Summary of Product Characteristics

1. Name of Medicinal Product:

Carboplatin Injection BP 150 mg/15mL

Carboplatin Injection BP 450 mg/45mL

2. Qualitative & Quantitative Formula:

Carboplatin Injection BP 150 mg/15mL and 450 mg/45mL:

Each mL contains:
Carboplatin BP 10 mg
Water for Injection BP q.s

Qualitative & Quantitative Formula

Name of Ingredients	Spec	Std qty per ml	% Overage	Actual qty per ml	Function
Carboplatin	BP	10 mg	2.0 %	10.2 mg	Active Pharmaceutical Ingredient
Water For Injections	BP	q.s. to ml	Nil	q.s. to ml	Vehicle

Actual quantity depends on assay on a dried basis

Average Fill Volume:
Carboplatin Injection BP 150 mg/15mL: NLT 15.0 mL
Carboplatin Injection BP 450 mg/45mL: NLT 45.0 mL

3. Pharmaceutical Form:

Carboplatin Injection BP 150 mg/15mL:
Description: A clear, colorless solution

Pack Style: A clear, colorless solution filled in a 15 mL amber moulded glass vial, USP Type I, stoppered with a 20 mm bromobutyl rubber plug, sealed with a 20 mm aluminium flip-off seal having red colour.

Carboplatin Injection BP 450 mg/15mL:
Description: A clear, colorless solution

Pack Style: A clear, colorless solution filled in a 45 mL amber moulded glass vial, USP Type I, stoppered with a 20 mm bromobutyl rubber plug, sealed

with a 20 mm aluminium flip-off seal having red colour.

4. Clinical Particulars:

4.1 Therapeutic indications:

1. Advanced ovarian carcinoma of epithelial origin in:
a) first-line therapy
b) second-line therapy after other treatments have failed
2. Small cell carcinoma of the lung.

4.2 Posology and method of administration

Posology

Carboplatin injection should be used by the intravenous route only. Adults: The recommended dose of carboplatin in previously untreated adults with normal renal function is 400mg/m2 given as a single short term intravenous infusion over 15 to 60 minutes. Alternatively see Calvert formula below. Dose (mg) = target AUC (mg/ml x min) x [GFR ml/min + 25] Note: With the Calvert formula, the total dose of carboplatin is calculated in mg not mg/m2.

Target AUC	Planned Chemotherapy	Patient Treatment status
5-7 mg/ml.min	single-agent carboplatin	previously untreated
4-6 mg/ml.min	single-agent carboplatin	previously treated
4-6 mg/ml.min	carboplatin plus cyclophosphamide	previously untreated

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/mm3 and the platelet count is at least 100,000 cells/mm3.

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 aluminum parts that may come in contact with carboplatin injection should not be used for preparation or administration. Aluminum 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.

Renal impairment: "Patients with creatinine clearance values below 60 mL/min are at increased 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/m2 I.V. 16-40 mL/min 200 mg/m2 I.V.

Insufficient data exist on the use of carboplatin injection in patients with creatinine clearance 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, dosage adjustment, initially or subsequently, may be necessary during the first and the subsequent therapeutic courses depending on the physical condition of the patient.

Children: Specific dosage recommendations for use in children and infants cannot be made due to insufficient use in paediatrics at this time.

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

Therapy should not be repeated until 4 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.

Determination of hematologic 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 during preparation and administration. Preparation must be carried out by personnel who have been trained in the safe use while wearing protective gloves, a 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 values below 60 ml/min are at increased 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 clearance 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 population
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. Method of administration
Carboplatin injection should be used by the intravenous route only.

4.3 Contraindications
Carboplatin is contraindicated in:

- patients with severe myelosuppression
- patients with pre-existing severe renal impairment (with creatinine clearance < 30 mL/min), unless in the judgment of the physician and patient, the possible benefits of treatment outweigh the risks.
- patients with a history of hypersensitivity to carboplatin and other platinum-containing compounds

- patients with bleeding tumors
- concomitant use with yellow fever vaccine.

4.4 Special warnings and precautions for use:

Warnings:

Carboplatin should only be administered under the supervision of a qualified physician who is experienced in the use of chemotherapeutic agents. Diagnostic and treatment facilities should be readily available for management of therapy and possible complications.

