Carbotor™ IV Injection

Carboplatin Injection BP

DESCRIPTION

Carbotor™ is a preparation of Carboplatin. Carboplatin produces predominantly interstrand DNA cross-links rather than DNA-protein cross-links. This effect is apparently cell-cycle nonspecific. The aquation of Carboplatin, which is thought to produce the active species, occurs at a slower rate than in the case of Cisplatin. Despite this difference, it appears that both Carboplatin and Cisplatin induce equal numbers of drug-DNA cross-links, causing equivalent lesions and biological effects. The differences in potencies for Carboplatin and Cisplatin appear to be directly related to the difference in aquation rates.

INDICATIONS

- Initial Treatment of Advanced Ovarian Carcinoma
- Secondary Treatment of Advanced Ovarian Carcinoma

DOSAGE AND ADMINISTRATION

Single-Agent Therapy: Carboplatin Injection, as a single agent, has been shown to be effective in patients with recurrent ovarian carcinoma at a dosage of 360 mg/m^2 IV on day 1 every 4 weeks. In general, however, single intermittent courses of Carboplatin should not be repeated until the neutrophil count is at least 2,000 and the platelet count is at least 100,000.

Combination Therapy with Cyclophosphamide: In the chemotherapy of advanced ovarian cancer, an effective combination for previously untreated patients consists of: Carboplatin—300 mg/m^2 IV on day 1 every 4 weeks for 6 cycles. Cyclophosphamide—600 mg/m^2 IV on day 1 every 4 weeks for 6 cycles. Intermittent courses of Carboplatin in combination with Cyclophosphamide should not be repeated until the neutrophil count is at least 2,000 and the platelet count is at least 100,000.

Dose Adjustment Recommendations: The suggested dose adjustments for single agent or combination therapy shown in the table below are modified from controlled trials in previously treated and untreated patients with ovarian carcinoma. Blood counts were done weekly, and the recommendations are based on the lowest post-treatment platelet or neutrophil value.

Platelets	Neutrophils	Adjusted Dose (From Prior Course)
>100,000	>2,000	125%
50-100,000	500-2,000	No Adjustment
<50,000	<500	75%

Carboplatin is usually administered by an infusion lasting 15 minutes or longer. No pre- or post-treatment hydration or forced diuresis is required.

Patients with Impaired Kidney Function: Patients with creatinine clearance values below 60 mL/min are at increased risk of severe bone marrow suppression. In renally-impaired patients who received single-agent Carboplatin therapy, the incidence of severe leukopenia, neutropenia, or thrombocytopenia has been about 25% when the dosage modifications in the table below have been used.

Baseline Creatinine Clearance	Recommended Dose on Day 1
41-59 mL/min	250 mg/m^2
16-40 mL/min	200 mg/m^2

Formula Dosing: A simple formula for calculating dosage, based upon a patient's glomerular filtration rate (GFR in mL/min) and Carboplatin target area under the concentration versus time curve (AUC in mg/mL•min), has been proposed by Calvert. In these studies, GFR was measured by ^{51}Cr-EDTA clearance.

Calvert formula for Carboplatin Dosing: Total Dose (mg) = (target AUC) x (GFR + 25)

Note: With the Calvert formula, the total dose of Carboplatin is calculated in mg, not mg/m^2.

CONTRAINDICATIONS

- Hypersensitivity
- Severe bone marrow depression or significant bleeding.

SIDE EFFECTS

- Alopecia
- Cardiovascular events (cardiac failure, embolism, cerebrovascular accidents)
- Cancer-associated hemolytic uremic syndrome
- Malaise, anorexia, hypertension, dehydration, and stomatitis

WARNING AND PRECAUTION

Carboplatin injection should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate treatment facilities are readily available. Bone marrow suppression is dose related and may be severe, resulting in infection and/or bleeding. Anemia may be cumulative and may require transfusion support. Vomiting is another frequent drug-related side effect. Anaphylactic-like reactions to Carboplatin have been reported and may occur within minutes of Carboplatin administration. Epinephrine, corticosteroids, and antihistamines have been employed to alleviate symptoms.

Needles or intravenous administration sets containing aluminum parts that may come in contact with Carboplatin injection should not be used for the preparation or administration of the drug. Aluminum can react with Carboplatin causing precipitate formation and loss of potency.

USE IN PREGNANCY AND LACTATION

Pregnancy Category D. It is not known whether Carboplatin is excreted in human milk. Because there is a possibility of toxicity in nursing infants secondary to Carboplatin treatment of the mother, it is recommended that breast-feeding be discontinued if the mother is treated with Carboplatin injection.

SPECIAL INSTRUCTIONS FOR HANDLING AND DISPOSAL

Carboplatin injection should be prepared for administration by professionals who have been trained in the safe use of cytotoxic drugs.

The personnel carrying out these procedures should be adequately protected with clothing, gloves, masks and eye protection.

Personnel regularly involved in the preparation and handling of Carboplatin should have bi-annual blood examinations.

In the event of contact with the skin or eyes, the affected area should be washed with copious amounts of water or normal saline.

A bland cream may be used to treat the transient stinging of skin. Medical advice should be sought if the eyes are affected.

In the event of spillage, personnel wearing protective clothing should sponge up the spilled material. The area should be rinsed twice with water, and all solutions, and contaminated clothing and sponges put into a plastic bag and sealed. The bag should be disposed of as below.

Syringes, containers, absorbent materials, solution and any other material which has come into contact with Carboplatin should be placed in a thick plastic bag or other impervious container and incinerated at 1000 °C. Tightly sealed containers may explode.

PREPARATION OF INTRAVENOUS SOLUTIONS

Carboplatin injection is a premixed aqueous solution of 10 mg/mL Carboplatin. Carboplatin aqueous solution can be further diluted to concentrations as low as 0.5 mg/mL with 5% Dextrose in water or 0.9% Sodium Chloride injection.

When prepared as directed, Carboplatin aqueous solutions are stable for 8 hours at room temperature (25 °C). Since no antibacterial preservative is contained in the formulation, it is recommended that Carboplatin aqueous solutions be discarded 8 hours after dilution.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light and wet place. Protect from freezing. Keep out of reach of children. Wear gloves at all times when handling containers.

PACKAGING

Carbotor™ 150 IV Injection: Each box contains one multi-dose vial of Carboplatin BP 150 mg/15 mL injection.

Carbotor™ 450 IV Injection: Each box contains one multi-dose vial of Carboplatin BP 450 mg/45 mL injection.

SK+F ONCOLOGY

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
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R/PM0741 V01