AUSTRALIAN PRODUCT INFORMATION – DBL™ Carboplatin Injection (Carboplatin)

1. NAME OF THE MEDICINE

Carboplatin

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DBL Carboplatin Injection is a sterile solution of carboplatin in Water for Injections and is presented in vials containing 5, 15, or 45 mL of 10 milligrams/mL carboplatin.

Each mL of DBL Carboplatin Injection contains carboplatin 10 mg.

For the full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Solution for injection.

DBL Carboplatin Injection is a clear, colourless or slightly yellow solution free from particulates. The solution does not contain any preservatives. The pH of the injection ranges between 4.0 to 7.0.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Carboplatin is indicated in the treatment of:

- advanced stage ovarian cancer of epithelial origin
- small cell lung carcinoma
- carcinoma of the head and neck
- carcinoma of the testis
- paediatric cerebral tumours
- soft tissue sarcoma
- neuroblastoma.

4.2 Dose and method of administration

Dosage

Adult: The recommended dose of carboplatin in previously untreated adults with normal renal function is 400 milligrams/m^2 given as a single intravenous infusion over 15 to 60 minutes. Therapy should not be repeated until four weeks after the previous carboplatin course.

It is recommended that according to clinical circumstances the initial dosage may require reduction by 20 to 25% in patients with risk factors such as increasing age, previous myelosuppressive therapy and poor performance status.

Dosage modification may be required when carboplatin is used in combination with other myelosuppressive drugs or radiation therapy, to minimise additive myelosuppressive effects.

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

Dosage Adjustment

Renal impairment

In patients with initial impaired renal function reduction of dosage of carboplatin may be required. Haematological nadirs and renal function should be monitored in these circumstances.

A suggested dosage schedule in patients with impaired renal function based on creatinine clearance is as follows:

Creatinine Clearance	**Dose of Carboplatin**
>40 mL/min	400 milligrams/m^2
20-39 mL/min	250 milligrams/m^2
0-19 mL/min	150 milligrams/m^2

Children

Sufficient usage of carboplatin in paediatrics has not occurred to allow specific dosage recommendations to be made. Physicians are advised to refer to recently published literature for information on the current dosing regimens for particular tumours.

Method of Administration

Preparation of carboplatin solution

Equipment containing aluminium components should be avoided (see section 4.4 Special warnings and precautions for use).

DBL Carboplatin Injection is a ready to use solution containing 10 milligrams/mL carboplatin in Water for Injections.

The injections may be further diluted in 5% glucose intravenous infusion. To reduce microbiological hazard, use as soon as practicable after preparation. If storage is necessary, hold at 2-8°C for not more than 24 hours.

Contains no antimicrobial agent. Product is for single use in one patient only. Discard any residue.

These products contain no antimicrobial agent. In order to reduce microbiological contamination hazard, infusion should be commenced as soon as practicable after preparation. Infusion should be completed within 24 hours of preparation and any residue discarded.

Compatibilities

Carboplatin has been found to be stable for 24 hours when admixed with 5% glucose in water.

Handling guidelines

1. Carboplatin should be prepared for administration only by professionals who have been trained in the safe use of the preparation.
2. Operations such as 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 transient stinging of the skin. Medical advice should be sought if the eyes are affected.

(b) In the event of spillage, operators should put on gloves and mop up 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. The bag should be prominently labelled with the words "Cytotoxic Waste" or similar.

Disposal

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 or more.

4.3 Contraindications

Carboplatin is contraindicated in patients with the following conditions:

- severe myelosuppression.
- pre-existing severe renal impairment; dose adjustment may allow use in the presence of mild renal impairment (see section 4.2 Dose and method of administration).
- history of severe allergic reactions to carboplatin, other platinum-containing compounds (e.g., cisplatin) or mannitol.
- severe bleeding.
- pregnancy or lactation.

4.4 Special warnings and precautions for use

Carboplatin should only be administered to patients 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 appropriate management of therapy and possible

complications, particularly in the case of administration of high drug dosages.

Carboplatin is a highly toxic drug with a narrow therapeutic index and a therapeutic effect is unlikely to occur without some evidence of toxicity.

Bone Marrow Function

Carboplatin should be administered with caution to patients with significant bleeding or with bone marrow depression.