Myelosuppression

Severity of myelosuppression is increased in patients with prior treatment with the drug, in particular with cisplatin. Myelosuppression as a result of carboplatin treatment is closely related to the renal clearance of the drug, and it can also be enhanced in those with impaired kidney function. Therefore, in patients with abnormal renal function, or those receiving concomitant therapy with nephrotoxic drugs, myelosuppression, especially thrombocytopenia, may be more severe and prolonged. Initial carboplatin dosages in these groups of patients should be appropriately reduced. and the effects carefully monitored through frequent blood counts between courses. Combination therapy with other myelosuppressive drugs may require modification of dosage/timing of schedules in order to minimise additive effects.

Carboplatin can cause nausea and vomiting. Pre-medication with anti-emetics has been reported to be useful in reducing the incidence and intensity of these effects.

Renal and Hepatic function

Renal and hepatic function impairment may be encountered with Carboplatin. Very high doses of carboplatin (5 times single agent recommended dose) have resulted in severe abnormalities in hepatic and renal function. Although no clinical evidence on compounding nephrotoxicity has been accumulated, it is recommended not to combine Carboplatin with aminoglycosides or other nephrotoxic compounds. Renal and hepatic function tests must be done regularly and the drug should be discontinued if abnormal renal or hepatic function is seen.

The incidence and severity of nephrotoxicity may increase in patients who have impaired kidney function before carboplatin treatment. It is not clear whether an appropriate hydration programme might overcome such an effect but dosage reduction or discontinuation of therapy is required in the presence

of severe alteration in renal function test.
Impairment of renal function is more likely in patients who have previously experienced nephrotoxicity as a result of Cisplatin therapy.
In patients with impaired renal function, the effect of carboplatin on the hematopoietic system is more pronounced and longer-acting than in patients with normal renal function. In this risk group, therapy with carboplatin must be performed with special caution.

Allergic Reactions

As with other platinum-based drugs, allergic reactions to Carboplatin have been commonly reported, including following multiple courses of carboplatin. Allergic reactions appearing most often during administration may occur and necessitate discontinuation of infusion and an appropriate symptomatic treatment. Patients should therefore be observed carefully for possible allergic reactions and managed with appropriate supportive therapy, including antihistamines, adrenaline and/or glucocorticoids. Cross reactions, sometimes fatal, have been reported with all the platinum compounds .

Hematologic Toxicity

Leukopenia, neutropenia, and thrombocytopenia are dose-dependent and dose-limiting. Peripheral blood counts should be monitored during carboplatin treatment frequently and, in cases of toxicity, until recovery is achieved. Blood counts should be performed prior to commencement of Carboplatin therapy, and at weekly intervals thereafter and the drug should be discontinued if abnormal depression of the bone marrow is seen. This will monitor toxicity and help determine the nadir and recovery of haematological parameters, and assist in subsequent dosage adjustments.
Median day of nadir is day 21 in patients receiving single agent carboplatin and day 15 in patients receiving carboplatin in combination with other chemotherapeutic agents. In general, single intermittent courses of carboplatin should not be repeated until leukocyte, neutrophil, and platelet counts have returned to normal. Lowest levels of platelets are generally seen between days 14 and 21 of initial therapy. A greater reduction is seen in patients who previously received extensive myelosuppressive chemotherapy. Lowest levels of white cells occur generally between days 14 and 28 of initial therapy. Therapy should not be repeated until 4 weeks after the previous carboplatin course and/or until the neutrophil count is above 2,000 cells/mm3 or platelets greater than 100,000 cells/mm3. This recovery usually takes 5 to 6 weeks.
Anemia is frequent and cumulative; however, it rarely requires a transfusion.

Neurologic Toxicity

Although peripheral neurologic toxicity is generally common and mild, limited to paresthesia and decreased osteotendinous reflexes, its frequency is increased in patients older than 65 years and/or in patients previously treated with cisplatin. Monitoring and neurological examinations should be carried out at regular intervals.

Visual disturbances, including loss of vision, have been reported after the use of carboplatin in doses higher than those recommended in patients with renal impairment. Vision appears to recover totally or to a significant extent within weeks of stopping these high doses.

Geriatric Use

In studies involving combination therapy with carboplatin and cyclophosphamide, elderly patients treated with carboplatin were more likely to develop severe thrombocytopenia than younger patients. Because renal function is often decreased in the elderly, renal function should be considered when determining dosage.

