CARBOPLATIN INJECTION IP (450/45ML)
CARBOPLATIN INJECTION IP (150/15ML)

CARBOWEMB
450mg/150mg Injection

Composition :

Each ml contains :

Carboplatin I.P. 10 mg

Excipients q.s.

DESCRIPTION

Carboplatin is a platinum coordination compound. The chemical name for carboplatin is platinum, diammine [1,1-cyclobutane-dicarboxylato(2-)-0,0']-,(SP-4-2), and carboplatin has the following structural formula:

CLINICAL PHARMACOLOGY

Carboplatin, like cisplatin, 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 AND USAGE

Carboplatin is indicated for the treatment of:

1. advanced ovarian carcinoma of epithelial origin in:
- first line therapy
- second line therapy, after other treatments have failed.
2. small cell carcinoma of the lung.

DOSAGE & ADMINISTRATION

Dosage and Administration:

Carboplatin should be used by the intravenous route only. The recommended dosage of Carboplatin in previously untreated adult patients with normal kidney function, i.e. creatinine clearance > 60 ml/min is 400 mg/m^2 as a single short term IV dose administered by a 15 to 60 minutes infusion. Alternatively, the Calvert formula shown below may be used to determine dosage:

Dose (mg) = target AUC (mg/ml x min) x [GFR ml/min + 25]

Dose (mg) = target AUC (mg/ml x min) x [GFR ml/min + 25]		
Target AUC	**Planned chemotherapy**	**Patient treatment status**
5-7mg/ml .min	single agent Carboplatin	Previously untreated
4-6 mg/ml .min	single agent Carboplatin	Previously treated
4-6mg/ml .min	Carboplatin plus cyclophosphamide	Previously untreated

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

Therapy should not be repeated until four weeks after the previous Carboplatin course and/or until the neutrophil count is at least 2,000 cells/mm^3 and the platelet count is at least 100,000 cells/mm^3.

Initial dosage should be reduced by 20-25% in patients with risk factors such as previous myelosuppressive therapy and or poor performance status (ECOG-Zubrod 2-4 or Karnofsky below 80).

Determination of haematologic nadir by weekly blood counts during initial courses is recommended for future dosage adjustment and scheduling of carboplatin.

Needles or intravenous sets containing aluminium parts that may come in contact with carboplatin injection should not be used for preparation or administration. Aluminium reacts with carboplatin injection causing precipitate formation and/or loss of potency.

The safety measures for dangerous substances are to be complied with preparation and administration. Preparation must be carried out by personnel who have been trained in the safe use while wearing protective gloves, face mask and protective clothes.

Impaired renal function:

In patients with impaired renal function, dosage of carboplatin should be reduced (refer to Calvert formula) and haematological nadirs and renal function monitored.

Patients with creatinine clearance below 60 ml/min are at increase risk of severe myelosuppression. The frequency of severe leukopenia, neutropenia, or thrombocytopenia has been maintained at about 25% with the following dosage recommendations:

Baseline Creatinine Clearance	Initial Dose (Day 1)
41-59 ml/min	250 mg/m^2 I.V.
16-40 ml/min	200 mg/m^2 I.V.

Insufficient data exist on the use of carboplatin injection in patients with creatinine of 15 ml/min or less to permit a recommendation for treatment.

All of the above dosing recommendations apply to the initial course of treatment. Subsequent dosages should be adjusted according to the patient's tolerance and to the acceptable level of myelosuppression.

Combination Therapy:

The optimal use of Carboplatin in combination with other myelosuppressive agents requires dosage adjustments according to the regimen and schedule to be adopted.

Elderly:

In patients of more than 65 years of age, adjustment of the carboplatin dose to the general condition is necessary during the first and the subsequent therapeutic courses.

Paediatric population

There is insufficient information to support a dosage recommendation in the paediatric population.

CONTRAINDICATIONS

Carboplatin is contraindicated in:
- Hypersensitivity to the active substance(s)
- patients with severe myelosuppression
- patients with pre-existing severe renal impairment (with creatinine clearance of ≤ 30 ml per minute) unless in the judgment of the physician and patient, the possible benefits of treatment outweigh the risks
- patients with bleeding tumors
- concomitant use with yellow fever vaccine
- patients with a history of severe allergic reaction or other platinum containing compounds.

Dosage adjustment may allow use in the presence of mild impairment

WARNINGS & PRECAUTIONS

Carboplatin is contraindicated in:
- Hypersensitivity to the active substance (s)
- patients with severe myelosuppression
- patients with pre-existing severe renal impairment (with creatinine clearance of ≤ 30 ml per minute) unless in the judgment of the physician and patient, the possible benefits of treatment outweigh the risks
- patients with bleeding tumors
- concomitant use with yellow fever vaccine
- patients with a history of severe allergic reaction or other platinum containing compounds.

Dosage adjustment may allow use in the presence of mild impairment

PREGNANCY AND LACTATION

Pregnancy

Carboplatin can cause foetal harm when administered to a pregnant woman. Carboplatin has been shown to be embryotoxic and teratogenic in rats receiving the drug during organogenesis. No controlled studies in pregnant women have been conducted.