Bone marrow suppression (leucopenia, neutropenia and thrombocytopenia) is dose dependent and is the dose-limiting toxicity of carboplatin. Although at the recommended drug doses, the haematologic toxicity of carboplatin is usually moderate and reversible, severe myelosuppression (especially thrombocytopenia) may occur in patients with renal impairment and in patients who are concurrently receiving (or have received) other myelosuppressive drugs or radiation therapy.

Peripheral blood counts and renal function should be monitored closely. Blood counts should be performed prior to commencement of carboplatin therapy and weekly thereafter. Aside from monitoring toxicity, this practice will help determine the nadir and recovery of the haematological parameters and assist in subsequent dose adjustments. Lowest levels in white cells and platelets are generally seen between days 14 and 28, and days 14 and 21 respectively after initial therapy. A greater reduction in platelets is seen in patients who previously received extensive myelosuppressive chemotherapy than non-treated patients. White blood cell counts less than 2×10^9 cells/L (2,000 cells/mm^3) or platelets less than 50×10^9 cells/L (50,000 cells/mm^3) should cause consideration of postponement of carboplatin therapy until bone marrow recovery is evident, which is usually 5 to 6 weeks. Transfusions may be required.

The occurrence, severity and protraction of toxicity are likely to be greater in patients who have received extensive prior treatment for their disease, have poor performance status and who are more advanced in age. Dosage reduction may be necessary in cases of severe toxicity. Treatment of severe haematologic toxicity may consist of supportive care, anti-infective agents for complicating infections, transfusions of blood products, autologous bone marrow rescue, peripheral stem cell transplantation and haematopoietic agents (colony-stimulating factors).

Carboplatin courses should not, in general, be repeated more frequently than every four weeks in order to ensure that the nadir in blood counts has occurred and that there has been recovery to a satisfactory level.

Hypersensitivity Reactions

Hypersensitivity and anaphylactic reactions to carboplatin have been reported. These allergic reactions have been similar in nature and severity to those reported with other platinum containing compounds. Symptoms include rash, urticaria, erythema, pruritus, bronchospasm and hypotension. Patients should be monitored for possible anaphylactoid reactions and appropriate equipment and medication should be readily available to treat such reactions (e.g., antihistamines, corticosteroids, adrenaline (epinephrine), oxygen) whenever carboplatin is administered.

There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction, see section 4.8). Kounis syndrome can develop in patients with and without cardiac risk factors. Kounis

syndrome may present with a combination of cardiac and allergic symptoms, or as standalone acute allergic coronary arteriospasm. Coronary vasospasm may be eliminated with steroids, antihistamines in addition to spasmolytics treatment.

Central Nervous System (CNS)/Hearing Functions

Neurotoxicity, such as paraesthesias and decreased deep tendon reflexes, and ototoxicity are more likely to be seen in patients who have received cisplatin previously. Routine neurologic examination is advisable during carboplatin therapy, particularly in patients previously treated with cisplatin and in patients over 65 years of age. Ototoxicity is cumulative. The frequency and severity of hearing disorder increases with high dose regimens and repeated doses, or prior treatment with cisplatin (as cisplatin is also ototoxic). Assessment of hearing should be performed prior to initiating therapy and regularly during treatment or when auditory symptoms occur. Clinically important deterioration of auditive function may require dosage modifications or discontinuation of therapy. The risk of ototoxicity may be increased by concomitant administration of other ototoxic drugs (e.g., aminoglycosides) (see section 4.5 Interactions with other medicines and other forms of interactions).

Delayed onset hearing loss has been reported in paediatric patients. Long-term audiometric follow-up in this population is recommended.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

Cases of RPLS have been reported in patients receiving carboplatin in combination chemotherapy. RPLS is a rare, reversible after treatment discontinuation, rapidly evolving neurological condition, which can include seizure, hypertension, headache, confusion, blindness, and other visual and neurological disturbances. Diagnosis of RPLS is based upon confirmation by brain imaging, preferably MRI.

Blood and Lymphatic System Disorders

Haemolytic anaemia with the presence of serologic drug-induced antibodies has been reported in patients treated with carboplatin. This event can be fatal.

Haemolytic uraemic syndrome (HUS) is a potentially life-threatening side effect. Carboplatin should be discontinued at the first sign of any evidence of microangiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or lactate dehydrogenase (LDH). Renal failure may not be reversible with discontinuation of therapy and dialysis may be required.

