NIVOREST

Nivolumab INN

Everest

COMPOSITION

NIVOREST 100: Each 10 mL solution contains Nivolumab INN 100 mg (10 mg/mL).
NIVOREST 40: Each 4 mL solution contains Nivolumab INN 40 mg (10 mg/mL).

PHARMACOLOGY

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. 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, In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth.
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. In murine syngeneic tumor models, dual blockade of PD-1 and CTLA-4 resulted in increased anti-tumor activity.

INDICATION

NIVOREST is a programmed death receptor-1 (PD-1)-blocking antibody indicated for the treatment of:

Melanoma

In adult and pediatric (12 years and older) patients with unresectable or metastatic melanoma, as a single agent or in combination with ipilimumab.
For the adjuvant treatment of adult and pediatric patients 12 years and older with completely resected Stage IIB, Stage IIC, Stage III, or Stage IV melanoma.

Non-Small Cell Lung Cancer (NSCLC)

In adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer in the neoadjuvant setting, in combination with platinum-doublet chemotherapy.
Adult patients with resectable (tumors ≥4 cm or node positive) non-small cell lung cancer and no known EGFR mutations or ALK rearrangements, for neoadjuvant treatment, in combination with platinum-doublet chemotherapy, followed by single-agent OPDIVO as adjuvant treatment after surgery.
Adult patients with metastatic non-small cell lung cancer expressing PD-L1 (≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, as first-line treatment in combination with ipilimumab.
Adult patients with metastatic or recurrent non-small cell lung cancer with no EGFR or ALK genomic tumor aberrations as first-line treatment, in combination with ipilimumab and 2 cycles of platinum-doublet chemotherapy.
Adult patients with metastatic non-small cell lung cancer and progression on or after platinum-based chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving NIVOREST.

Malignant Pleural Mesothelioma

Adult patients with unresectable malignant pleural mesothelioma, as first-line treatment in combination with ipilimumab.

Renal Cell Carcinoma (RCC)

Adult patients with intermediate or poor risk advanced renal cell carcinoma, as a first-line treatment in combination with ipilimumab.
Adult patients with advanced renal cell carcinoma, as a first-line treatment in combination with cabozantinib.
Adult patients with advanced renal cell carcinoma who have received prior anti- angiogenic therapy.

Classical Hodgkin Lymphoma (cHL)

Adult patients with classical Hodgkin lymphoma that has relapsed or progressed aftera: autologous hematopoietic stem cell transplantation (HSCT) and brentuximab vedotin, or, 3 or more lines of systemic therapy that includes autologous HSCT.

Squamous Cell Carcinoma of the Head and Neck (SCCHN)

Adult patients with recurrent or metastatic squamous cell carcinoma of the head and neck with disease progression on or after a platinum-based therapy.

Urothelial Carcinoma

Adjuvant treatment of adult patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection of UC.
Adult patients with unresectable or metastatic urothelial carcinoma, as first-line treatment in combination with cisplatin and gemcitabine.
Adult patients with locally advanced or metastatic urothelial carcinoma who: have disease progression during or following platinum-containing chemotherapy; have disease progression within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.

Colorectal Cancer

Adult and pediatric (12 years and older) patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer (CRC) in combination with ipilimumab.
Adult and pediatric (12 years and older) patients with microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan.

Hepatocellular Carcinoma (HCC)

Adult patients with unresectable or metastatic hepatocellular carcinoma (HCC), as a first-line treatment in combination with ipilimumab.
In combination with ipilimumab in adult patients with unresectable or metastatic HCC who have been previously treated with sorafenib.

Esophageal Cancer

Adult patients with completely resected esophageal or gastroesophageal junction cancer with residual pathologic disease, who have received neoadjuvant chemoradiotherapy (CRT).
Adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with fluoropyrimidine- and platinum- containing chemotherapy whose tumors express PD-L1 (≥1).
Adult patients with unresectable advanced or metastatic esophageal squamous cell carcinoma as first-line treatment in combination with ipilimumab whose tumors express PD-L1 (≥1).
Adult patients with unresectable advanced, recurrent or metastatic esophageal squamous cell carcinoma (ESCC) after prior fluoropyrimidine- and platinum-based chemotherapy.

Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

Adult patients with advanced or metastatic gastric cancer, gastroesophageal junction cancer, and esophageal adenocarcinoma whose tumors express PD-L1 (≥1) in combination with fluoropyrimidine- and platinum-containing chemotherapy.

[a] 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 confirmatory trials.

DOSAGE AND ADMINISTRATION

The recommended dosages of intravenous NIVOREST as a single agent are presented in Table 1.

Administer NIVOREST as a 30-minute intravenous infusion.

Table 1: Recommended Dosages for Intravenous NIVOREST as a Single Agent

Indication	Recommended NIVOREST Dosage	Duration of Therapy
Metastatic non-small cell lung cancer	240 mg every 2 weeks or 480 mg every 4 weeks	Until disease progression or Unacceptable toxicity
Advanced renal cell carcinoma		
Classical Hodgkin lymphoma		
Squamous cell carcinoma of the head and neck		
Locally advanced or metastatic urothelial carcinoma		
Esophageal squamous cell carcinoma		
Unresectable or metastatic melanoma	Adult patients and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks	Until disease progression or unacceptable toxicity
	Pediatric patients age 12 years and older and weighing less than 40 kg: 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks	
Adjuvant treatment of melanoma	Adult patients and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks	Until disease recurrence or unacceptable toxicity for up to 1 year
	Pediatric patients	

	Pediatric patients age 12 years and older and weighing less than 40 kg: 3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks	
Adjuvant treatment of urothelial carcinoma (UC)	240 mg every 2 weeks or 480 mg every 4 weeks	Until disease recurrence or unacceptable toxicity for up to 1 year
Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following prior treatment for metastatic disease	Adult patients and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks	Until disease progression or unacceptable toxicity
	Pediatric patients age 12 years and older and weighing less than 40 kg: 3 mg/kg every 2 weeks	
Adjuvant treatment of resected esophageal or gastroesophageal junction cancer	240 mg every 2 weeks or 480 mg every 4 weeks	Until disease progression or unacceptable toxicity for a total treatment duration of 1 year

The recommended dosages of NIVOREST in combination with other therapeutic agents are presented in Table 2. Administer NIVOREST on the same day as other therapeutic agents. Refer to the respective Prescribing Information for each therapeutic agent administered in combination with NIVOREST for the recommended dosage information, as appropriate.

Table 2: Recommended Dosages of Intravenous NIVOREST in Combination with Other Therapeutic Agents

Unresectable or metastatic melanoma	1 mg/kg every 3 weeks with ipilimumab 3 mg/kg	In combination with ipilimumab for a maximum of 4 doses or until unacceptable toxicity, whichever occurs earlier
	Adult patients and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks	After completing 4 doses of combination therapy, administer as single agent until disease progression or unacceptable toxicity
	Pediatric patients age 12 years and older and weighing less than 40 kg: 3 mg/kg every 2 weeks Or 6 mg/kg every 4 weeks	
Neoadjuvant treatment of resectable non-small cell lung cancer	360 mg every 3 weeks with platinum-doublet chemotherapy on the same day every 3 weeks	In combination with platinum-doublet chemotherapy for 3 cycles
Neoadjuvant and adjuvant treatment of resectable non-small cell lung cancer	Neoadjuvant: 360 mg every 3 weeks with platinum-doublet chemotherapy on the same day every 3 weeks	Neoadjuvant treatment in combination with chemotherapy for up to 4 cycles or until disease progression or unacceptable toxicity, followed by adjuvant treatment with Nivolumab as a single agent after surgery for up to 13 cycles (approximately 1 year) or until disease recurrence or unacceptable toxicity
	Adjuvant: 480 mg every 4 weeks	
Metastatic non-small cell lung cancer expressing PD-L1	360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks	In combination with ipilimumab until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression
Metastatic or recurrent nonsmall cell lung cancer	360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks and histology-based platinum-doublet chemotherapy every 3 weeks	In combination with Ipilimumab until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression
		2 cycles of histology based platinum-doublet chemotherapy
Malignant pleural mesothelioma	360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks	In combination with ipilimumab until disease progression, unacceptable toxicity, or up to 2 years in patients without disease progression
Advanced renal cell carcinoma	3 mg/kg every 3 weeks with ipilimumab 1 mg/kg	In combination with ipilimumab for 4 doses
	240 mg every 2 weeks or 480 mg every 4 weeks	After completing 4 doses of combination therapy with ipilimumab, administer as single agent until disease progression or unacceptable toxicity
	240 mg every 2 weeks or 480 mg every 4 weeks Administer Nivolumab in combination with Cabozantinib 40 mg orally once daily without food	NIVOREST: Until disease progression, unacceptable toxicity, or up to 2 years
		Cabozantinib: Until disease progression or unacceptable toxicity
First-line unresectable or metastatic urothelial carcinoma	360 mg every 3 weeks Administer Nivolumab in combination with cisplatin and gemcitabine on the same day every 3 weeks	In combination with cisplatin and gemcitabine for up to 6 cycles
	240 mg every 2 weeks or 480 mg every 4 weeks	After completing up to 6 cycles of combination therapy, administer as single agent until disease progression, unacceptable toxicity, or up to 2 years from first dose
Microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer	Adult patients and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 3 weeks with ipilimumab 1 mg/kg	In combination with ipilimumab for a maximum of 4 doses
	Pediatric patients age of 4 doses 12 years and older and weighing less than 40 kg: 3 mg/kg every 3 weeks with ipilimumab 1 mg/kg	
	Adult patients and pediatric patients age 12 years and older and weighing 40 kg or more: 240 mg every 2 weeks or 480 mg every 4 weeks	After completing a maximum of 4 doses of combination therapy, administer as single agent until disease progression or unacceptable toxicity, or up to 2 years
	Pediatric patients age 12 years and older and weighing less than 40 kg:	