Other

Auditory defects have been reported during carboplatin therapy. Ototoxicity may be more pronounced in children. Cases of hearing loss with a delayed onset have been reported in pediatric patients. A long-term audiometric follow-up in this population is recommended.

Administration of live or live-attenuated vaccines in patients immunocompromised by chemotherapeutic agents including carboplatin, may result in serious or fatal infections. Vaccination with a live vaccine should be avoided in patients receiving carboplatin. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

Its carcinogenic potential has not been studied but compounds with similar mechanisms of action and mutagenicity have been reported to be carcinogenic.

4.5 Interaction with other medicinal products and other forms of interaction:

Concomitant use contraindicated

Yellow fever vaccine: risk of generalised vaccinal disease mortal.

Concomitant use not recommended

- Live attenuated vaccines (except yellow fever): Risk of systemic, possibly fatal disease. This risk is increased in subjects who are already immunosuppressed by their underlying disease. Use an inactivated vaccine where this exists

(poliomyelitis).
- Phenytoin, fosphenytoin: Risk of exacerbation of convulsions (resulting from the decrease of phenytoin digestive absorption by the cytotoxic drug) or 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
- Cyclosporine (and by extrapolation tacrolimus and sirolimus): Excessive immunosuppression with risk of lymphoproliferation
- Concurrent therapy with nephrotoxic drugs or ototoxic drugs such as aminoglycosides, vancomycin, capreomycin and diuretics may increase or exacerbate toxicity due to Carboplatin induced changes in renal clearance.
- Aminoglycosides: The concomitant use of carboplatin with aminoglycosides antibiotics should be approached with caution due to the cumulative nephrotoxicity and ototoxicity, particularly in renal failure patients.
- Loop diuretics: The concomitant use of carboplatin with loop diuretic should be approached with caution due to the cumulative nephrotoxicity and ototoxicity.
Combination therapy with other myelosuppressive agents may require dose changes or rescheduling of doses in order to minimize the additive myelosuppressive effects
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 eventuality 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. Caution should be exercised when carboplatin is used concomitantly with warfarin, as cases of increased INR have beeen reported.

4.6 Fertility, pregnancy and lactation

Pregnancy

Carboplatin can cause fetal harm when administered to a pregnant woman. The safe use of Carboplatin in pregnancy has not been established. No controlled studies in pregnant women have been conducted. Carboplatin has been shown to be embryotoxic and teratogenic in rats receiving the drug during organogenesis. Both men and women receiving carboplatin should be informed of the potential risk of adverse effects on reproduction.
Women of childbearing potential should be fully informed of the potential hazard to the foetus if this drug is used during pregnancy or should they

become pregnant during carboplatin therapy. Women with child- bearing potential should be advised to avoid becoming pregnant.
In cancer chemotherapy, carboplatin should not be used in pregnant women or women of childbearing potential who might become pregnant unless the potential benefits to the mother outweigh the possible risks to the foetus. Carboplatin has been shown to be mutagenic in vivo and in vitro.

Breast-feeding
It is not known whether Carboplatin is excreted in human milk. If treatment becomes necessary during the lactation period, breastfeeding must be stopped

Fertility
Gonadal suppression resulting in amenorrhea or azospermia may occur in patients receiving antineoplastic therapy. These effects appear to be related to dose and length of therapy and may be irreversible. Prediction of the degree of testicular or ovarian functional impairment is complicated by the common use of combinations of several antineoplastics, which makes it difficult to assess the effects of individual agents.
Men of sexually mature age treated with carboplatin are advised not to father a child during treatment and up to 6 months afterwards. Male patients should seek advice about spermatic preservation prior to initiation of the therapy because of the possibility of irreversible infertility due to therapy with carboplatin.

4.7 Effects on ability to drive and use machines
No studies of the effects on the ability to drive and use machines have been performed. However, carboplatin may cause nausea, vomiting, vision abnormalities, and ototoxicity; therefore, patients should be warned of the potential effect of these events on the ability to drive or to use machines.