Secondary Leukaemia

Acute promyelocytic leukaemia (APL) and myelodysplastic syndrome (MDS)/acute myeloid leukaemia (AML) have been reported years after therapy with carboplatin and other antineoplastic treatments.

Hepatobiliary Disease

Cases of hepatic veno-occlusive disease (sinusoidal obstructive syndrome) have been reported. Some of them were fatal.

Gastrointestional Effects

Carboplatin can induce emesis. The incidence and severity of emesis may be reduced by pre-treatment with antiemetics or by carboplatin administration as a continuous IV infusion over 24 hours, or as IV administration of divided doses over 5 consecutive days rather than a single infusion. Selective inhibitors of type 3 (5HT-3), serotonergic receptors (e.g., ondansetron) or substituted benzamides (e.g., metoclopamide) may be particularly effective antiemetics and combination therapy may be considered for patients experiencing severe or refractory emetogenic effects.

Tumour Lysis Syndrome (TLS)

Patients at high risk of TLS such as patients with high proliferative rate, high tumour burden and high sensitivity to cytotoxic agents should be monitored closely and appropriate precaution taken.

Immunosuppresant Effects/Increased Susceptibility to Infections

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.

Carboplatin should be administered with caution to patients with herpes zoster, existing or recent chicken pox, or recent exposure to chicken pox, due to the risk of severe generalised disease. It should also be administered with caution to patients with other infections.

The myelosuppressive effects of carboplatin may adversely affect dental procedures, resulting in an increased incidence of microbial infection, delayed healing and gingival bleeding. Where possible, dental work should be completed prior to initiation of carboplatin therapy, or deferred until blood counts have returned to normal. Patients should be instructed on proper oral hygiene during treatment, including caution in the use of toothbrushes, dental floss and toothpicks.

Aluminium

Aluminium-containing equipment should not be used (see sections 4.5 Interactions with other medicines and other forms of interactions and 6.2 Incompatibilities).

Use in Renal Impairment

Carboplatin is excreted primarily in the urine and renal function should be assessed prior to and during therapy. Creatinine clearance appears to be the most sensitive measure of kidney function in patients receiving carboplatin. Dose adjustment criteria for patients with impaired renal function are provided in Section 4.2 Dose and method of administration.

Myelosuppression as a result of carboplatin treatment is closely related to the renal clearance of the drug. Therefore, in patients who have abnormal renal function or who are receiving concomitant therapy with nephrotoxic drugs, myelosuppression, especially thrombocytopenia, may be more severe and prolonged.

Renal toxicity is not usually dose-limiting. Unlike cisplatin therapy, pre-treatment and post-treatment hydration is not necessary as the drug has a relatively low nephrotoxic potential.

However, about 25% of patients show decreases in creatinine clearance and, less frequently, rises in serum creatinine and blood urea nitrogen may be seen. Impairment of renal function is more likely to be seen in patients who have previously experienced nephrotoxicity as a result of cisplatin therapy. Concomitant administration of other nephrotoxic drugs (e.g., aminoglycoside antibiotics) may increase the risk of nephrotoxicity (see section 4.5 Interactions with other medicines and other forms of interactions).

Use in the Elderly

Carboplatin-induced peripheral neuropathy appears to be more common in those over 65 years of age than in younger patients. Elderly patients may have decreased renal and haematopoietic function, and may be more susceptible to other effects of the drug (see section 4.8 Adverse effects (undesirable effects)).

Paediatric Use

Safety and efficacy in children have not been established.

Effects on Laboratory Tests

No data available.

4.5 Interactions with other medicines and other forms of 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 in contact with carboplatin should not be used for preparation or administration of the drug (see section 6.2 Incompatibilities).

Concomitant administration of carboplatin and aminoglycosides results in an increased risk of nephrotoxicity and/or ototoxicity, and the drugs should be used concurrently with caution. The use of other nephrotoxic drugs results in a potentiation of renal effects by carboplatin.

Carboplatin is mostly used in combination with antineoplastic drugs having similar cytotoxic effects. In these circumstances additive toxicity is likely to occur. Combination therapy with other myelosuppressive medicines may require modification of the dose or timing of carboplatin therapy to minimise additive myelosuppressive effects. Dosage reduction is recommended if carboplatin is administered concurrently with radiation therapy.

