SK+F

ESKAYEF PHARMACEUTICALS LTD.

Murapara, Rupganj, Narayanganj 1464, Bangladesh.

Packaging Material Code: R/PM2416
Version No.: V01

100 mm

280 mm

Nab-Paclitor™

Paclitaxel USP (Protein-Bound Particles
for Injectable Suspension) (Albumin-Bound)

DESCRIPTION

Nab-Paclitor™ is a preparation of Paclitaxel Protein-Bound Particles (Albumin-Bound). Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is a microtubule inhibitor that promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization. This stability results in the inhibition of the normal dynamic reorganization of the microtubule network which is essential for vital interphase and mitotic cellular functions. Paclitaxel induces abnormal arrays or "bundles" of microtubules throughout the cell cycle and multiple asters of microtubules during mitosis.

INDICATIONS

Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is indicated for the treatment of:

- Metastatic breast cancer, after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
- Locally advanced or metastatic non-small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.
- Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with Gemcitabine.

DOSAGE AND ADMINISTRATION

Nab-Paclitor™ recommended dose for-

- **Metastatic Breast Cancer (MBC):** 260 mg/m^2 intravenously over 30 minutes every 3 weeks.
- **Non-Small Cell Lung Cancer (NSCLC):** 100 mg/m^2 intravenously over 30 minutes on Days 1, 8, and 15 of each 21-day cycle; administer carboplatin on Day 1 of each 21-day cycle immediately after Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-bound) use.
- **Adenocarcinoma of the Pancreas:** 125 mg/m^2 intravenously over 30-40 minutes on Days 1, 8 and 15 of each 28-day cycle; administer Gemcitabine on Days 1, 8 and 15 of each 28-day cycle immediately after Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-bound) use.

Use in Patients with Hepatic Impairment: Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is not recommended for use in patients with AST greater than 10 x the upper limit of normal (ULN); or bilirubin greater than 5 x ULN or patients with metastatic adenocarcinoma of the pancreas who have moderate to severe hepatic impairment. For MBC or NSCLC, reduce starting dose in patients with moderate to severe hepatic impairment.
Dose Reductions for Adverse Reactions: Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicities.

Reconstitution:

1. Aseptically, reconstitute each vial by injecting 20 mL of 0.9% Sodium Chloride Injection.
2. Slowly inject the 20 mL of 0.9% Sodium Chloride Injection, over a minimum of 1 minute, using the sterile syringe to direct the solution flow onto the INSIDE WALL OF THE VIAL.

3. DO NOT INJECT the 0.9% Sodium Chloride Injection, directly onto the lyophilized cake as this will result in foaming.
4. Once the injection is complete, allow the vial to sit for a minimum of 5 minutes to ensure proper wetting of the lyophilized cake/powder.
5. Gently swirl and/or invert the vial slowly for at least 2 minutes until complete dissolution of any cake/powder occurs. Avoid generation of foam.
6. If foaming or clumping occurs, stand solution for at least 15 minutes until foam subsides.

Each mL of the reconstituted formulation will contain 5 mg/mL Paclitaxel. The reconstituted suspension should be milky and homogenous without visible particulates. If particulates or settling are visible, the vial should be gently inverted again to ensure complete resuspension prior to use. Discard the reconstituted suspension if precipitates are observed. Discard any unused portion.
Calculate the exact total dosing volume of 5 mg/mL suspension required for the patient and slowly withdraw the dosing volume of the reconstituted suspension from the vial(s) into a syringe: Dosing volume (mL)=Total dose (mg)/5 (mg/mL).

Inject the appropriate amount of reconstituted Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) into an empty, sterile intravenous bag [plasticized polyvinyl chloride (PVC) containers, PVC or non-PVC type intravenous bag]. The use of specialized DEHP-free solution containers or administration sets is not necessary to prepare or administer Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) infusions. The use of medical devices containing silicone oil as a lubricant (i.e., syringes and intravenous bags) to reconstitute and administer Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) may result in the formation of proteinaceous strands. Visually inspect the reconstituted Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) suspension in the intravenous bag prior to administration. Discard the reconstituted suspension if proteinaceous strands, particulate matter, or discoloration are observed.

Stability of Reconstituted Suspension in the Vial: Reconstituted Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) in the vial should be used immediately, but may be refrigerated at 2 °C to 8 °C (36 °F to 46 °F) for a maximum of 24 hours, if necessary. If not used immediately, each vial of reconstituted suspension should be replaced in the original carton to protect it from bright light. Discard any unused portion.
Stability of Reconstituted Suspension in the Infusion Bag: The suspension for infusion when prepared as recommended in an infusion bag should be used immediately, but may be refrigerated at 2 °C to 8 °C (36 °F to 46 °F) and protected from bright light for a maximum of 24 hours. The total combined refrigerated storage time of reconstituted Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) in the vial and in the infusion bag is 24 hours. This may be followed by storage in the infusion bag at ambient temperature

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(approximately 25 °C) and lighting conditions for a maximum of 4 hours.

