Navigo™

Nivolumab IV Infusion

Presentation
Navigo™ 40 IV infusion: Each vial contains Nivolumab INN 40 mg in 4 ml sterile solution for IV infusion.

Description
Nivolumab is a human immunoglobulin G4 (IgG4) 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. Combined nivolumab (anti-PD-1) and ipilimumab (anti-CTLA-4) mediated inhibition results in enhanced T-cell function that is greater than the effects of either antibody alone, and results in improved anti-tumor responses in metastatic melanoma and advanced RCC.

Indications and Uses
Nivolumab is a programmed death receptor-1 (PD-1)-blocking antibody indicated for:
•Melanoma
•Non-Small Cell Lung Cancer (NSCLC)
•Malignant Pleural Mesothelioma
•Renal Cell Carcinoma (RCC)
•Classical Hodgkin Lymphoma (cHL)
•Squamous Cell Carcinoma of the Head and Neck (SCCHN)
•Urothelial Carcinoma
•Colorectal Cancer
•Hepatocellular Carcinoma (HCC)
•Esophageal Cancer
•Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

Dosage and Administrations
Administer by intravenous infusion after dilution based upon recommended infusion rate for each indication.
Unresectable or metastatic melanoma
- 240 mg every 2 weeks or 480 mg every 4 weeks
- 1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks

Adjuvant treatment of melanoma
- 240 mg every 2 weeks or 480 mg every 4 weeks. (2.2)

Neoadjuvant treatment of resectable (tumors ≥4 cm or node positive) non-small cell lung cancer
- 360 mg with platinum-doublet chemotherapy on the same day every 3 weeks for 3 cycles

Metastatic non-small cell lung cancer
- 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks
- 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks and 2 cycles of platinum-doublet chemotherapy
- 240 mg every 2 weeks or 480 mg every 4 weeks

Malignant pleural mesothelioma
- 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks

Advanced renal cell carcinoma
- 3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks
- 240 mg every 2 weeks or 480 mg every 4 weeks administered in combination with cabozantinib 40 mg once daily without food
- 240 mg every 2 weeks or 480 mg every 4 weeks

Classical Hodgkin lymphoma
- 240 mg every 2 weeks or 480 mg every 4 weeks

Recurrent or metastatic squamous cell carcinoma of the head and neck
- 240 mg every 2 weeks or 480 mg every 4 weeks

Adjuvant treatment of urothelial carcinoma
- 240 mg every 2 weeks or 480 mg every 4 weeks

Locally advanced or metastatic urothelial carcinoma
- 240 mg every 2 weeks or 480 mg every 4 weeks

Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer
- Adult and pediatric patients weighing 40 kg or greater: 240 mg every 2 weeks or 480 mg every 4 weeks
- Pediatric patients weighing less than 40 kg: 3 mg/kg every 2 weeks
- Adult and pediatric patients weighing 40 kg or greater: 3 mg/kg followed by ipilimumab 1 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks

Hepatocellular carcinoma
- 1 mg/kg followed by ipilimumab 3 mg/kg on the same day every 3 weeks for 4 doses, then 240 mg every 2 weeks or 480 mg every 4 weeks

Adjuvant treatment of resected esophageal or gastroesophageal cancer
- 240 mg every 2 weeks or 480 mg every 4 weeks for total treatment duration of 1 year

Esophageal squamous cell carcinoma
- 240 mg every 2 weeks or 480 mg every 4 weeks in combination with chemotherapy regimen of fluoropyrimidine- and platinum-containing chemotherapy
- 3 mg/kg every 2 weeks or 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks
- 240 mg every 2 weeks or 480 mg every 4 weeks

Gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma (GC, GEJC, or EAC)
- 360 mg every 3 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 3 weeks
- 240 mg every 2 weeks with fluoropyrimidine- and platinum-containing chemotherapy every 2 weeks

