with Axitinib, for the first-line treatment of adult patients with advanced renal cell carcinoma (RCC).
  2. In combination with Lenvatinib, for the first-line treatment of adult patients with advanced RCC.
  3. Adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.
- Endometrial Carcinoma
  1. In combination with Carboplatin and Paclitaxel, followed by Pembrolizumab as a single agent, for the patients with primary advanced or recurrent endometrial carcinoma.
  2. In combination with Lenvatinib, for advanced endometrial carcinoma that is mismatch repair proficient (pMMR) or not MSI-H, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
  3. As a single agent for advanced endometrial carcinoma that is MSI-H or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
- Adult and pediatric patients with unresectable or metastatic tumor mutational burden-high (TMB-H) [≥10 mutations/megabase (mut/Mb)] solid tumors, that have progressed following prior treatment and who have no satisfactory alternative treatment options. (The safety and effectiveness of Pembrolizumab in pediatric patients with TMB-H central nervous system cancers have not been established.)
- Recurrent or metastatic cutaneous squamous cell carcinoma (cSCC) or locally advanced cSCC that is not curable by surgery or radiation.
- Triple-Negative Breast Cancer
  1. High-risk early-stage triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.
  2. In combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumors express PD-L1 (CPS ≥10).

PATIENT SELECTION

Single Agent

Select patients for treatment with Pembrolizumab as a single agent based on the presence of positive PD-L1 expression in:

- Stage III NSCLC who are not candidates for surgical resection or definitive chemoradiation.
- Metastatic NSCLC.
- First-line treatment of metastatic or unresectable, recurrent HNSCC.
- Previously treated recurrent locally advanced or metastatic esophageal cancer.
- Recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.

Select patients for single-agent Pembrolizumab based on MSI-H/dMMR or TMB-H status from tumor specimens.
In high-grade gliomas, test TMB-H, MSI-H, and dMMR on primary tumor tissue obtained before starting Temozolomide, since treatment may create subclonal mutations.

For non-CRC solid tumors, confirm MSI-H/dMMR with an FDA-approved test when possible.

If confirmatory testing cannot be performed, TMB ≥10 mut/Mb (FDA-approved test) may be used for patient selection.

Combination Therapy

Select patients with PD-L1 CPS ≥1 for Pembrolizumab used with neoadjuvant therapy, then with or without chemotherapy during RT, and continued as adjuvant treatment in resectable, locally advanced HNSCC.
For Pembrolizumab with chemotherapy, select patients with PD-L1 CPS ≥1 in:

- Locally advanced unresectable or metastatic gastric or GEJ adenocarcinoma
- Esophageal or GEJ carcinoma

(No FDA-approved PD-L1 test exists for selecting esophageal carcinoma patients treated with Platinum + Fluoropyrimidine + Pembrolizumab.)
For Pembrolizumab with chemotherapy ± Bevacizumab, select based on positive PD-L1 in persistent, recurrent, or metastatic cervical cancer.
For pMMR/not MSI-H advanced endometrial cancer, select based on MMR or MSI status when using Pembrolizumab + Lenvatinib.
For Pembrolizumab with chemotherapy in locally recurrent unresectable or metastatic TNBC, select based on positive PD-L1 expression.

DOSAGE AND ADMINISTRATION

Administer Pembrolizumab as a 30-minute intravenous infusion. The recommended dosages of Pembrolizumab are presented below:

Indication	Recommended Dosage of Pembrolizumab	Duration/Timing of Treatment
Monotherapy		
Adult patients with unresectable or metastatic melanoma	200 mg every 3 weeks or 400 mg every 6 weeks	Until disease progression or unacceptable toxicity
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	Until disease progression, unacceptable toxicity, or up to 24 months
Adult patients with high-risk BCG-unresponsive NMIBC	200 mg every 3 weeks or 400 mg every 6 weeks	Until persistent or recurrent high-risk NMIBC, disease progression, unacceptable toxicity, or up to 24 months
Pediatric patients with cHL, PMBCL, MSI-H or dMMR Cancer, MCC, or TMB-H Cancer	2 mg/kg every 3 weeks (up to a maximum of 200 mg)	Until disease progression, unacceptable toxicity, or up to 24 months
Pediatric patients (12 years and older) for adjuvant treatment of melanoma	2 mg/kg every 3 weeks (up to a maximum of 200 mg)	Until disease recurrence, unacceptable toxicity, or up to 12 months
Combination Therapy		
Adult patients with resectable NSCLC	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to chemotherapy when given on the same day.	Neoadjuvant treatment in combination with chemotherapy for 12 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity, followed by adjuvant treatment with Pembrolizumab as a single agent after surgery for 39 weeks or until disease recurrence or unacceptable toxicity.
Adult patients with NSCLC, MPM, HNSCC, HER2-negative Gastric Cancer, Esophageal Cancer, or BTC	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to chemotherapy when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months
Adult patients with locally advanced or metastatic urothelial cancer.	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab after Enfortumab Vedotin when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months.
Adult patients with MIBC	200 mg every 3 weeks (neoadjuvant) 200mg every 3 weeks or 400 mg every 6 weeks (adjuvant) Administer Pembrolizumab after Enfortumab Vedotin when given on the same day.	Neoadjuvant: • Administer Pembrolizumab 200 mg every 3 weeks for 3 doses in combination with Enfortumab Vedotin or until disease progression that precludes curative-intent cystectomy or unacceptable toxicity. Adjuvant: • Administer Pembrolizumab 200 mg every 3 weeks for 14 doses or 400 mg every 6 weeks for 7 doses in combination with Enfortumab Vedotin or until disease recurrence or unacceptable toxicity
Adult patients with locally advanced HNSCC	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to Cisplatin when given on the same day.	Neoadjuvant: •Administer Pembrolizumab for 6 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity. Adjuvant: •Administer Pembrolizumab in combination with RT with or without Cisplatin. •Continue Pembrolizumab as a single agent. •Continue Pembrolizumab until disease recurrence or unacceptable toxicity or up to one year
Adult patients with HER2-positive Gastric Cancer	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to Trastuzumab and chemotherapy when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months
Adult patients with Cervical Cancer	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to chemoradiotherapy or prior to chemotherapy with or	Until disease progression, unacceptable toxicity, or for Pembrolizumab, up to 24 months

	without Bevacizumab when given on the same day.	
Adult patients with RCC	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab in combination with Axitinib 5 mg orally twice daily† or Administer Pembrolizumab in combination with Lenvatinib 20 mg orally once daily.	Until disease progression, unacceptable toxicity, or for Pembrolizumab, up to 24 months
Adult patients with Endometrial Carcinoma	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to Carboplatin and Paclitaxel when given on the same day. or Administer Pembrolizumab in combination with Lenvatinib 20 mg orally once daily.	Until disease progression, unacceptable toxicity, or for Pembrolizumab, up to 24 months
Adult patients with high-risk early-stage TNBC	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to chemotherapy when given on the same day.	Neoadjuvant treatment in combination with chemotherapy for 24 weeks (8 doses of 200 mg every 3 weeks or 4 doses of 400 mg every 6 weeks) or until disease progression or unacceptable toxicity, followed by adjuvant treatment with Pembrolizumab as a single agent for up to 27 weeks (9 doses of 200 mg every 3 weeks or 5 doses of 400 mg every 6 weeks) or until disease recurrence or unacceptable toxicity.
Adult patients with locally recurrent unresectable or metastatic TNBC	200 mg every 3 weeks or 400 mg every 6 weeks Administer Pembrolizumab prior to chemotherapy when given on the same day.	Until disease progression, unacceptable toxicity, or up to 24 months

*Refer to the Prescribing Information for the agents administered in combination with Pembrolizumab for recommended dosing information, as appropriate.
*When Axitinib is used in combination with Pembrolizumab, dose escalation of Axitinib above the initial 5 mg dose may be considered at intervals of six weeks or longer.
*Patients who experience disease progression or unacceptable toxicity related to Pembrolizumab with neoadjuvant treatment in combination with chemotherapy should not receive adjuvant single agent Pembrolizumab.

Dose Reduction

Pembrolizumab has no recommended dose reduction; instead, therapy is withheld for most Grade 3 immune-mediated toxicities, and permanently discontinued for any Grade 4 event, recurrent Grade 3 requiring systemic steroids, or when the patient cannot taper corticosteroids to ≤10 mg Prednisone/day within 12 weeks.

CONTRAINDICATION

None

Adverse Reaction

The following adverse reactions are described elsewhere in the labeling:

Pembrolizumab monotherapy: fatigue, musculoskeletal pain, rash, diarrhea, pyrexia, cough, decreased appetite, pruritus, dyspnea, constipation, pain, abdominal pain, nausea, hypothyroidism.

Pembrolizumab + chemotherapy/chemoradiotherapy: fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, pyrexia, alopecia, peripheral neuropathy, mucosal inflammation, stomatitis, headache, weight loss, abdominal pain, arthralgia, myalgia, insomnia, palmar-plantar erythrodysesthesia, urinary tract infection, hypothyroidism, radiation skin injury, dysphagia, dry mouth, musculoskeletal pain.