In patients who have previously received cisplatin, neurotoxicity such as paraesthesias, decreased deep tendon reflexes, and ototoxicity are more likely to be seen. The frequency and severity of hearing disorder increases with prior treatment with cisplatin (as cisplatin is also ototoxic). Paraesthesias present prior to treatment, especially if caused by cisplatin, may persist or worsen during carboplatin therapy.

In patients receiving carboplatin concomitantly with paclitaxel, myalgias and arthralgias commonly occur. Fatigue has also been reported in patients receiving this combination.

Pain, most likely related to tumour size, and asthenia occur frequently in patients receiving carboplatin in conjunction with cyclophosphamide. Visual disturbances have been reported in patients receiving usual dosages of carboplatin in conjunction with cyclophosphamide.

Concomitant administration of carboplatin with other emetogenic drugs, or administration to

patients who have previously received emetogenic drugs, has increased the incidence of nausea and vomiting.

Vaccination with a live vaccine should be avoided in patients receiving carboplatin (see section 4.4 Special warnings and precautions for use).

A decrease in phenytoin serum levels has been observed with concurrent administration of carboplatin and phenytoin/fosphenytoin. This may lead to exacerbation of seizures.

4.6 Fertility, pregnancy and lactation

Effects on Fertility

Both men and women receiving carboplatin should be informed of the potential risk of adverse effects on reproduction. Women of child-bearing potential should be advised to avoid becoming pregnant by using effective contraception during treatment and for at least 7 months after therapy. For women who are pregnant or become pregnant during therapy, genetic counselling should be provided.

Carboplatin is genotoxic. Men being treated with carboplatin are advised not to father a child during and for at least 4 months after treatment.

Male and female fertility may be impacted by treatment with carboplatin. Most forms of chemotherapy have been associated with reduction of oogenesis and spermatogenesis and patients receiving carboplatin should be warned of this potential. Although not reported with carboplatin, this has been reported with other platinum agents. Recovery of fertility after exposure can occur but is not guaranteed. Both men and women should seek advice for fertility preservation before treatment with carboplatin.

Use in Pregnancy – Category D

This category specifies medicines which have caused or may be expected to cause an increased incidence of human fetal malformations or irreversible damage. These medicines may also have adverse pharmacological effects.

Carboplatin has been shown to be embryotoxic and mutagenic. Use in pregnancy is not recommended. Women of child-bearing potential should use adequate contraception and carboplatin should only be used in women of child-bearing potential if the expected benefits outweigh the risks of such therapy.

If the patient becomes pregnant while being treated with carboplatin, she should be advised of the potential hazard to the fetus.

Use in Lactation

Carboplatin and its active metabolites have been identified in human milk of treated mothers. To avoid possible harmful effects in infants, breast-feeding should be discontinued during carboplatin therapy and for 1 month following last dose of treatment or treatment should be discontinued, taking into account the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (undesirable effects)

Myelosuppression is the dose-limiting toxicity of carboplatin. It is generally reversible and is not cumulative when carboplatin is used as single agent and at the recommended frequencies of administration.

Adverse effects which have been observed in studies to date can be grouped under the following organ systems:

Blood and lymphatic system disorders: Leucopenia (55%), thrombocytopenia (32%), anaemia (59%). Myelosuppression is dose-related, and appears to be most common and more severe in patients who have received prior antineoplastic therapy (especially cisplatin), those who have received or who are currently receiving other myelosuppressive drugs or radiation therapy, and those with renal impairment. Transfusional support has been required in about one-fifth of patients.

Platelet and leukocyte/granulocyte nadirs usually occur two to three weeks from drug administration. Recovery is generally adequate to allow the administration of the subsequent carboplatin dose four weeks after a previous administration. Anaemia (haemoglobin less than 11 g/dL), which may be symptomatic, occurs in a substantial proportion of patients. This effect may be cumulative and transfusions may be needed particularly in patients receiving prolonged therapy (e.g., more than 6 cycles).

Haemolytic anaemia (sometimes fatal) has also been reported.

Clinical sequelae of bone marrow/haematologic toxicity such as fever, infections, sepsis/septic shock and haemorrhage may be expected.

Haemolytic uraemic syndrome has been reported.

