SUMMARY OF PRODUCT CHARACTERISTIC

1. NAME OF THE MEDICINAL PRODUCT

Biocarb 150

Carboplatin Injection BP

150mg/15ml Biocarb 450

Carboplatin Injection BP 450mg/45ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Carboplatin BP 10mg

Water for Injection BP q.s.

For full list excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection

A clear, colourless to pale yellow colour solution filled in an amber glass vial.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Carboplatin is used to treat ovarian cancer.

Carboplatin is also used for other types of cancer, including lung, head and neck, endometrial, esophageal, bladder, breast, and cervical; central nervous system or germ cell tumors; osteogenic sarcoma; and as preparation for a stem cell or bone marrow transplant.

4.2 Posology and method of administration

Pretreatment platelet count and performance status are important prognostic factors for severity of myelosuppression in previously treated patients.

The suggested dose adjustment 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%
20-100,000	500-2,000	No adjustment
< 50,000	< 500	75%
*Percentages apply to carboplatin as a single agent or both Carboplatin and cyclophosphamide in combination. In the controlled studies, dosages were also		

adjusted at a lower level (50 to 60%) for severe myelosuppression. Escalations above 125% were not recommended for these studies

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 sever leucopenia, 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
16-40ml/min	200 mg/m^2

The data available for patients with severely impaired kidney function (creatinine clearance below 15 ml/min) are too limited to permit a recommendation for treatment.

These dosing recommendation apply to the initial course of treatment. Subsequent dosages should be adjusted according to the patient's tolerance based on the degree of bone marrow suppression.

4.3 Contraindications

Carboplatin is contraindicated in patients with a history of severe allergic reactions to Cisplatin or other platinum containing compounds.

Carboplatin should not be employed in patients with severe bone marrow depression or significant bleeding.

4.4 Warnings and precautions

Bone marrow depression (leucopenia, neutropenia, and thrombocytopenia) is dose dependent and is also the dose limiting toxicity. Peripheral blood counts should be frequently monitored during carboplatin treatment and when appropriate, until recovery is achieved. Median nadir occurs at day 21 in patients receiving single agent carboplatin. In general, single intermittent courses of carboplatin should not be repeated until leukocyte, neutrophil and platelet counts have recovered. Since anemia is cumulative, transfusions may be needed during treatment with carboplatin particularly in patients receiving prolonged therapy.

Bone marrow suppression is increased in patients who have received prior therapy, especially regimens including cisplatin. Marrow suppression is also increased in patients with impaired kindney function. Initial carboplatin dosages

in these patients should be appropriately reduced and blood counts should be carefully monitored between courses. The use of Carboplatin in combination with other bone marrow suppressing therapies must be carefully managed with respect to dosage and timing in order to minimize additive effects. Carboplatin has limited nephrotoxic potential, but concomitant treatment with aminoglycosides has resulted in increased renal and/or audiologic toxicity and caution must be exercised when a patient receives both drugs. Clinically significant hearing loss has been reported to occur in pediatric patients when carboplatin was administered at higher than recommended doses in combination with other ototoxic agents. Carboplatin can induce emesis; can be more severe in patients previously receiving emetogenic therapy. The incidence and intensity of emesis have been reduced by using pre-medication with antiemetics, although no conclusive efficacy data exist with the following schedules of carboplatin, lengthening the duration of single intravenous administration to 24 hours or dividing the total dose over five consecutive daily pulse doses has resulted in reduced emesis.

Although peripheral neurotoxicity is infrequent, its incidence is increased in patients older than
65 years and in patients previously treated with cisplatin. Pre-existing cisplatin induced neurotoxicity does not worsen in about 70% of the patients receiving carboplatin as secondary treatment.

Loss of vision, which can be complete for light and colors, has been reported after the use of carboplatin with doses higher than those recommended in the package insert. Vision appears to recover totally or to a significant extent within weeks of stopping these high doses.

As in the case of other platinum coordination compounds, allergic reactions to carboplatin have been reported. These may occur within minutes of administration and should be managed with appropriate supportive therapy. There is increased risk of allergic reactions including anaphylaxis in patients previously exposed to platinum therapy.