Important Administration Instructions

- DO NOT SUBSTITUTE FOR OR WITH OTHER Paclitaxel FORMULATIONS. Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) has different dosage and administration instructions from other Paclitaxel products.
- Closely monitor the infusion site for extravasation or drug infiltration during administration. Limiting the infusion of Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) to 30 minutes may reduce the risk of infusion-related reactions.

CONTRAINDICATIONS:

Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) is contraindicated in patients with:

- Baseline neutrophil counts of < 1,500 cells/mm^3
- A history of severe hypersensitivity reactions to Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound)

SIDE EFFECTS:

- Metastatic Breast Cancer: The most common adverse reactions are alopecia, neutropenia, sensory neuropathy, abnormal ECG, fatigue/asthenia, myalgia/arthralgia, AST elevation, alkaline phosphatase elevation, anemia, nausea, infections, and diarrhea.
- Non-Small Cell Lung Cancer: The most common adverse reactions are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue.
- Adenocarcinoma of the Pancreas: The most common adverse reactions are neutropenia, fatigue, peripheral neuropathy, nausea, alopecia, peripheral edema, diarrhea, pyrexia, vomiting, decreased appetite, rash, and dehydration.

PRECAUTIONS AND WARNINGS:

- Paclitaxel Protein-Bound particles for injectable suspension (Albumin-Bound) can cause sensory neuropathy frequently, which may require dose reduction or treatment interruption.
- Sepsis occurred in patients with or without neutropenia who received protein-bound Paclitaxel in combination with Gemcitabine; interrupt Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and Gemcitabine until sepsis resolves, and if neutropenia, until neutrophils are at least 1500 cells/mm^3, then resume treatment at reduced dose levels.
- Pneumonitis occurred with the use of Protein-Bound Paclitaxel in combination with Gemcitabine; permanently discontinue treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and Gemcitabine.
- Severe hypersensitivity reactions with fatal outcomes have been reported. Do not re-challenge with this drug.
- Exposure and toxicity of Paclitaxel can be increased in patients with hepatic impairment, consider dose reduction and closely monitor patients with hepatic impairment.
- Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) contains albumin derived from human blood, which has a theoretical risk of viral transmission.
- Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) can cause fetal harm. Advise patients of potential risks to a fetus and to use effective contraception.

USE IN PREGNANCY AND LACTATION

Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) can cause fetal harm when administered to a pregnant woman. There are no available human data on Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) use in pregnant women to inform the drug-associated risk.
There are no data on the presence of Paclitaxel in human milk, or its effect on the breastfed child or milk production. Because of the potential for serious adverse reactions in a breastfed child from Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound), advise lactating women not to breastfeed during treatment with Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) and for two weeks after the last dose.

PEDIATRIC USE

Safety and effectiveness in pediatric patients have not been established.

DRUG INTERACTION:

The metabolism of Paclitaxel is catalyzed by CYP2C8 and CYP3A4. Caution should be exercised when administering Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) concomitantly with medicines known to inhibit or induce either CYP2C8 or CYP3A4.

OVERDOSE:

The primary anticipated complications of overdosage would consist of bone marrow suppression, sensory neurotoxicity, and mucositis. No known antidote exists for Paclitaxel Protein-Bound Particles for Injectable Suspension (Albumin-Bound) overdosage.

PHARMACEUTICAL PRECAUTION

Do not store above 25 °C temperature. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Nab-Paclitor™ for injectable Suspension:
Each box contains

- One vial of Paclitaxel USP 100 mg (Protein-Bound Particles for Injectable Suspension) (Albumin-Bound)
- One infusion set,
- Two 10 mL 0.9% Sodium Chloride ampoules,
- One 20 mL disposable syringe

SK+F ONCOLOGY
Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
RUPGANJ, NARAYANGANJ, BANGLADESH
TM TRADEMARK
R/PM2416 V01

PM SPECIFICATION

Creative ID: CSD_02

Job Name: NAB Paclitor Injection Insert		**Size:** L - 280 mm, W - 100 mm			**Paper:** 80 gsm Art Paper
No. of Color: 4 Extra	**Pantone Color Code**	Black C	2347 C	232 C	Process blue C

	Creative Service Department	Marketing Department	PD/QC/Contract Customer	Approved By
Comments				
Signature & Date				