4.8 Undesirable 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), and 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, febrile neutropenia, haemolytic-uraemic syndrome, haemolytic anaemia
Immune system disorders	Common	Hypersensitivity, anaphylactoid type reaction
Metabolism and nutrition disorders	Not known	Dehydration, anorexia, hyponatraemia, Tumour lysis syndrome
Nervous system disorders	Common	Peripheral neuropathy, paraesthesia, decreased osteotendinous reflexes, sensory disturbance, dysgeusia
	Not known	Cerebrovascular accident*, encephalopathy, 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, veno-occlusive disease (fatal)
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	Decreased renal clearance of creatinine, increased blood urea, increased blood alkaline phosphatase, increased aspartate aminotransferase, abnormal liver function tests, decreased blood sodium, decreased blood potassium, decreased blood calcium, decreased blood magnesium.
	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.

Blood and lymphatic system disorders:

Myelosuppression is the dose-limiting toxicity of Carboplatin. It is generally reversible and not cumulative when Carboplatin is used as a single agent at recommended frequencies of administration. In patients with normal baseline values, thrombocytopenia with platelet counts below 50,000/mm3 occurs in 25% of patients, neutropenia with granulocyte counts below 1,000/mm3 in 18% of patients, and leukopenia with WBC counts below 2,000/mm3 in 14% of patients. The nadir usually occurs on day 21. Myelosuppression can be worsened by combination of carboplatin injection with other myelosuppressive compounds or forms of treatment.

Anaemia with haemoglobin values below 8 g/dL has been observed in 15% of patients with normal baseline values. The incidence of anaemia is increased with increasing exposure to carboplatin injection. Myelosuppression

may be more severe and prolonged in patients with impaired renal function, extensive prior treatment, in particular in patients previously treated with cisplatin, poor performance status and age above 65. These effects, although usually reversible, have resulted in infectious and hemorrhagic complications in 4% and 5% of patients given carboplatin injection, respectively. These complications have led to death in less than 1% of patients.

Gastrointestinal disorders:

Nausea without vomiting occurs in 15% of patients receiving carboplatin; vomiting has been reported in 65% of the patients and about one-third of these suffer severe emesis. Previously treated patients (in particular patients previously treated with cisplatin) appear to be more prone to vomiting. Nausea and vomiting usually disappear within 24 hours after treatment and are usually responsive to (and may be prevented by) anti-emetic medication. Vomiting is more likely when carboplatin injection is given in combination with other emetogenic compounds. The other gastro-intestinal complaints corresponded to pain in 8% of patients, diarrhoea, and constipation in 6 % of patients.

Nervous system disorders:

The incidence of peripheral neuropathies after treatment with Carboplatin is 4%. In the majority of patients neurotoxicity is limited to paraesthesia and decreased deep tendon (osteotendinous) reflexes. The frequency and intensity of this side effect increases in patients older than 65 years and in those previously treated with cisplatin, as well as those receiving prolonged treatment with carboplatin injection. Paraesthesia present before commencing carboplatin therapy particularly if related to prior cisplatin treatment may persist or worsen during treatment with carboplatin.

Clinically significant-sensory disturbances (i.e, visual disturbances and taste modifications) have occurred in 1% of patients.

The overall frequency of neurologic side effects seems to be increased in patients receiving carboplatin injection in combination. This may also be related to longer cumulative exposure.

Neoplasms, benign and malignant and unspecified (incl. cysts and polyps) Secondary acute malignancies after cytostatic combination therapies containing carboplatin have been reported.

Eye disorders:

Transient visual disturbances, sometimes including transient sight loss, have been commonly reported with platinum therapy. This is usually associated with high dose therapy in renally impaired patients.

Ear and labyrinth disorders:

Auditory defects out of the speech range with impairments in the high frequency (4,000 – 8,000 Hz) were found in serial audiometric investigations with a frequency of 15%. Very rare cases of hypoacusia have been reported.
In patients who have been previously treated with cisplatin and have a hearing organ predamaged due to cisplatin, a further exacerbation in the hearing function sometimes occurs during treatment with carboplatin. At higher than recommended doses, in combination with other ototoxic agents, clinically significant hearing loss has been reported to occur in paediatric patients when carboplatin was administered.

Hepatobiliary disorders:

Modification of liver function in patients with normal baseline values was observed, including elevation of total bilirubin in 5%, SGOT in 15%, and alkaline phosphatase in 24% of patients. These modifications were generally mild and reversible in about one-half the patients. Elevations in SGPT occur less frequently.
In a limited series of patients receiving very high dosages of carboplatin injection and autologous bone marrow transplantation, severe elevation of liver function tests has occurred.
Cases of an acute, fulminant liver cell necrosis occured after high-dosed administration of carboplatin.