Carboplatin may cause fetal harm when administered to a pregnant woman. There are no adequate and well controlled studies in pregnant women.

4.5 Interaction with other medicinal products and other forms of interaction

Aceclofenac: Carboplatin may decrease the excretion rate of Aceclofenac which could result in a higher serum level.

Busulfan: The risk or severity of adverse effects can be increased when Carboplatin is combined with Busulfan

Digoxin: Carboplatin may decrease the excretion rate of Digoxin which could result in a higher serum level.

Glipizide: Carboplatin may decrease the excretion rate of Glipizide which could

result in a higher serum level.

4.6 Pregnancy and Nursing Mothers:

Pregnancy:

Carboplatin injection may cause fatal harm when administered to a pregnant woman. If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant.

Nursing mothers:

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.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Adverse

effects

Hematologic

Toxicity

Bone marrow suppression is the dose-limiting toxicity of carboplatin. Thrombocytopenia with platelet counts below 50,000/mm^3 occurs in 25% of the patients; neutropenia with granulocyte counts below 1,000/mm^3 occurs in 16% of the patients; leucopenia with WBC counts below 2,000/mm^3 occurs in 15% of the patients. The nadir usually occurs about day 21 in patients receiving single agent therapy. By day 26, 90% of patients have platelet counts above 100,000/mm^3, 74% have neutrophil counts above 2,000/mm^3; 67% have leukocyte counts above 4,000/mm^3 marrow suppression is usually more severe in patients with impaired kidney function. Patients with poor performance status have also experienced a higher incidence of severe leucopenia and thrombocytopenia. Anemia with hemoglobin less than 11 g/dL occurs in majority of the patients who start therapy with a baseline above the value. The incidence of anemia increases with increasing exposure to carboplatin. Transfusions may be required in some patients treated with carboplatin. Bone marrow depression may be more severe when carboplatin is combined with other bone marrow suppressing drugs or with radiotherapy.

Gastrointestinal Toxicity

Vomiting occurs in 65% of the patients and in about one-third of these patients it is severe. Nausea alone occurs in an additional 10% to 15% of patients. Both nausea and vomiting usually cease within 24 hours of treatment and are often responsive to antiemetic measures. Emesis was increased when carboplatin was used in combination with other emetogenic compounds. Other gastrointestinal effects observed frequently were pain, in 17% of the patients; diarrhea in 6%; and constipation in 6%.

Neurologic Toxicity

Peripheral neuropathies have been observed in 4% of the patients receiving carboplatin with mild paresthesias occurring most frequently. Patients older than 65 years appear to have an increased risk for peripheral neuropathies. Clinical ototoxicity and other sensory abnormalities such as visual disturbances and change in taste occur rarely. Central nervous system symptoms have been reported in fewer patients and appear to be most often related to the use of antiemetics. Although the overall incidence of peripheral neurologic side effects induced by carboplatin is low, prolonged treatment may result in cumulative neurotoxicity.

Nephrotoxicity

Development of abnormal renal function test results is uncommon, with carboplatin. Creatinine clearance has proven to be the most sensitive measure of kidney function in patients receiving carboplatin, and it appears to be the most useful test for correlating drug clearance and bone marrow suppression.

Hepatic Toxicity

The incidences of abnormal liver function tests in patients with normal baseline values were reported as follows: total bilirubin, 5%; SGOT, 15%; and alkaline phosphatase, 24%. These abnormalities have generally been mild and reversible in about one-half of the cases. In a limited series of patients receiving very high dosages of carboplatin and autologous bone marrow transplantation, severe abnormalities of liver function tests were reported.

Electrolyte Changes

Abnormally decreased serum electrolyte values may be found in some patients. Electrolyte supplementation was not routinely administered concomitantly with carboplatin, and these electrolyte abnormalities were rarely associated with symptoms.

