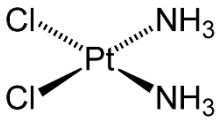
DBL CISPLATIN INJECTION

NAME OF MEDICINE

Cisplatin



CAS Registry No.: 15663-27-1

DESCRIPTION

DBL Cisplatin Injection is a clear, colourless to pale yellow sterile solution of Cisplatin 1 mg/mL, Mannitol BP 1 mg/mL and Sodium Chloride BP 9 mg/mL in Water for Injections BP. The solution does not contain any preservative.

PHARMACOLOGY

Cisplatin is an antineoplastic agent with biochemical properties similar to those of bifunctional alkylating agents. The drug inhibits DNA synthesis by producing intrastrand and interstrand crosslinks in DNA. Protein and RNA synthesis are also inhibited to a lesser extent. Cisplatin does not appear to be cell-cycle specific.

PHARMACOKINETICS

Distribution

There is good uptake of cisplatin by the kidneys, liver and intestine.

More than 90% of platinum containing species remaining in the blood are bound (possibly irreversibly) to plasma proteins.

The clearance of total platinum from plasma is rapid during the first four hours after intravenous administration, but then proceeds more slowly because of covalent binding to serum proteins.

Levels of unbound platinum fall with a half-life of 20 minutes to 1 hour depending on the rate of drug infusion.

Elimination and excretion

The elimination of intact drug and various platinum-containing biotransformation products is via the urine. About 15 - 25% of administered platinum is rapidly excreted in the first 2 - 4 hours after administration of cisplatin. This early excretion is mostly of intact cisplatin. In the first 24 hours after administration, 20 - 80% is excreted, the remainder representing drug bound to tissues or plasma protein.

PRECLINICAL SAFETY DATA

Genotoxicity

Cisplatin is mutagenic in bacteria and produces chromosome aberrations in animal cells in tissue culture. Non-clinical findings in mice treated with cisplatin (5 mg/kg intraperitoneally) showed that cisplatin caused direct damage to primordial follicle oocytes, leading to apoptosis.

Carcinogenicity

Carcinogenicity of cisplatin is possible but not proven.

INDICATIONS

DBL Cisplatin Injection is indicated for the palliative treatment of metastatic non-seminomatous germ cell carcinoma, advanced-stage refractory ovarian carcinoma, advanced-stage refractory bladder carcinoma and refractory squamous cell carcinoma of the head and neck. It may be used as a single agent or in combination with other chemotherapeutic agents. It may be employed, in appropriate circumstances, in addition to other modalities, e.g., radiotherapy or surgery.

CONTRAINDICATIONS

Use of cisplatin is contraindicated in the following conditions:

- Renal impairment (see **DOSAGE AND ADMINISTRATION**)
- Hearing disorders (see **PRECAUTIONS - Ototoxicity**)
- Bone marrow depression
- Generalised infections
- During pregnancy or lactation
- In patients with a history of hypersensitivity to cisplatin or platinum-containing compounds.

PRECAUTIONS

Cisplatin is a highly toxic drug with a relatively narrow therapeutic index, and a therapeutic effect is unlikely to occur without some evidence of toxicity. Cisplatin should be administered only under constant supervision by physicians experienced in therapy with cytotoxic agents and only when potential benefits of cisplatin therapy outweigh the possible risks. Appropriate facilities should be available for adequate management of complications should they arise.

To minimise the risk of nephrotoxicity, hydrate before, during and after therapy (see **DOSAGE AND ADMINISTRATION**). Prior to initial therapy, then before subsequent doses, the following parameters should be monitored: renal function including Glomerular Filtration Rate (GFR), Blood Urea Nitrogen (BUN), serum creatinine and creatinine clearance; electrolytes (magnesium, sodium, potassium and calcium) to detect hypomagnesaemia or hypocalcaemia; auditory function; red blood cells, white blood cells and platelets; liver function and neurological status.

Ototoxicity

Ototoxicity is cumulative and occurs mainly with high dose regimes. Tinnitus or occasional decreased ability to hear normal conversation are indications of ototoxicity, which have been frequently observed. Abnormalities of audiometric testing are more common and hearing loss can be unilateral or bilateral; frequency and severity increase with repeated doses, and may not be reversible, but mostly occur in the 4,000 - 8,000 Hz range.

Audiometric testing should be performed, if possible prior to initiation of therapy and at regular intervals thereafter, particularly if the clinical symptoms of tinnitus or hearing impairment occur. Radiotherapy may enhance ototoxicity. Clinically important deterioration of auditive function may require dosage modifications or discontinuation of therapy.

