NEW ZEALAND DATA SHEET
CARBOPLATIN SOLUTION FOR INJECTION

1. PRODUCT NAME

Carboplatin Accord

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Carboplatin Accord Injection is a sterile solution of carboplatin in water for injections. The vials contain 50 mg, 150 mg or 450 mg of carboplatin as a 10 mg/mL solution. The solution does not contain any preservatives.

For the full list of excipients, see **Section 6.1 List of Excipients**.

3. PHARMACEUTICAL FORM

Carboplatin Accord is a solution for injection.

It is clear, colourless or slightly yellow solution free from particulates and is presented in vials.

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

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

Adults: The recommended dose of carboplatin in previously untreated adults with normal renalfunction is 400 mg/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.

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.

Impaired Renal Function: In patients with initial impaired renal function reduction of dosage of carboplatin may be required. Haematologicial nadirs and renal function should be monitoredin 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

Method of administration

For instructions on dilution of the medicine before administration, see **Section 6.6 Special Precautions for Disposal and Other Handling.**

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 presenceof 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).
- 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 the 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 cells counts less than $2x10^9$ cells/L (2,000 cells/mm^3) or platelets less than $50x10^9$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 havereceived extensive prior treatment for their disease, have poor performance status and who aremore advance in age. Dosage reduction may be necessary is 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 weeksin order to ensure that the nadir in blood counts has occurred and that there has been recoveryto a satisfactory level.

Hypersensitivity reactions

Hypersensitivity and anaphylactic reactions to carboplatin have been reported. These allergicreactions 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, epinephrine, oxygen) whenever carboplatin is administered.

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 treatedwith cisplatin and in patients over 65 years of age. Ototoxicity is cumulative. The frequency and severity of hearing disorders 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-uremic syndrome (HUS) is a potentially life-threatening side effect. Carboplatin should be discontinued at the first sign of any evidence of microangiopathic haemolyticanaemia, 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 leukemia (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.

Gastrointestinal effects

Gastrointestinal, carboplatin can induce emesis. The incidence and severity of emesis may bereduced by pre-treatment with antiemetics or by carboplatin administration as a continuous IVinfusion over 24 hours, or as IV administration of divided doses over 5 consecutive days ratherthan a single infusion. Selective

inhibitors of type 3 (5-HT3), serotonergic receptors (e.g. ondansetron) or substituted benzamides (e.g. metoclopramide) 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 andhigh sensitivity to cytotoxic agents should be monitored closely and appropriate precaution taken.

Immunosuppressant 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 orinactivated 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, resultingin 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 deferreduntil 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 **Section 4.5 Interactions with Other Medicines and Other Forms of Interactions and Section 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. Pre-treatment and post-treatment hydration is not necessary. 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 renalfunction is more likely to be seen in patients who have previously experience 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 elderly patients

Carboplatin-induced peripheral neuropathy appears to be more common in those over 65 yearsof age than in younger patients. Elderly patients may have decreased renal and haematopoieticfunction, and may be more susceptible to other effects of the drug (see **Section 4.8 Undesirable Effects**).

Paediatric population

Safety and efficacy in children have not been established.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

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**).

Concurrent therapy with nephrotoxic drugs may increase or exacerbate toxicity due to carboplatin-induced changes in renal clearance. Patients receiving aminoglycoside antibioticsor other nephrotoxic drugs should not be treated with carboplatin.

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 drugs may require modification of the dose or timing of carboplatin therapy to minimize 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 andseverity 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 persistor 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 inpatients receiving usual dosages of carboplatin in conjunction with cyclophosphamide.

An increased incidence of emesis has been reported when carboplatin and other emetogenic drugs are given concurrently or carboplatin is administered to patients who previously received emetogenic therapy.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

Fertility

Both men and women receiving carboplatin should be informed of the potential risk of adverseeffects on reproduction. Women of childbearing potential should be advised to avoid becomingpregnant by using effective contraception during treatment and up to 6 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 up to three months after treatment and to seek advice on conservation of sperm priorto treatment because of the possibility of irreversible infertility due to therapy with carboplatin.

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 fertilitypreservation before treatment with carboplatin.

Pregnancy – Category D

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

Carboplatin has been shown to be embryotoxic and mutagenic. Use in pregnancy is not recommended. Women of childbearing 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.

Breast-feeding

It is not known whether carboplatin is excreted in breast milk. To avoid possible harmfuleffects in the infant, breast-feeding is not advised during carboplatin therapy.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINERY

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

4.8 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/septicshock and haemorrhage may be expected.