Gastrointestinal disorders: Nausea and vomiting (53%), nausea only (25%), diarrhoea (6%), constipation (3%). Nausea and vomiting generally are delayed 6 to 12 hours after administration of carboplatin and disappear within 24 hours, but may persist for up to 3 days in some patients. Vomiting may be delayed for 24 hours or longer after treatment in some patients. Nausea and vomiting are readily controlled (or may be prevented) with antiemetic medication. Gastrointestinal pain, diarrhoea, constipation, mucositis and stomatitis have also been reported.

Renal and urinary disorders: Decrease in creatinine clearance (25%); increases in uric acid (25%), blood urea nitrogen (16%) and serum creatinine (7%). Acute renal failure has been reported rarely. Risk of carboplatin-induced nephrotoxicity (e.g., impaired creatinine clearance) becomes more prominent at relatively high dosages or in patients previously treated with cisplatin.

Investigations: Decreases in serum magnesium (37%), potassium (16%) and, rarely, calcium (5%). Carboplatin may also cause decreases in serum sodium levels. These changes have not been severe enough to cause clinical symptoms.

Nervous system disorders: Peripheral neuropathy (6%) which was mild, and dysgeusia (<1%). In the majority of patients, neurotoxicity manifests mainly as paraethesias and decreased deep tendon reflexes. The effect, more common in patients over 65 years of age, appears to be cumulative, occurring mainly in patients receiving prolonged therapy and/or in those who have received prior cisplatin therapy. Central neurotoxicity has also been reported, although this may be related to concomitant antiemetic therapy. Fatigue has been reported in patients receiving carboplatin concomitantly with paclitaxel. Dysgeusia has been reported in patients taking carboplatin.

Ear and labyrinth disorders: Subclinical decrease in hearing acuity as determined by audiogram, in the high frequency (4,000 to 8,000 Hz) range (15%); clinical ototoxicity, usually manifested as tinnitus (1%). Pre-existing hearing impairment may persist or worsen with carboplatin therapy. In patients who developed hearing loss as a result of cisplatin therapy, the impairment may persist or worsen.

Hepatobiliary disorders: Increases in liver enzymes have been transient in the majority of cases. Alkaline phosphatase (ALP) (30%), aspartate aminotransferase (AST) (15%), bilirubin (4%). Substantial abnormalities in liver function test have been reported in patients treated with carboplatin at high doses and autologous bone marrow transplantation.

Immune system disorders: In less than 2% of patients, reactions similar to those seen after cisplatin have been observed. Erythematous rash, fever, perioral tingling, urticaria, pruritus, bronchospasm, hypotension, hypoxia and pyrexia have been observed. Anaphylaxis and anaphylactoid reactions have also occurred, while exfoliative dermatitis has been reported rarely. In a few cases, no cross-reactivity was present. The frequency of allergic reactions is higher in patients who receive carboplatin in conjunction with other antineoplastic agents. Hypersensitivity reactions may occur within a few minutes after IV administration of carboplatin.

Eye disorders: Visual abnormalities, such as transient sight loss (which can be complete for light and colours) or other disturbances may occur in patients treated with carboplatin. Improvement and/or total recovery of vision usually occurs within weeks after the drug is discontinued. Cortical blindness has been reported in patients with impaired renal function receiving high-dose carboplatin.

Neoplasms – benign, malignant and unspecified: There have been rare reports of acute myelogenous leukaemias and myelodysplatic syndromes arising in patients who have been treated with carboplatin, mostly when given in combination with other potentially leukaemogenic agents.

Cardiac disorders: Cardiac failure, ischaemic coronary artery disorders (e.g., myocardial infarction, cardiac arrest, angina, myocardial ischaemia), Kounis syndrome (acute allergic coronary arteriospasm).

Vascular disorders: Cerebrovascular events.

Skin and subcutaneous tissue disorders: Exfoliative dermatitis may rarely occur. Erythematous rash, pruritus, urticaria and alopecia have also been reported in association with carboplatin.

Musculoskeletal and connective tissue disorders: Myalgia/arthralgia. This can commonly occur in patients receiving carboplatin together with paclitaxel (see section 4.5 Interactions with other medicines and other forms of interactions).