Myelosuppression

This may occur in patients treated with cisplatin. Haematological toxicity is dose-related and cumulative. The nadirs in circulating platelets and leucocytes generally occur between days 18 - 23 (range 7.3 - 45) with most patients recovering by day 39 (range 13 - 62). Leucopenia and thrombocytopenia are more pronounced at doses greater than 50 mg/m^2.

Peripheral blood counts should be monitored frequently in patients receiving cisplatin. Although the haematologic toxicity is usually moderate and reversible, severe thrombocytopenia and leucopenia may occur. In patients who develop thrombocytopenia special precautions are

recommended: care in performing invasive procedures; search for signs of bleeding or bruising; test of urine, stools and emesis for occult blood; avoiding aspirin and other NSAIDs. Patients who develop leucopenia should be observed carefully for signs of infection and might require antibiotic support and blood product transfusions.

Subsequent courses of cisplatin should not be instituted until platelets are present at levels greater than 100,000/mm^3 and white cells greater than 4,000/mm^3.

Anaemia

Anaemia (decrease of greater than 2g/dL haemoglobin) occurs in a significant number of patients, usually after several courses of treatment. Anaemia occurs at approximately the same frequency but generally with a later onset than leucopenia and thrombocytopenia. Transfusions of packed red cells may be necessary in severe cases.

Rarely, the drug has caused haemolytic anaemia; Coombs-positive results have been reported in a few of these cases. Further courses with cisplatin in sensitised individuals may cause increased haemolysis.

A high incidence of severe anaemia requiring transfusion of packed red cells has been observed in patients receiving combination chemotherapy including cisplatin.

Nausea and vomiting

Marked nausea and vomiting occur in almost all patients treated with cisplatin and are occasionally so severe that dosage reduction or discontinuance of treatment is necessary.

Anaphylaxis

Reactions secondary to cisplatin therapy have been occasionally reported in patients who were previously exposed to cisplatin. Patients who are at particular risk are those with a prior history or family history of atopy. Facial oedema, wheezing, tachycardia, hypotension and skin rashes of urticarial non-specific maculopapular type can occur within a few minutes of administration. Serious reactions seem to be controlled by IV adrenaline, corticosteroids or antihistamines.

Patients receiving cisplatin should be observed carefully for possible anaphylactic-like reactions and the necessary supportive equipment and medication should be readily available to treat such reactions.

Cardiovascular toxicity

Cisplatin has been found to be associated with cardiovascular toxicity (see **ADVERSE EFFECTS**). Patients may experience clinically heterogeneous venous thromboembolic events, myocardial infarction, cerebrovascular accidents, thrombotic microangiopathy and cerebral arteritis. Cases of pulmonary embolism (including fatalities) have been reported (see **ADVERSE EFFECTS**).

Hypomagnesaemia and hypocalcaemia

Hypomagnesaemia occurs quite frequently with cisplatin administration, while hypocalcaemia occurs less frequently. The loss of magnesium seems to be associated with renal tubular damage which prevents resorption of this cation. Where both electrolytes are deficient, tetany may result. It does not appear to be dose related. Monitoring of electrolytes is necessary.

Neurotoxicity and seizures

Cisplatin is known to induce neurotoxicity; therefore, neurologic examination is warranted in patients receiving a cisplatin-containing treatment. Peripheral neuropathy, postural hypotension, myasthenic syndromes, seizures and visual loss may occur with cisplatin treatment. This appears to be more common after prolonged treatment. Since neurotoxicity may result in irreversible damage, the development of clinically significant symptoms should generally contraindicate further cisplatin usage.

Immunosuppressant effects/increased susceptibility to infections

Administration of live or live-attenuated vaccines in patients immunocompromised by chemotherapeutic agents including cisplatin, may result in serious or fatal infections. Extreme caution should be used where patients have recently been exposed to infections, particularly chicken pox and herpes zoster. Vaccination with a live vaccine should be avoided in patients receiving cisplatin. Killed or inactivated vaccines may be administered; however, the response to such vaccines may be diminished.

Dental

The bone marrow depressant effects of cisplatin may result in an increased incidence of microbial infection, delayed healing and gingival bleeding. Dental work should be avoided during cisplatin therapy.

Others

As patients undergoing treatment with cisplatin are at an increased risk of bleeding, bruising and infection, it is recommended that extreme care be used when performing necessary invasive procedures.