	3 mg/kg every 2 weeks or 6 mg/kg every 4 weeks	
Hepatocellular carcinoma	1 mg/kg every 3 weeks with ipilimumab 3 mg/kg	In combination with ipilimumab for a maximum of 4 doses
	240 mg every 2 weeks or 480 mg every 4 weeks	After completing a maximum of 4 doses of combination therapy, administer as single agent until disease progression, unacceptable toxicity, or up to 2 years
Esophageal squamous cell carcinoma	240 mg every 2 weeks Or 480 mg every 4 weeks Administer Nivolumab in combination with fluoropyrimidine- and platinum-containing chemotherapy	NIVOREST Until disease progression, unacceptable toxicity, or up to 2 years
		Chemotherapy: Until disease progression or unacceptable toxicity
	3 mg/kg every 2 weeks or 360 mg every 3 weeks with ipilimumab 1 mg/kg every 6 weeks	In combination with ipilimumab until disease progression, unacceptable toxicity, or up to 2 years
Gastric cancer, Gastroesophageal junction cancer, and Esophageal adenocarcinoma	240 mg every 2 weeksm with fluoropyrimidine and platinum-containing chemotherapy every 2 weeks Or 360 mg every 3 weeks with fluoropyrimidine and platinum-containing chemotherapy every 3 weeks	Until disease progression, unacceptable toxicity, or up to 2 years

DOSAGE MODIFICATIONS

No dose reduction for NIVOREST is recommended. In general, withhold NIVOREST for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue NIVOREST for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone or equivalent per day within 12 weeks of initiating steroids.

Dosage modifications for NIVOREST or NIVOREST in combination for adverse reactions that require management different from these general guidelines are summarized in Table 3 and Table 4.

When NIVOREST is administered in combination with ipilimumab, withhold or permanently discontinue both ipilimumab and NIVOREST for an adverse reaction meeting these dose modification guidelines.