Reporting of suspected adverse reactions:
Healthcare professionals are requested to report any suspected adverse reactions via Pharmacy and the Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

There is no known antidote for Carboplatin Injection overdosage. The anticipated complications of overdosage would be secondary to bone marrow suppression and/or hepatic toxicity.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Carboplatin is an antineoplastic in the class of alkylating agents and is used to treat various forms of cancer. Alkylating agents are so named because of their ability to add alkyl groups to many electronegative groups under conditions present in cells. They stop tumor growth by cross- linking guanine bases in DNA double-helix strands - directly attacking DNA. This makes the strands unable to uncoil and separate. As this is necessary in DNA replication, the cells can no longer divide. In addition, these drugs add methyl or other alkyl groups onto molecules where they do not belong which in turn inhibits their correct utilization by base pairing and causes a miscoding of DNA. Alkylating agents are cell cycle-nonspecific. Alkylating agents work by three different mechanisms all of which achieve the same end result - disruption of DNA function and cell death.

Mechanism of action

Vincristine is an antineoplastic drug with broad-spectrum anti-tumor activity in man. The drug may act by mitotic inhibition, causing an arrest of cell division in metaphase. The drug is relatively marrow-sparing and is thus suitable for use in combination with other cancer chemotherapeutic agents.

5.2 Pharmacokinetic properties

The Cmax values and areas under the plasma concentration versus time curves from 0 to infinity (AUC inf) increase linearly with dose, although the increase was slightly more than dose proportional. Carboplatin exhibits linear pharmacokinetics.

Carboplatin is not bound to plasma protein. However, the platinum itself from carboplatin irreversibly binds to plasma proteins and is slowly eliminated with a minimum half-life of 5 days.

The major route of elimination of carboplatin is renal excretion. After 24 hours, all of the platinum is recovered in the urine as carboplatin. Whether biliary excretion occurs is not known. Initial plasma half-life (alpha) = 1.1 to 2 hours; Post distribution plasma half-life (beta) = 2.6 -
5.9 hours.

5.3 Preclinical safety data

Both in vivo and in vitro laboratory tests have failed to demonstrate conclusively that this product is mutagenic. No evidence of carcinogenicity was found following intraperitoneal administration in rats and mice, although this study was limited.

In several animal species, carboplatin can include teratogenic effects, as well as embryo lethality, with doses that are nontoxic to the pregnant animal.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

- Water for Injection

6.2 Incompatibilities

About 5% of the initial carboplatin concentration was lost over 24 hours when solutions were diluted in sodium chloride 0.9% and stored at 25^0C

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store at a temperature not exceeding 30^0C. Protect from light. Do not freeze.

6.5 Nature and contents of

container Single vial contains

150mg/15ml Single vial

contains 450mg/45ml

6.6 Special precautions for disposal and

other handling Cytotoxic Handling

Guidelines

Administration:

Should be administered only by or under the direct supervision of a qualified physician who is experienced in the use of cancer chemotherapeutic agents.

Preparation (Guidelines)

1. Chemotherapeutic agents should be prepared for administration only by professionals who have been trained in the safe use of preparation.
2. Operations such as reconstitution and transfer to syringes should be carried out only in the designated area.
3. The personnel carrying out these procedures should be adequately protected with clothing, gloves and eye shield.
4. Pregnant personnel are advised not to handle chemotherapeutic agents.

Contamination

(a) 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.

(b) In the event of spillage, operators should put on gloves and mop the spilled material with a sponge kept in the area for that purpose. Rinse the area twice with water. Put all solutions and sponges into a plastic bag and then seal it.

Disposal

Syringes, containers, absorbent materials, solution and any other contaminated material should be placed in a thick plastic bag or other impervious container and incinerated.

7.0 REGISTRANT

Marketing Authorization holder

Name: Zydus Healthcare Limited

Address: Ackruti Star, Unit No.: 103, MIDC, Andheri (E), Mumbai – 400 093, India

8.0 MARKETING AUTHORIZATION NUMBER

17511

9.0 DATE OF FIRST REGISTRATION

09/04/2026

10.0 DATE OF REVIDION OF THE TEXT

09/04/2026