Alcohol and aspirin should be avoided because of the risk of gastrointestinal bleeding.

Use in hepatic impairment

Liver function should be monitored periodically.

Use in renal impairment

Cisplatin is contraindicated in patients with renal impairment (see **CONTRAINDICATIONS**).

Cumulative and dose-related renal insufficiency is the major dose-limiting toxicity of cisplatin. The most commonly observed change in renal function has been a fall in glomerular filtration rate reflected by a rise in serum creatinine and a reduction in effective renal plasma flow.

Pre- and post-treatment hydration may reduce nephrotoxicity (see **DOSAGE AND ADMINISTRATION**).

Renal function must return to normal before further doses are given (see **DOSAGE AND ADMINISTRATION**).

Special care has to be taken when cisplatin-treated patients are given concomitant therapies with other potentially nephrotoxic drugs (see **INTERACTIONS WITH OTHER MEDICINES**).

Effects on fertility

Female

Based on non-clinical (see **PRECLINICAL SAFETY DATA**) and clinical findings, female fertility may be compromised by treatment with cisplatin. Use of cisplatin has been associated with cumulative dose-dependent ovarian failure, premature menopause and reduced fertility.

Male

Cisplatin can affect male fertility. Impairment of spermatogenesis and azoospermia have been reported (see **ADVERSE EFFECTS**). Although the impairment of spermatogenesis can be reversible, males undergoing cisplatin treatment should be warned about the possible adverse

effects on male fertility.

Both men and women should seek advice on fertility preservation before treatment.

Use in pregnancy (Category D†)

The safety of cisplatin in pregnancy has not been established. Cisplatin can cross the placental barrier. In mice, cisplatin is teratogenic and embryotoxic. Cisplatin may be toxic to the foetal urogenital tract. Therefore cisplatin is considered to be potentially harmful to the fetus when administered to a pregnant woman and its use in pregnant women is not recommended. Patients should be advised to avoid becoming pregnant.

If the patient becomes pregnant whilst receiving the drug she should be advised of the hazard to the fetus. Cisplatin should only be used if the potential benefits outweigh the risk of therapy.

Women of childbearing potential should use effective contraception during treatment with cisplatin and for at least 26 weeks following the last dose. Men with female partners of childbearing potential should be advised to use effective contraception during treatment with cisplatin and for at least 14 weeks after the last dose.

For patients with end-stage renal disease, the washout period of cisplatin will be longer (up to 7 weeks); effective contraception for men is advised for at least 19 weeks and for female patients, for at least 31 weeks after the last dose.

Use in lactation

Limited data from published literature report presence of cisplatin in human milk. Advise pregnant women not to breastfeed during treatment with cisplatin.

Paediatric use

Cisplatin can also be used in children. Cases of delayed-onset hearing loss have been reported in the paediatric population. Long term follow-up in this population is recommended.

INTERACTIONS WITH OTHER MEDICINES

Cisplatin is mostly used in combination with antineoplastic drugs having similar cytotoxic effects.

† *Category D: Drugs which have caused, are suspected to cause or be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects.*

In these circumstances additive toxicity is likely to occur.

Other known drug interactions are reported below.

Nephrotoxic drugs

Potentially nephrotoxic medicines, e.g., aminoglycoside antibiotics and loop diuretics when given concurrently or within 1-2 weeks after cisplatin administration, may potentiate the nephrotoxic effects of cisplatin. Concomitant use of other potentially nephrotoxic drugs (e.g., amphotericin B) is not recommended during cisplatin therapy.

The renal toxicity of ifosfamide may be greater when used with cisplatin or in patients who have previously been given cisplatin.

Ototoxic drugs

Concurrent and/or sequential administration of potentially ototoxic medicines, e.g., aminoglycoside antibiotics and loop diuretics, may potentiate the ototoxic effects of cisplatin, especially in the presence of renal impairment.

Ifosfamide may increase hearing loss due to cisplatin.

Renally excreted drugs

Reduction of the lithium blood levels was noticed in a few cases after treatment with cisplatin combined with bleomycin and etoposide. It is therefore recommended to monitor the lithium values.

Antigout agents

Cisplatin may raise the concentration of blood uric acid. Thus, in patients concurrently receiving antigout agents such as allopurinol, colchicine, probenecid or sulfinpyrazone, dosage adjustment of these drugs may be necessary to control hyperuricemia and gout.