Renal and urinary disorders:

Renal toxicity is not usually dose limiting in patients receiving Carboplatin, nor does it require preventative measures such as high volume fluid hydration or forced diuresis. When given in usual doses, development of abnormal renal function has been uncommon, despite the fact that carboplatin injection has been administered without high-volume fluid hydration and/or forced diuresis. Elevation of serum creatinine occurs in 6% of patients, elevation of blood urea nitrogen in 14%, and of uric acid in 5% of patients. These are usually mild and are reversible in about one-half the patients. Creatinine clearance has proven to be the most sensitive renal function measure in patients receiving carboplatin injection. Twenty- seven percent (27%) of patients who have a baseline value of 60 mL/min or greater, experience a reduction in creatinine clearance during carboplatin injection therapy.
The incidence and severity of nephrotoxicity may increase in patients who have impaired kidney function before carboplatin treatment. It is not clear whether an appropriate hydration programme might overcome such an effect, but dosage reduction or discontinuation of therapy is required in the presence of severe alteration in renal function tests.

Immune system disorders:

Anaphylactic-type reactions, sometimes fatal, may occur in the minutes following injection of the product, including: tachycardia, bronchospasm, dyspnoea, hypotension, dizziness, wheezing, urticaria, facial oedema, and anaphylactic shock. These reactions are similar to those observed after administration of other platinum-containing compounds and should be managed with appropriate supportive therapy.

Skin and subcutaneous tissue disorders:

Alopecia is common.

Investigations:

Decreases in serum sodium, potassium, calcium, and magnesium occur in 29%, 20%, 22%, and 29% of patients, respectively. In particular, cases of early hyponatraemia have been reported. The electrolyte losses are minor and mostly take a course without any clinical symptoms.

Cardiovascular disorders:

Isolated cases of cardiovascular incidents (cardiac insufficiency, embolism) as well as isolated cases of cerebrovascular accidents have been reported.

Isolated cases of cardiovascular incidents (cardiac insufficiency, embolism) as well as isolated cases of cerebrovascular accidents have been reported.

General disorders and administration site conditions:

Reactions at the site of injection (burning, pain, reddening, swelling, urticarial, necrosis in connection with extravasation) have been reported.
Fever and chills as well as mucositis have occasionally been observed.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the National Regulatory Authority.

4.9 Overdose:

There is no known antidote for Carboplatin overdose. The anticipated complications of overdosage would be related to myelosuppression as well as impairment of hepatic and renal and auditory function. Use of higher than recommended doses of carboplatin has been associated with loss of vision. If necessary, however the patient may need supportive treatment relating to myelosuppression, renal and hepatic impairment. Reports of doses up to 1,600 mg/m2 indicate patients feeling extremely ill with diarrhoea and alopecia developing.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

ATC Code: Antineoplastic agent; L01X A02 Carboplatin is an antineoplastic agent. Its reactivity has been demonstrated against several murine and human cell lines. Carboplatin exhibited comparable activity to cisplatin against a wide range of tumours regardless of the implant site. Alkaline elution techniques and DNA binding studies have demonstrated the qualitatively similar modes of action of carboplatin and cisplatin. Carboplatin, like cisplatin, induces changes in the superhelical conformation of DNA which is consistent with a "DNA shortening effect".

5.2 Pharmacokinetic properties:

Carboplatin has biochemical properties similar to that of cisplatin, thus producing predominately intrastrand and interstrand DNA crosslinks. Following administration of carboplatin in man, linear relationships exist between dose and plasma concentrations of total and free ultrafiltrable platinum. The area under the plasma concentration versus time curve for total platinum also shows a linear relationship with the dose when creatinine clearance ≥ 60 ml/min. Repeated dosing during four consecutive days did not produce an accumulation of platinum in plasma. Following the administration of carboplatin reported values for the terminal elimination half-lives of free ultrafiltrable platinum and carboplatin in man are approximately 6 hours and 1.5 hours respectively. During the initial phase, most of the free ultrafiltrable platinum is present as carboplatin. The terminal half-life for total plasma platinum is 24 hours. Approximately 87% of plasma platinum is protein bound within 24 hours following administration. Carboplatin is excreted primarily in the urine, with recovery of approximately 70% of the administered platinum within 24 hours. Most of the drug is excreted in the first 6 hours. The total body and renal clearance of free ultrafilterable platinum correlate with the rate of glomerular filtration but not tubular secretion.