Table 3: Recommended Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity	Dosage Modification
Immune-Mediated Adverse Reactions.		
Pneumonitis	Grade 2	Withhold[a]
	Grade 2 or 4	Permanently discontinue
Colitis For colitis in patients treated with combination therapy with ipilimumab, see Table 4.	Grade 2 or 3	Withhold[a]
	Grade 4	Permanently discontinue
Hepatitis with no tumor involvement of the liver For liver enzyme elevations in patients treated with combination therapy with ipilimumab, see Table 4.	AST/ALT increases to >3 and ≤8 times ULN or Total bilirubin increases to >1i5 and ≤3 times ULN	Withhold[a]
	AST or ALT increases to >8 times ULN or Total bilirubin increases to >3 times ULN	Permanently discontinue
Hepatitis with tumor involvement of the liverb For liver enzyme elevations in patients treated with combination therapy with ipilimumab, see Table 4.	Baseline AST/ALT is >1 and ≤3 times ULN and increases to >5 and ≤10 times ULN or Baseline AST/ALT is >3 and ≤5 times ULN and increases to >8 and ≤10 times ULN	Withhold[a]
	AST/ALT increases to >10 times ULN or Total bilirubin increases to >3 times ULN	Permanently discontinue
Endocrinopathiesc	Grade 3 or 4	Withhold until clinically stable or permanently discontinue depending on severity
Nephritis with Renal Dysfunction	Grade 2 or 3 increased blood creatinine	Withhold[a]
	Grade 4 increased blood creatinine	Permanently discontinue
Exfoliative Dermatologic Conditions	Suspected SJS, TEN, or DRESS	Withhold[a]
	Confirmed SJS, TEN, or DRESS	Permanently discontinue
Myocarditis	Grades 2, 3, or 4	Permanently discontinue
Neurological Toxicities	Grade 2	Withhold[a]
	Grade 3 or 4	Permanently discontinue
Other Adverse Reactions		
Infusion-Related Reactions	Grade 1 or 2	Interrupt or slow the rate of infusion
	Grade 3 or 4	Permanently discontinue

a Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of last dose or inability to reduce prednisone to 10 mg per day (or equivalent) or less within 12 weeks of initiating steroids.
b If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue NIVOREST based on recommendations for hepatitis with no liver involvement.
c Depending on clinical severity, consider withholding for Grade 2 endocrinopathy until symptom improvement with hormone replacement. Resume once acute symptoms have resolved.
ALT = alanine aminotransferase, AST = aspartate aminotransferase, DRESS = Drug Rash with Eosinophilia and Systemic Symptoms, SJS = Stevens Johnson Syndrome, TEN = toxic epidermal necrolysis, ULN = upper limit normal

Table 4: Recommended Dosage Modifications for Adverse Reactions in Patients Treated with Combination Therapy

Treatment	Adverse Reaction	Severity	Dosage Modification
NIVOREST in combination with ipilimumab	Colitis	Grade 2	Withhold[a]
		Grade 3 or 4	Permanently discontinue
	Hepatitis with no tumor involvement of the liver or Hepatitis with tumor involvement of the livere/ non-HCC	AST/ALT increases to >3 times ULN and ≤5 times ULN or Total bilirubin increases to ≥1i5 and ≤3 times ULN.	Withhold[a]
		AST or ALT >5 times ULN or Total bilirubin >3 times ULN.	Permanently discontinue
	Hepatitis with tumor involvement of the liverb/HCC	Baseline AST/ALT is >1 and ≤3 times ULN and increases to >5 and ≤10 times ULN or Baseline AST/ALT is >3 and ≤5 times ULN and increases to >8 and ≤10 times ULNi	Withhold[a]
		AST/ALT increases to >10 times ULN or Total bilirubin increases to >3 times ULNi	Permanently discontinue
NIVOREST in combination with ipilimumab	Liver enzyme elevations	ALT or AST >3 times ULN but ≤10 times ULN with concurrent total bilirubin <2 times ULN	Withhold[c] both NIVOREST and cabozantinib until adverse reactions recoverd to Grades 0-1
		ALT or AST >10 times ULN or >3 times ULN with concurrent total bilirubin ≥2 times ULN	Permanently discontinue[c] both NIVOREST and cabozantinib

CONTRAINDICATION

None

WARNINGS AND PRECAUTIONS

Severe and Fatal Immune-Mediated Adverse Reactions

NIVOREST

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NIVOREST is a monoclonal antibody that belongs to a class of drugs that bind to either the programmed death-receptor 1 (PD-1) or the PD-ligand 1 (PD-L1), blocking the PD-1/PD-L1 pathway, thereby removing inhibition of the immune response, potentially breaking peripheral tolerance and inducing immune-mediated adverse reactions. Important immune-mediated adverse reactions listed under Warnings and Precautions may not include all possible severe and fatal immune-mediated reactions.