Pembrolizumab + chemotherapy + Bevacizumab: peripheral neuropathy, alopecia, anemia, fatigue/asthenia, nausea, neutropenia, diarrhea, hypertension, thrombocytopenia, constipation, arthralgia, vomiting, urinary tract infection, rash, leukopenia, hypothyroidism, decreased appetite.

Pembrolizumab + Axitinib: diarrhea, fatigue/asthenia, hypertension, hepatotoxicity, hypothyroidism, decreased appetite, palmar-plantar erythrodysesthesia, nausea, stomatitis/mucosal inflammation, dysphonia, rash, cough, constipation.

Pembrolizumab + Lenvatinib: hypothyroidism, hypertension, fatigue, diarrhea, musculoskeletal disorders, nausea, decreased appetite, vomiting, stomatitis, weight loss, abdominal pain, urinary tract infection, proteinuria, constipation, headache, hemorrhagic events, palmar-plantar erythrodysesthesia, dysphonia, rash, hepatotoxicity, acute kidney injury.
Pembrolizumab + Enfortumab Vedotin: rash, peripheral neuropathy, fatigue, pruritus, diarrhea, alopecia, weight loss, decreased appetite, dry eye, nausea, constipation, dysgeusia, urinary tract infection.

WARNINGS AND PRECAUTION

Severe and Fatal Immune-Mediated Reactions

Pembrolizumab blocks PD-1, removing immune inhibition and potentially triggering immune-mediated toxicity in any organ system, during or after treatment. Early detection is critical. Monitor for clinical symptoms and check LFTs, creatinine, and thyroid function regularly. For TNBC neoadjuvant use, also monitor cortisol. Exclude infections before labeling a toxicity immune-mediated.
Manage promptly with corticosteroids (1–2 mg/kg/day) and taper over ≥1 month; use additional immunosuppressants if needed. Withhold or permanently discontinue Pembrolizumab based on severity. Endocrine and mild dermatologic events may not require systemic steroids.

Immune-Mediated Pneumonitis

Occurs in ~3–8% depending on population; can be fatal. Often requires high-dose steroids. Leads to treatment interruption or discontinuation; recurrence occurs in ~20–25% after rechallenge.

Immune-Mediated Colitis

Incidence was seen about 1–2%. Monitor for diarrhea; rule out CMV especially in steroid-refractory cases. Most require steroids; small minority need additional immunosuppression. Recurrence ~23% after rechallenge.

Hepatotoxicity and Immune-Mediated Hepatitis

As monotherapy, incidence <1%. With Pembrolizumab + Axitinib, Grade 3–4 ALT/AST elevations are significantly more frequent; close monitoring required. Most improve with steroids; recurrence more common with Axitinib than Pembrolizumab.

Immune-Mediated Endocrinopathies

Adrenal insufficiency: Pembrolizumab can cause primary or secondary adrenal insufficiency. For Grade ≥2 events, begin symptomatic management with hormone replacement and withhold treatment based on severity. Adrenal insufficiency occurred in 0.8% of patients, with most requiring systemic corticosteroids. Permanent discontinuation was rare (<0.1%), and treatment was withheld in 0.3% of patients, all of whom were able to restart Pembrolizumab after symptoms improved.

Hypophysitis: Pembrolizumab can cause immune-mediated hypophysitis, which may present with headache, photophobia, visual field defects, and can lead to hypopituitarism. Start hormone replacement as needed, and withhold or permanently discontinue treatment based on severity. Hypophysitis occurred in 0.6% of patients, with most requiring systemic corticosteroids. It led to permanent discontinuation in 0.1% and withholding in 0.3% of patients, all of whom were able to restart Pembrolizumab after symptom improvement.

Thyroid disorders: Pembrolizumab can cause immune-mediated thyroid disorders, including thyroiditis, hyperthyroidism, and hypothyroidism. Thyroiditis may occur with or without endocrine dysfunction, and hypothyroidism can follow hyperthyroidism. Manage with thyroid hormone replacement or medical therapy for hyperthyroidism, and adjust Pembrolizumab (withhold or permanently discontinue) based on severity. Thyroiditis occurred in 0.6% of patients, hyperthyroidism in 3.4% (higher in resected NSCLC: 11%), and hypothyroidism in 8% overall, with even higher rates in HNSCC (16%), cHL (17%), and resected

NSCLC (22%). Most thyroid disorders required long-term hormone therapy; treatment discontinuation was rare, and patients who had therapy withheld were able to restart after improvement. Pembrolizumab can also cause Type 1 diabetes mellitus (0.2%), sometimes presenting with DKA; all affected patients required lifelong insulin, with rare discontinuation and all withheld cases successfully re-initiated after stabilization.