Preparation and Administration

- The required volume of Nivolumab should be withdrawn and transfer into an intravenous container
- Nivolumab should be diluted with either 0.9% Sodium Chloride Injection, USP or 5% Dextrose Injection, USP to prepare an infusion with a final concentration ranging from 1 mg/mL to 10 mg/mL. The total volume of infusion must not exceed 160 mL.
- For adult and pediatric patients with body weight 40 kg or greater, total volume of infusion should not exceed 160 mL.
- For adult and pediatric patients with body weight less than 40 kg, total volume of infusion should not exceed 4 mL/kg of body weight.
- Diluted solution should be mixed by gentle inversion and should not be shaken
- Partially used vials or empty vials of NAVILUMAB should be discarded
- The product does not contain a preservative
- After preparation, the diluted solution should be stored either:
    - At room temperature and room light for not more than 8 hours from the time of preparation to end of the infusion. Diluted solution should be discarded if not used within 8 hours from the time of preparation; or
    - Under refrigeration at 2°C to 8°C (36°F to 46°F) and protected from light for not more than 7 days from the time of preparation to end of infusion. Diluted solution should be discarded if not used within 7 days from the time of preparation.
- Should not be frozen
- Administer the infusion, after dilution, over 30 minutes through an intravenous line containing a sterile, non-pyrogenic, low protein binding in-line filter (pore size of 0.2 micrometer to 1.2 micrometer).
- Do not co-administer other drugs through the same intravenous line.

Side Effects
Most common adverse reactions (incidence ≥20%) in patients were:
- As a single agent: fatigue, rash, musculoskeletal pain, pruritus, diarrhea, nausea, asthenia, cough, dyspnea, constipation, decreased appetite, back pain, arthralgia, upper respiratory tract infection, pyrexia, headache, abdominal pain, vomiting, and urinary tract infection
- In combination with ipilimumab: fatigue, diarrhea, rash, pruritus, nausea, musculoskeletal pain, pyrexia, cough, decreased appetite, vomiting, abdominal pain, dyspnea, upper respiratory tract infection, arthralgia, headache, hypothyroidism, constipation, decreased weight, and dizziness
- In combination with platinum-doublet chemotherapy: nausea, constipation, fatigue, decreased appetite, and rash
- In combination with cabozantinib: diarrhea, fatigue, hepatotoxicity, palmar-plantar erythrodysaesthesia syndrome, stomatitis, rash, hypertension, hypothyroidism, musculoskeletal pain, decreased appetite, nausea, dysgeusia, abdominal pain, cough and upper respiratory tract infection
- In combination with fluoropyrimidine- and platinum-containing chemotherapy: nausea, peripheral neuropathy, decreased appetite, fatigue, constipation, stomatitis, diarrhea, vomiting, abdominal pain, and musculoskeletal pain

Contraindications
None

Warning & Precautions
- Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis and hepatotoxicity, immune-mediated endocrinopathies, immune-mediated dermatologic adverse reactions, and immune-mediated nephritis and renal dysfunction
- Monitor for early identification and management. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. Withhold or permanently discontinue based on severity and type of reaction
- Infusion-related reactions: Interrupt, slow the rate of infusion, or permanently discontinue Nivolumab based on severity of reaction
- Complications of allogeneic HSCT: Fatal and other serious complications can occur in patient who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1 blocking antibody
- Embryo-Fetal toxicity: Can cause fetal harm. Advise females of reproductive potential of potential risk to a fetus and to use effective contraception
- 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 clinical trials.

Use in specific population
Pregnancy: Nivolumab can cause fetal harm when administered to a pregnant woman.
Lactation: There are no data on the presence of nivolumab in human milk, the effects on the breastfed child, or the effects on milk production.
Contraception: Based on its mechanism, Nivolumab can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with Nivolumab and for at least 5 months following the last dose of Nivolumab.
Pediatric Use: The safety and effectiveness of Nivolumab have not been established in pediatric patients less than 12 years old with MSI-H or dMMR mCRC or in pediatric patients less than 18 years old for the other approved indications.
Geriatric Use: No overall difference in safety was reported between elderly patients and younger patients. In elderly patients with intermediate or poor risk, no overall difference in effectiveness was reported.

Storage
Store at 2-8° C (in a refrigerator). Do not freeze. Keep away from light and out of reach of children.

Commercial Packaging
Navigo™ 40 IV infusion: Each box contains 1 vial of 4 ml sterile solution for IV infusion

Manufactured by
Incepta Pharmaceuticals Ltd
Savar, Dhaka, Bangladesh
™ Trademark

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