Haemolytic uremic syndrome (HUS) 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, 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. Mild and transient elevations of serum creatinine and of blood urea nitrogen concentrations may occur. 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 notbeen 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 paraesthesias 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. CNS effects may also occur. In some cases the neurotoxicity seen with carboplatin may be the result of a combination with some delayedeffect of 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 byaudiogram, in the high frequency (4,000-8,000Hz) range (15%); clinical ototoxicity, usuallymanifested 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 forlight 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 functionreceiving high-dose carboplatin.

Neoplasms benign, malignant and unspecified: There have been rare reports of acute myelogenous leukemias and myelodysplastic syndromes arising in patients who have beentreated with carboplatin, mostly when given in combination with other potentially leukemogenic agents.

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

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 Admimistration 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. Haemolytic uraemic syndrome has occurred rarely. Pain,most likely related to

tumour size, and asthenia occur frequently in patients receiving carboplatin in conjunction with cyclophosphamide.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

There are no known antidotes for carboplatin overdosage, thus every possible measure should be taken to avoid an overdose; this includes full awareness of the potential danger of an overdose, careful calculation of the dose to be administered and availability of adequate diagnostic and treatment facilities. Acute overdosage with carboplatin may result in an enhancement of its expected toxic effects (e.g. severe myelosuppression, intractable nausea and vomiting, severe neurosensorial toxicities, liver failure, kidney failure, etc.). Death may follow. Signs and symptoms of overdosage should be managed with supportive measures.

The patient may need to be sustained through complications relating to myelosuppression, renal impairment and hepatic impairment. Diarrhoea and alopecia may develop.

For advice on the management of overdose please contact the National Poisons Centre on 0800POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Carboplatin, an analogue of cisplatin, is an antineoplastic agent which interferes with DNA intra-strand and inter-strand 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 0-29% of carboplatin isproteinbound. By 24 hours 85-89% is protein bound.

Elimination

After a one-hour infusion of the drug (dose range 20 to 520 mg/m^2) plasma levels of total platinum and ultrafilterable (free) platinum decay bi-phasically following first order kinetics. For ultrafilterable platinum reported values for the initial phases of the half life ($t_{alpha\ ½}$) are about 90 minutes and in the later phase the half life ($t_{beta\ ½}$) is about 6 hours. Total platinum elimination has a similar initial half life while in the later phase the half life of total platinum may be greater than 24 hours. 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 first6 hours.

Excretion

Excretion of carboplatinis by glomerular filtration. Patients with poor renal function have a higher Area Under Curvefor 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.

Carcinogenicity

No data available.

Reproductive and developmental toxicity

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

24 months from date of manufacture stored at or below 25°C

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Carboplatin Accord should be stored at or below 25ºC. Do not freeze. Protect from light.

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

These products contain no antimicrobial agent. However, 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.

6.5 NATURE AND CONTENTS OF CONTAINER

Three strengths are available as follows: 50 mg/5 mL, 150 mg/15 mL and 450 mg/45 mL in glass vials in packs of 1.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Preparation

Equipment containing aluminium components should be avoided (see **Section 4.4 Special Warnings and Precautions for Use**). Carboplatin Accord is a ready to use solution containing 10 mg/mL carboplatin is water for injections.

The injections may be further diluted in 5% Glucose Intravenous Infusion B.P. 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.

Handling

1. Carboplatin should be prepared for administration only by professionals who have beentrained 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 withclothing, 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 intocontact with carboplatin should be placed in a thick plastic bag or other impervious container and incinerated at 1000°C or more.

7. MEDICINE SCHEDULE

Prescription Only Medicine

8. SPONSOR

Pharmacy Retailing (NZ) Limited Trading as Healthcare Logistics
58 Richard Pearse Drive
Airport Oaks
Auckland 2022
New Zealand

Phone: 0800 004 375

9. DATE OF FIRST APPROVAL

15 December 2022

10. DATE OF REVISION

06 February 2023

Version 2.0

Section Changed	Summary of new information
Throughout	Minor editorial changes
4.3	Included example of platinum compound, cisplatin
4.4	Added warning for carboplatin as highly toxic drug. Updated the following Warnings and Precautions for use; Bone marrow function, Central nervous system (CNS)/Hearing functions, Aluminium, Use in renal impairment.
4.5	Updated information on interaction with other nephrotoxic drugs and when use in combination with antineoplastic drugs.
4.6	Updated information on use in women of child-bearing potential
4.7	Updated Effects on ability to drive and use machinery

4.8	Updated the following Undesirable effects; Blood and lymphatic system disorders, Nervous system disorders, General Disorders and Administration Site Conditions.
4.9	Updated Overdose
5.2	Added subheading Distribution, Revised subheading from Elimination to Excretion