Nephritis: Pembrolizumab can cause immune-mediated nephritis, occurring in 0.3% of patients, including rare Grade 4–2 events. Most affected patients (89%) required systemic corticosteroids. Nephritis led to permanent discontinuation in 0.1% and temporary withholding in another 0.1%, with all withheld patients successfully restarting treatment without recurrence. Overall, nephritis resolved in 56% of cases.

Dermatologic immune reactions: ~1–2%; includes rare SJS/TEN. Steroids needed in ~40%. Most resolve; small recurrence rate.

Other immune-mediated toxicities (<1%): Myocarditis, pericarditis, vasculitis, encephalitis, neuropathies (including Guillain-Barré), uveitis (may mimic VKH), pancreatitis, gastritis/duodenitis, myositis/rhabdomyolysis, arthritis, hypoparathyroidism, and hematologic immune disorders (e.g., hemolytic anemia, aplastic anemia, HLH). Solid-organ transplant rejection has occurred.

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. Interrupt or slow the rate of infusion for mild (Grade 1) or moderate (Grade 2) infusion-related reactions. For severe (Grade 3) or life-threatening (Grade 4) infusion-related reactions, stop infusion and permanently discontinue Pembrolizumab.

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. Transplant-related complications include hyperacute graft-versus-host-disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT.

Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1 blocking antibody prior to or after an allogeneic HSCT.

Increased Mortality in Patients with Multiple Myeloma when Pembrolizumab is Added to a Thalidomide Analogue and

Dexamethasone

In two randomized trials in patients with multiple myeloma, the addition of Pembrolizumab to a thalidomide analogue plus dexamethasone, a use for which no PD-1 or PD-L1 blocking antibody is indicated, resulted in increased mortality. 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. Animal models link the PD-1/PD-L1 signaling pathway with maintenance of pregnancy through induction of maternal immune tolerance to fetal tissue. Advise women of the potential risk to a fetus.

Advise females of reproductive potential to use effective contraception during treatment with Pembrolizumab and for 4 months after the last dose.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pembrolizumab can harm the fetus based on its mechanism of action. PD-1/PD-L1 signaling is required for maternal immune tolerance during pregnancy, and blocking this pathway may disrupt that tolerance. Human IgG4 crosses the placenta, so the drug can reach the fetus. No human pregnancy data exist. In animal and literature-based models, PD-1/PD-L1 blockade increased fetal loss but did not cause structural malformations; however, offspring showed immune-mediated abnormalities. Pregnant women should be warned of potential risks. Background U.S. rates of major birth defects are 2–4% and miscarriage 15–20%.

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. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited systemic exposure in the breastfed child to Pembrolizumab are unknown. 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.

Females and Males of Reproductive Potential

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating Pembrolizumab.

Contraception

Pembrolizumab can cause fetal harm when administered to a pregnant. Advise females of reproductive potential to use effective contraception during treatment with Pembrolizumab and for 4 months after the last dose.

Pediatric Use

Pembrolizumab monotherapy is established as safe and effective in pediatric patients with melanoma, cHL, PMBCL, MCC, MSI-H/dMMR tumors, and TMB-H cancers, based on adult efficacy data supported by pediatric PK and safety findings. In KEYNOTE-051 (n=173; ages 6 months–17 years), patients received 2 mg/kg every 3 weeks for a median of 2.1 months. Adverse events occurring ≥10% more often in children than adults included fever, vomiting, headache, abdominal pain, lymphopenia, and leukopenia; lab abnormalities with ≥10% higher incidence included leukopenia, neutropenia, thrombocytopenia, and Grade 3 anemia. Safety and effectiveness in other pediatric indications remain unestablished.

Geriatric Use

Across trials in melanoma, NSCLC, HNSCC, urothelial cancer, TNBC, endometrial cancer, RCC, and cervical cancer, Pembrolizumab showed generally similar safety and effectiveness in patients ≥65 years compared with younger adults. An exception was classical Hodgkin lymphoma, where patients ≥65 years had a higher rate of serious adverse reactions (50% vs. 24%) and too few elderly participants to assess efficacy differences. Another key signal was with Pembrolizumab plus Enfortumab Vedotin: patients ≥75 years had more fatal adverse reactions, with rates of 7% vs. 4% in urothelial cancer and 12% vs. 4% in MIBC. In all other evaluated studies, no meaningful age-related differences in outcomes were observed.

PHARMACEUTICAL INFORMATION

Storage

Store vials under refrigeration at 2°C to 8°C (36°F to 46°F) in original carton to protect from light. Do not freeze. Do not shake. Keep out of the reach of children.

How Supplied

PEMREST Injection: Each box contains a clear glass vial containing Pembrolizumab INN 100 mg in 4 mL solution (25 mg/ mL).

Manufactured by
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