Anticonvulsant agents

Plasma levels of anticonvulsant agents may become subtherapeutic during cisplatin therapy. In patients receiving cisplatin and phenytoin, serum concentrations of the latter may be decreased, possibly as a result of decreased absorption and/or increased metabolism. In these patients, serum levels of antiepileptics should be monitored and dosage adjustments made as necessary.

Anticoagulants

It is advisable to check the international normalised ratio (INR) when oral anticoagulants such as coumarins/warfarin are used simultaneously with cisplatin.

Paclitaxel

Administration of cisplatin prior to an infusion with paclitaxel may reduce the clearance of paclitaxel by 33% and can therefore intensify neurotoxicity.

Incompatibilities

Cisplatin 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 cisplatin should not be used for preparation or administration of the drug. The stability of cisplatin is adversely affected by the presence of bisulphite, metabisulphite, sodium bicarbonate and fluorouracil.

ADVERSE EFFECTS

Ear and labyrinth disorders

Unilateral or bilateral tinnitus and/or high frequency hearing loss (>4000Hz) has been observed in up to 31% of patients treated with cisplatin and is usually reversible. The damage to the hearing system appears to be dose related and cumulative, and it is reported more frequently in very young or very old patients. Auditory function should be monitored more closely during treatment.

Eye disorders

Retinal toxicity manifests as blurred vision and altered colour perception. Optic neuritis, papilloedema and cortical blindness have been reported rarely following the administration of cisplatin. These events are usually reversible after drug withdrawal. Retinal pigmentation has also been reported.

Infections and infestations

Infection (infectious complications have led to death), sepsis

Blood and lymphatic system disorders

Thrombotic microangiopathy (haemolytic uraemic syndrome), bone marrow failure, neutropenia,

Coombs positive haemolytic anaemia.

Myelosuppression often occurs during cisplatin therapy. Mild bone marrow toxicity may occur with both leucopenia and thrombocytopenia. These effects are usually reversible after ceasing treatment. Cisplatin may also induce anaemia: this is not clearly dose related and is occasionally caused by haemolysis. Leucopenia and thrombocytopenia are dose-related and more pronounced at doses greater than 50 mg/m^2. Leucocyte and platelet nadirs generally occur between days 18 and 23 of treatment, with recovery in most patients by day 39. Anaemia occurs at approximately the same frequency.

There have been rare reports of acute myelogenous leukemias and myelodysplastic syndromes arising in patients who have been treated with cisplatin, mostly when given in combination with other potentially leukemogenic agents.

Immune system disorders

Anaphylactic and anaphylactic-like reactions, consisting principally of flushing, facial oedema, wheezing, tachycardia and hypotension have been reported in patients previously exposed to cisplatin. The reactions usually occur within a few minutes of cisplatin administration and may be controlled by IV adrenaline, corticosteroids and/or antihistamines.

Metabolism and nutritional disorders

Cisplatin may cause dehydration in patients. Cisplatin may also cause serious electrolyte disturbances, mainly represented by hypomagnesemia, hypocalcaemia, and hypokalaemia, and associated with renal tubular dysfunction. Hypomagnesemia and/or hypocalcaemia may become symptomatic, with muscle irritability or cramps, clonus, tremor, carpopedal spasm, and/or tetany. Hypomagnesaemia and hypocalcaemia may develop during cisplatin therapy or following discontinuance of the drug. Other reported toxicities are hyperuricemia, hyponatremia, hypophosphataemia and syndrome of inappropriate antidiuretic hormone (SIADH). Hyperuricaemia may occur in patients receiving cisplatin, principally as a result of drug-induced nephrotoxicity. Hyperuricaemia is more pronounced with doses greater than 50 mg/m^2, with peak levels occurring between 3-5 days after administration of the drug. Allopurinol may be used to reduce serum uric acid levels. Regular monitoring of serum electrolyte levels and replacement where necessary are advisable.

Nervous system disorders

Convulsion, leukoencephalopathy, reversible posterior leukoencephalopathy syndrome, haemorrhagic stroke, ischaemic stroke, ageusia, cerebral arteritis, myelopathy.

Peripheral neuropathies occur infrequently with usual doses of the drug. They are generally sensory in nature (e.g., paraesthesia of the upper and lower extremities), but can also include motor difficulties, reduced or absent reflexes and leg weakness. Autonomic neuropathy, seizures, slurred speech, loss of taste and memory loss have also been reported. These neuropathies usually appear after prolonged therapy, but have also developed after a single drug dose. Areflexia and loss of proprioception and vibratory sensation may be seen, especially if cisplatin is given at higher doses or more frequently than recommended. In some patients they may be irreversible however, they have been partially or completely reversible in others following discontinuance of cisplatin therapy. Cerebrovascular accident has been reported in patients treated with cisplatin. Lhermitte's sign has been reported.