Breastfeeding

It is not known whether Carboplatin is excreted in breast milk.

To avoid possible harmful effects in the infant, breast-feeding must be stopped during carboplatin therapy.

DRUG INTERACTIONS

Carboplatin may interact with aluminium to form a black precipitate. Needles, syringes, catheters or IV administration sets that contain aluminium parts which may come into contact with carboplatin, should not be used for the preparation or administration of the drug.

Due to the increase of thrombotic risk in cases of tumoral diseases, the use of anticoagulative treatment is frequent. The high intra-individual variability of the coagulabilty during diseases, and the possibility of interaction between oral anticoagulants and anticancer chemotherapy, may require an increase in frequency of INR monitoring if a patient is treated with oral anticoagulants.

Concomitant use contraindicated

Yellow fever vaccine: risk of generalized disease mortal.

Concomitant use not recommended

- Live attenuated vaccines (except yellow fever): Risk of systemic, possible fatal disease. This is increased in subjects who are already immunosuppressed by their underlying disease. Use inactivated vaccine where this exist (poliomyelitis).
- Phenytoin, fosphenytoin: Risk of exacerbation of convulsions (resulting from the decrease of phenytoin digestive absorption by the cytotoxic drug), risk of toxicity enhancement or loss of efficacy of the cytotoxic drug (due to increased hepatic metabolism by phenytoin).

Concomitant use to take into consideration

ADVERSE EFFECTS

The frequency of adverse reactions reported is based on a cumulative database of 1,893 patients receiving single agent carboplatin injection and post-marketing experience.

The list is presented by system organ class, MedDRA preferred term, and frequency using the following frequency categories:

very common (≥1/10)

common (≥1/100, <1/10)

uncommon (≥1/1,000, ≤1/100)

rare (≥1/10,000, ≤1/1,000)

very rare (<1/10,000), not known (cannot be estimated from the available data)

System Organ Class	**Frequency**	**MedDRA Term**
Neoplasms, benign and malignant and unspecified (incl cysts and polyps)	Not known	Treatment related secondary malignancy
Infections and infestations	Common	Infections*
	Not known	Pneumonia
Blood and lymphatic system disorders	Very common	Thrombocytopenia, neutropenia, leukopenia, anaemia
	Common	Haemorrhage*
	Not known	Bone marrow failure, haemolytic-uraemic syndrome
	Rare	febrile neutropenia,
Immune system disorders	Common	Hypersensitivity, anaphylactoid type reaction
Metabolism and nutrition disorders	Not known	Dehydration, anorexia, Tumor lysis syndrome
	Rare	hyponatraemia
Nervous system disorders	Common	Neuropathy peripheral, paraesthesia, decrease of osteotendinous reflexes, sensory disturbance, dysgeusia
	Not known	Cerebrovascular accident* Reversible Posterior Leukoencephalopathy Syndrome (RPLS).
Eye disorders	Common	Visual disturbance (incl. rare cases of loss of vision)
Ear and labyrinth disorders	Common	Ototoxicity
Cardiac disorders	Common	Cardiovascular disorder*
	Not known	Cardiac failure*
Vascular disorders	Not known	Embolism*, hypertension, hypotension
Respiratory, thoracic and mediastinal disorders	Common	Respiratory disorder, interstitial lung disease, bronchospasm
Gastrointestinal disorders	Very common	Vomiting, nausea, abdominal pain
	Common	Diarrhoea, constipation, mucous membrane disorder
	Not known	Stomatitis, Pancreatitis.
Skin and subcutaneous tissue disorders	Common	Alopecia, skin disorder
	Not known	Urticaria, rash, erythema, pruritus
Musculoskeletal and connective tissue disorders	Common	Musculoskeletal disorder
Renal and urinary disorders	Common	Urogenital disorder
General disorders and administration site conditions	Common	Asthenia
	Not known	Injection site necrosis, injection site reaction, injection site extravasation, injection site erythema, malaise
Investigations	Very Common	Creatinine renal clearance decreased, blood urea increased, blood alkaline phosphatase increased, aspartate aminotransferase increased, liver function test abnormal, blood sodium decreased, blood potassium decreased, blood calcium decreased, blood magnesium decreased.
	Common	Blood bilirubin increased, blood creatinine increased, blood uric acid increased

* Fatal in <1%, fatal cardiovascular events in <1% included cardiac failure, embolism, and cerebrovascular accident combined.

STORAGE CONDITION :

Storage : Store at 15^{0}C - 30^{0}C. Store protected from light and free from contact with metals.

Marketed by :

wembrace

Wembrace Biopharma Pvt. Ltd.
B-6/9,Commercial Complex,
Safdarjung Development Enclave,
New Delhi-110 029
Good To Talk
WEMBRACE CONSUMER CARE
EMAIL:-WECARE@WEMBRACE.IN
TOLL FREE CUSTOMER CARE :-18002029010
Mfd. by : Albino Lifesciences Pvt. Ltd.
(WHO-GMP Certified Company)
Village: Gaunspura, P.O.: Noorpur Bet,
Hambran, Ludhiana-141008
Connect with us

30 EXCELLENT YEARS

ISO 9001