Metabolism and nutrition disorders: Electrolyte abnormalities (hypokalaemia, hypocalcaemia, hyponatraemia and/or hypomagnesaemia).

General disorders and administration site conditions: Alopecia (2%), flu-like syndrome (1%), reaction at injection site (<1%). Taste abnormalities, and adverse respiratory and genitourinary effects have also been reported. Pain, most likely related to tumour size, and asthenia occur frequently in patients receiving carboplatin in conjunction with cyclophosphamide.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 Overdose

No overdosage occurred during clinical trials. Should it occur, the patient may need to be sustained through complications relating to myelosuppression, renal impairment and hepatic impairment. From reports in which doses up to 1600 milligrams/m^2 were used, patients were said to feel extremely unwell and developed diarrhoea and alopecia.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of Action

Carboplatin, an analogue of cisplatin, is an antineoplastic agent which interferes with DNA intrastrand and interstrand crosslinks in cells exposed to the drug. DNA reactivity has been correlated with cytotoxicity.

Clinical Trials

No data available.

5.2 Pharmacokinetic properties

Distribution

Initially protein binding is low. During the first 4 hours after administration 0 to 29% of carboplatin is protein bound. By 24 hours 85 to 89% is protein bound.

Elimination

After a one-hour infusion of the drug (dose range 20 to 520 milligrams/m^2) plasma levels of total platinum and ultrafilterable (free) platinum decay biphasically following first order kinetics. For ultrafilterable platinum reported values for the initial phase of the half life ($t_{alpha\ 1/2}$) are about 90 minutes and in the later phase the half life ($t_{beta\ 1/2}$) is about 6 hours. Total platinum elimination has a similar initial half life while in the later phase the half life is longer (approximately 5 days). Carboplatin is a stable molecule. All free platinum is in the form of carboplatin in the first 4 hours.

65% of the carboplatin dose is eliminated in the urine within 24 hours of administration with 32% of the dose being excreted as unchanged drug. Most of the drug is excreted in the first 6 hours.

Excretion

Excretion of carboplatin is by glomerular filtration. Patients with poor renal function have a higher Area Under Curve for total platinum and a reduction in dosage is recommended.

5.3 Preclinical safety data

Genotoxicity

Carboplatin has been shown to be mutagenic in mammalian cells. Patients should be advised of its mutagenic potential and should use effective contraception for an adequate duration of time after ceasing therapy (see section 4.6 Fertility, pregnancy and lactation).

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

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

Parenteral drugs should be inspected visually for particulate matter and discolouration, prior administration, whenever solution and container permit. If particulate matter observed, shake

and re-inspect. Vials with visible particulate matter should not be used.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store below 25°C. Do not freeze. Protect from light.

6.5 Nature and contents of container

DBL Carboplatin Injection is available as below,

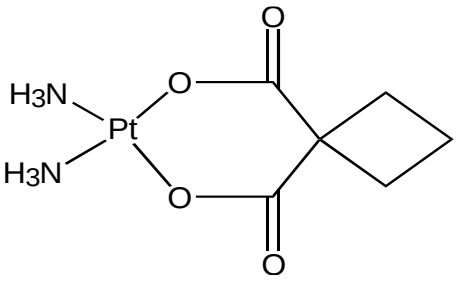
Strength	**Packs**
50 mg/5 mL	1 × 5 mL glass vial
150 mg/15 mL	1 × 20 mL glass vial
450 mg/45 mL	1 × 50 mL glass vial

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

Chemical structure



CAS number

41575-94-4

7. MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription Only Medicine

8. SPONSOR

Pfizer Australia Pty Ltd

Level 17, 151 Clarence Street

Sydney NSW 2000

Toll Free Number: 1800 675 229

www.pfizermedicalinformation.com.au

9. DATE OF FIRST APPROVAL

50 mg/5 mL: 13 August 1991

150 mg/15 mL: 31 January 1994

450 mg/45 mL: 31 January 1994

10. DATE OF REVISION

28 February 2024

™ = Trademark

Summary Table of Changes

Section changed	Summary of new information
4.6	Effects on Fertility Update to the duration of the effective use of contraception in child-bearing women and men after the last dose of treatment with carboplatin. Use in Lactation Update to breastfeeding information and the breast-feeding discontinuation and washout period.
5.2	Update to the elimination t½ of total plasma platinum post carboplatin treatment.