Cardiac disorders

Cardiovascular abnormalities (coronary disease, congestive heart failure, postural hypotension, thrombotic microangiopathy, arrhythmia, bradycardia, tachycardia, cardiac arrest, cardiac disorder etc.)

Vascular disorders

Raynaud's phenomenon

Venous thromboembolism

A significant increase in the risk of venous thromboembolic events has been reported in patients with advanced solid tumours and treated with cisplatin compared with non-cisplatin-based chemotherapy.

Vascular toxicity coincident with the use of cisplatin in combination with other antineoplastic agents have been reported rarely. The events are clinically heterogeneous and may include myocardial infarction, cerebrovascular accident (haemorrhagic and ischaemic stroke), thrombotic microangiopathy (haemolytic uremic syndrome) or cerebral arteritis. Various mechanisms have been proposed for these vascular complications.

Respiratory, thoracic and mediastinal disorders

Pulmonary embolism

Pulmonary toxicity has been reported in patients treated with cisplatin in combination with bleomycin or 5-fluorouracil.

Gastrointestinal disorders

Stomatitis, vomiting, nausea, anorexia, hiccups, diarrhoea

Cisplatin induces severe nausea and vomiting in almost all patients. Severe nausea and vomiting usually begin within 1-4 hours after treatment and may persist for up to a week after treatment. These side effects are only partially relieved by standard antiemetics. The severity of these symptoms may be reduced by dividing the total dose per cycle into smaller doses given once daily for five days. Reported toxicity includes gingival platinum line.

Hepatobiliary disorders

Mild and transient elevations of serum AST and ALT levels may occur infrequently. Liver damage has also been infrequently reported.

Skin and subcutaneous tissue disorders

Mild alopecia. Rarely, urticarial or maculopapular skin rashes have also been observed.

Musculoskeletal and connective tissue disorders

Myalgia, muscle spasms.

Renal and urinary disorders

Acute renal toxicity, which was highly frequent in the past and represented the major dose-limiting toxicity of cisplatin, has been greatly reduced by the use of 6 to 8-hour infusions as well as by concomitant intravenous hydration and forced diuresis. Cumulative toxicity, however, remains a problem and may be severe. Renal impairment, which is associated with tubular damage, may be first noted during the second week after a dose and is manifested by an increase in serum creatinine, BUN, serum uric acid and/or a decrease in creatinine clearance. Renal insufficiency is generally mild to moderate and reversible at the usual doses of the drug (recovery occurring as a rule within 2-4 weeks); however, high or repeated cisplatin doses can increase the severity and duration of renal impairment and may produce irreversible renal insufficiency (sometimes fatal). Renal failure has been reported also following intraperitoneal instillation of the drug.

Reproductive system and breast disorders

Impairment of spermatogenesis and azoospermia have been reported (see **PRECAUTIONS - Effects on fertility**).

General disorders and administration site conditions

Pyrexia, asthenia, malaise. Local effects such as pain, oedema, erythema, phlebitis, tissue cellulitis, fibrosis, and skin necrosis (following extravasation of the drug) may occur. Extravasation may result from infusion of solutions greater than 0.5 mg/mL cisplatin.

DOSAGE AND ADMINISTRATION

Dosage

The usual dose in adults and children when used as single agent therapy is 50-100 mg/m^2 as a single IV infusion every 3-4 weeks, or 15-20 mg/m^2 as a daily IV infusion for 5 days every 3-4 weeks.

Subsequent treatment with cisplatin

A repeat course of cisplatin should not be given until:

- the serum creatinine is below 140 micromol/L and/or the plasma urea is below 9 mmol/L and
- circulating blood elements are at an acceptable level (platelets at least 100,000/mm^3, WBC at least 4,000/mm^3).

At base line audiogram should be taken and the patient monitored periodically for auditory deterioration (see **PRECAUTIONS**).

With impaired hepatic function

Human studies show a high uptake of cisplatin in the liver. An elevated aspartate aminotransferase (AST) and alkaline phosphatase with clinical signs of liver toxicity has been reported in some cases. The adult dosage should be used with caution in patients with pre-existing hepatic dysfunction.

With impaired renal function

Cisplatin displays high tissue uptake in the kidneys, exhibits dose related and cumulative nephrotoxicity, and is excreted mainly in the urine. In addition, the plasma elimination half-life of cisplatin is prolonged in renal failure.