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue. Immune-mediated adverse reactions can occur at any time after starting treatment with a PD-1/PD-L1 blocking antibody. While immune-mediated adverse reactions usually manifest during treatment with PD-1/PD-L1 blocking antibodies, immune-mediated adverse reactions can also manifest after discontinuation of PD-1/PD-L1 blocking antibodies.

Early identification and management of immune-mediated adverse reactions are essential to ensure safe use of PD-1/PD-L1 blocking antibodies. Monitor patients closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

Withhold or permanently discontinue NIVOREST depending on severity. In general, if Nivolumab requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroid therapy.

Toxicity management guidelines for adverse reactions that do not necessarily require systemic steroids (e.g., endocrinopathies and dermatologic reactions) are discussed below.

Infusion-Related Reactions
NIVOREST can cause severe infusion-related reactions, which have been reported in <1% of patients in clinical trials. Discontinue NIVOREST in patients with severe or life-threatening infusion-related reactions. Interrupt or slow the rate of infusion in patients with mild or moderate infusion-related reactions.

Complications of Allogeneic Hematopoietic Stem Cell Transplantation
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 receptor blocking antibody. Transplant-related complications include hyperacute graftversus- 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 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 receptor blocking antibody prior to or after an allogeneic HSCT.

Embryo-Fetal Toxicity
Based on its mechanism of action and data from animal studies, NIVOREST can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of nivolumab to cynomolgus monkeys from the onset of organogenesis through delivery resulted in increased abortion and premature infant death. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with NIVOREST and for 5 months after the last dose.

Increased Mortality in Patients with Multiple Myeloma when NIVOREST Is Added to a Thalidomide Analogue and Dexamethasone
In randomized clinical trials in patients with multiple myeloma, the addition of a PD-1 blocking antibody, including NIVOREST, 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 clinical trials.

SIDE EFFECTS

The most common side effects are feeling tired, rash, pain in muscles, bones, and joints, itching, diarrhea, nausea, weakness, cough, shortness of breath, constipation, decreased appetite, back pain, upper respiratory tract infection, fever, headache, stomach-area (abdominal) pain, vomiting, urinary tract infection.

DRUG INTERACTIONS

When NIVOREST 3 mg/kg every 3 weeks was administered in combination with ipilimumab 1 mg/kg every 3 weeks, the CL of nivolumab and ipilimumab were unchanged compared to nivolumab or ipilimumab administered alone.

When NIVOREST 1 mg/kg every 3 weeks was administered in combination with ipilimumab 3 mg/kg every 3 weeks, the CL of nivolumab was increased by 29% compared to NIVOREST administered alone and the CL of ipilimumab was unchanged compared to ipilimumab administered alone.

When NIVOREST 3 mg/kg every 2 weeks was administered in combination with ipilimumab 1 mg/kg every 6 weeks, the CL of nivolumab was unchanged compared to NIVOREST administered alone and the CL of ipilimumab was increased by 30% compared to ipilimumab administered alone.

When NIVOREST 360 mg every 3 weeks was administered in combination with ipilimumab 1 mg/kg every 6 weeks and chemotherapy, the CL of nivolumab was unchanged compared to NIVOREST administered alone and the CL of ipilimumab increased by 22% compared to ipilimumab administered alone.

USE IN SPECIFIC POPULATIONS

Pregnancy
Based on findings from animal studies and its mechanism of action, NIVOREST can cause fetal harm when administered to a pregnant woman. There are no available data on NIVOREST use in pregnant women. Pregnant women should be advised of the potential risk to a fetus.

LACTATION

Risk Summary
There are no data on the presence of nivolumab in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment and for 5 months after the last dose of NIVOREST.

Females and Males of Reproductive Potential
Pregnancy Testing
Verify the pregnancy status of females of reproductive potential prior to initiating NIVOREST.

Contraception
NIVOREST can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with NIVOREST and for 5 months following the last dose.
Pediatric population
The safety and effectiveness of NIVOREST have been established in pediatric patients aged 12 years and older.

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

NIVOREST 100: Each box contains a clear glass vial containing Nivolumab 100 mg in 10 mL solution.
NIVOREST 40: Each box contains a clear glass vial containing Nivolumab 40 mg in 4 mL solution.

Manufactured by
Everest Pharmaceuticals Ltd.
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www.everestpharmabd.com

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