5.3 Preclinical safety data:

Carboplatin has been shown to be embryotoxic and teratogenic in rats. It is mutagenic in vivo and in vitro and although the carcinogenic potential of Carboplatin has not been studied, compounds with similar mechanisms of action and mutagenicity have been reported to be carcinogenic.

6. Pharmaceutical particulars:

6.1 List of Excipients
Water For Injection BP

6.2 Incompatibilities:
Aluminium – containing equipment should not be used
This medicinal product must not be mixed with other medicinal products except those mentioned in section 5.6.

6.3 Shelf life:
24 Months

6.4 Special precautions for storage:
Do not store above 30°C.
Keep container in the outer carton

6.5 Nature and contents of container:
Glass Container of USP Type I:
Clear and colourless USP Type I containers were chosen for the filling of products as containers of USP Type I are high resistant borosilicate glass, generally used for packing of acidic parenteral preparations. This glass has high silicon content, and it is the least reactive, which means that the glass is least likely to have a chemical reaction with whatever you place inside it. The glass will not leech into its contents, which can happen with a more reactive glass type. Type I glass containers are highly resistant to temperature changes. They have a low coefficient of expansion.
Since Carboplatin Injection has pH between 5.0 to 7.0, so USP Type I containers are most suitable for packing of Carboplatin Injection. Also amber colour glass vial are chosen because the product is light sensitive.
Closure:
20 mm Bromo Butyl Rubber Plug:
20 mm Bromo Butyl rubber Plug are Teflon coated made from suitable compounded and vulcanized rubber, non-porous having smooth finish and free from embedded particles and having self-sealing property, suitable to fit in 20 mm neck of glass vial.
20 mm Aluminium Flip off Seal:
Flip off Seal Made of Aluminium and Nontoxic Polypropylene.

6.6 Special precautions for disposal and other handling:
For single use only. Discard any unused contents. Dilution:

Carboplatin Concentrate for Solution for Infusion must be diluted before use. Carboplatin Concentrate for Solution for Infusion may be further diluted in Glucose 5% or Sodium Chloride 0.9% and administered as an intravenous infusion.

Handling:

Carboplatin should be prepared for administration only by professionals who have been trained in the safe use of chemotherapeutic agents.

Transfer to syringes and infusion containers should be carried out only in the designated area. Personnel carrying out these procedures should be adequately protected with clothing, gloves and an eye shield.

Pregnant personnel are advised not to handle chemotherapeutic agents.

Contamination:

In the event of contact of Carboplatin with eyes or skin, wash the affected area with copious amounts of water or normal saline. A bland cream may be used to treat transient stinging of skin. Medical advice should be sought if the eyes are affected.

In the event of spillage, two operators should put on gloves and mop up the spilled material with a sponge kept for that purpose. In the event of powder spillage, cover with a cloth and moisten with water before mopping up. Rinse the area twice with water. Put all solutions and sponges in a plastic bag, seal and label with the words 'CYTOTOXIC WASTE' and incinerate.

Disposal:

Syringes, containers, absorbent materials, solutions 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.

6.7 How Supplied

Carboplatin Injection is supplied as a Liquid injection in glass vials, USP Type I. The following packages are available:

Carboplatin Injection 150 mg/15 ml:

15 ml amber moulded Glass Vial, USP Type I Vial containing clear, colorless solution.

Carboplatin Injection 450 mg/45 ml:

50 ml amber moulded Glass Vial USP Type I Vial containing clear, colorless solution.

7. Marketing Authorization Holder:

Marketing Authorization Holder:
National Pharmacy Ltd
P.O. Box 17843-00500,
Nairobi, Kenya

Manufacturer:
Biozenta Lifescience Pvt. Ltd.,
Khasra NO. 59, 60 & 61, Bela Bathri,
Tehsil Haroli, Distt. Una
Himachal Pradesh 174301 India

8. Marketing authorization number(s)

Carboplatin Injection BP 150 mg/15mL: H2026/CTD12810/26838
Carboplatin Injection BP 450 mg/45mL: H2026/CTD12734/26842

9. Date of first authorization/renewal of the authorization:

Date of latest renewal of registration:
Carboplatin Injection BP 150 mg/15mL: 16 March 2026
Carboplatin Injection BP 450 mg/45mL: 16 March 2026

10. Date of revision of the text

16 March 2026