Caution should be exercised in patients with pre-existing renal dysfunction. Cisplatin is contraindicated in patients with serum creatinine levels greater than 0.2 mmol/L. Repeat courses are not advised until serum creatinine is below 0.14 mmol/L and/or blood urea below 9 mmol/L.

Administration

(a) **Pre-treatment hydration:** Patients should be adequately hydrated before and for 24 hours after administration of cisplatin to ensure good urinary output and minimise nephrotoxicity. Hydration may be achieved by IV infusion of 2 litres of either sodium chloride IV infusion 0.9% or glucose-saline (e.g., glucose 4% in one-fifth sodium chloride IV infusion 0.9%) over a 2 hour period. During the last 30 minutes of the pre-treatment hydration or after the hydration, 375 mL of 10% mannitol injection may be administered via a side-arm drip.

(b) **Preparation of Cisplatin infusion:** DBL Cisplatin Injection should be added to 1 litre of sodium chloride IV infusion 0.9%.
Aluminium containing equipment should not be used for administration of cisplatin (see **INTERACTIONS WITH OTHER MEDICINES** – Incompatibilities).

(c) **Treatment:** Following pre-hydration, administer the cisplatin infusion over 1-2 hours. It has been proposed that a longer infusion time of 6-8 hours may decrease gastrointestinal and renal toxicities.
The IV flask should be covered to preclude light.

(d) **Post-treatment hydration:** Adequate hydration and urinary output must be maintained during the 24 hours following infusion. It has been suggested that IV hydration continue after treatment with the aim to administer 2 litres of sodium chloride IV infusion 0.9% or glucose-saline over a period of 6-12 hours.

The product and its admixtures contain no antimicrobial agent. In order to reduce microbiological hazards it is recommended that further dilution be effected immediately prior to use and infusion commenced as soon as practicable after preparation of the admixture. Infusion should be completed within 24 hours of preparation and the residue discarded.

Handling precautions

As with all antineoplastic agents, trained personnel should prepare Cisplatin Injection. This should be performed in a designated area (preferably a cytotoxic laminar flow cabinet). Care should be taken to prevent inhaling particles and exposing the skin to cisplatin. Protective gown, mask, gloves and appropriate eye protection should be worn while handling cisplatin. In the event of contact with the eyes, wash with water or saline; where solution accidentally contacts skin or mucosa, the affected area should be immediately washed thoroughly with soap and water and in both cases seek medical advice. Seek immediate medical attention if the drug is ingested or inhaled. It is recommended that pregnant personnel not handle cytotoxic agents such as cisplatin.

Luer-Lock fitting syringes and giving sets to avoid leakage are recommended. Large bore needles are recommended to minimise pressure and possible formation of aerosols. Aerosols may also be reduced by using a venting needle during preparation.

Items used to prepare cisplatin, or articles associated with body waste should be disposed of by placing in a double sealed polythene bag, and incinerating at 1100°C.

Spills and disposal

If spills occur, restrict access to the affected area. Wear two pairs of gloves (latex rubber), a respirator mask, a protective gown and safety glasses. Limit the spread of the spill by covering with a suitable material such as absorbent towel or adsorbent granules. Spills may also be treated with 5% sodium hypochlorite. Collect up absorbent/adsorbent material and other debris from spill and place in a leak proof plastic container and label accordingly.

Cleanse the remaining spill area with copious amounts of water.

OVERDOSAGE

Acute overdosage with cisplatin may result in an enhancement of its expected toxic effects (e.g., kidney failure, severe myelosuppression, intractable nausea and vomiting, severe neurosensorial toxicities, liver failure etc.). Death may also occur. Signs and symptoms of overdosage should be managed with supportive measures. Patients should be monitored for 3 to 4 weeks in case of delayed toxicity. See **ADVERSE EFFECTS** for possible complications.

STABILITY

Cisplatin 0.15 mg/mL in sodium chloride IV infusion 0.9% is chemically stable for 24 hours when stored at room temperature and protected from light.

PRESENTATION AND STORAGE CONDITIONS

Code	Strength	Pack Size
1880	50 mg/50 mL	1 x 50 mL vial
1885	100 mg/100 mL	1 x 100 mL vial

Store below 25°C. Protect from light. Single use only. Discard unused portion.

MARKETING AUTHORISATION HOLDER

Pfizer (Thailand) Limited

Warning (based on the Ministry of Public Health's Announcement)

This drug may cause serious harm, should be used under the supervision of a physician.