Summary of Product Characteristics

1. Name of the Medical Product

Drug Product	**:**	Cisplatin Injection BP (50 mg / 50 mL)
Generic Name	**:**	Cisplatin Injection BP
Strength	**:**	Each mL of sterile preservative and pyrogen free aqueous clear and colourless to pale yellow solution containing 1.0 mg of Cisplatin BP in 1.0 mL of Water for Injection USP.

2. Quality and Quantitative Composition

Each mL contains:

Cisplatin BP	1.0 mg
Water for Injection USP	qs.

For the full list of excipients, see section 6.1

3. Pharmaceutical form

Sterile preservative and pyrogen free aqueous clear and colourless to pale yellow solution as parenteral preparation for Intravenous Infusion

4. Clinical Particulars

4.1 Therapeutic Indications

Cisplatin is intended for the treatment of:

Advanced or metastasised testicular cancer

Advanced or metastasised ovarian cancer

Advanced or metastasised bladder carcinoma

Advanced or metastasised squamous cell carcinoma of the head and neck

Advanced or metastasised non-small cell lung carcinoma

Advanced or metastasised small cell lung carcinoma.

Cisplatin is indicated in the treatment of cervical carcinoma in combination with other chemotherapeutics or with radiotherapy.

Cisplatin can be used as monotherapy and in combination therapy

4.2 Posology and method of administration

Cisplatin 1 mg/mL concentrate for solution for infusion is to be diluted before administration. For instructions on dilution of the product before administration.

The diluted solution should be administered only intravenously by infusion. For administration, any device containing aluminium that may come in contact with cisplatin (sets for intravenous infusion, needles, catheters, syringes) must be avoided.

Adults and children:

The cisplatin dosage depends on the primary disease, the expected reaction, and on whether cisplatin is used for monotherapy or as a component of combination chemotherapy. The dosage directions are applicable for both adults and children.

For monotherapy, the following two dosage regimens are recommended:

<< Single dose of 50 to 120 mg/m2 body surface every 3 to 4 weeks;

<<15 to 20 mg/m2/day for five days, every 3 to 4 weeks.

If cisplatin is used in combination chemotherapy, the dose of cisplatin must be reduced. A typical dose is 20 mg/m2 or more once every 3 to 4 weeks.

For treatment of cervical cancer cisplatin is used in combination with radiotherapy. A typical dose is 40 mg/m2 weekly for 6 weeks.

In patients with renal dysfunction or bone marrow depression, the dose should be reduced adequately.

The cisplatin solution for infusion prepared according to instructions should be administered by intravenous infusion over a period of 6 to 8 hours.

Adequate hydration must be maintained from 2 to 12 hours prior to administration until minimum 6 hours after the administration of cisplatin. Hydratation is necessary to cause sufficient diuresis during and after treatment with cisplatin. It is realised by intravenous infusion of one of the following solutions:

Sodium chloride solution 0.9%;

Mixture of sodium chloride solution 0.9% and glucose solution 5% (1:1).

Hydration prior to treatment with cisplatin:

Intravenous infusion of 100 to 200ml/hour for a period of 6 to 12 hours, with a total amount of at least 1L.

Hydration after termination of the administration of cisplatin:

Intravenous infusion of another 2 litres at a rate of 100 to 200 mL per hour for a period of 6 to 12 hours. Forced diuresis may be required should the urine secretion be less than 100 to 200 mL/hour after hydration. Forced diuresis may be realised by intravenously administering 37.5g mannitol as a 10% solution (375 ml mannitol solution 10%), or by administration of a diuretic if the kidney functions are normal.

The administration of mannitol or a diuretic is also required when the administrated cisplatin dose is higher than 60 mg/m2 of body surface.

It is necessary that the patient drinks large quantities of liquids for 24 hours after the cisplatin infusion to ensure adequate urine secretion.

4.3 Contraindications

Cisplatin is contraindicated in patients

Hypersensitivity to the active substance or to any of the excipients

With pre-existing renal impairment.

In dehydrated condition (pre- and post-hydration is required to prevent serious renal dysfunction);

With myelosuppression;

With pre-existing hearing impairment; - with neuropathy caused by cisplatin

Who are breastfeeding.

In combination with live vaccines, including yellow fever vaccine.

In combination with phenytoin in prophylactic use.

Due to the fact that cisplatin is nephrotoxic and neurotoxic (in particular ototoxic). These toxicities may be cumulative if disorders of this type pre-exist.

4.4 Special Warnings and precautions for use

Cisplatin reacts with metallic aluminium to form a black precipitate of platinum. All aluminium containing IV sets, needles, catheters and syringes should be avoided.

Cisplatin may only be administered under the supervision of a physician qualified in oncology with experience in the use of antineoplastic chemotherapy. Supportive equipment should be available to control anaphylactic reactions.

Cisplatin reacts with metallic aluminium to form a black precipitate of platinum. All aluminium containing IV sets, needles, catheters and syringes should be avoided.

The solution for infusion should not be mixed with other drugs or additives.

Appropriate monitoring and management of the treatment and its complications are only possible if adequate diagnosis and exact treatment conditions are available.

Cisplatin is proven to be cumulative ototoxic, nephrotoxic, and neurotoxic. The toxicity caused by cisplatin may be amplified by the combined use with other medicinal products, which are toxic for the said organs or systems.

Before, during and after administration of cisplatin, the following parameters resp. organ functions must be determined:

Renal function;

Hepatic function;

Hematopoiesis functions (number of red and white blood cells and blood platelets);

Serum electrolytes (calcium, sodium, potassium, magnesium).

These examinations must be repeated every week over the entire duration of the treatment with cisplatin.

Repeating administration of cisplatin must be delayed until normal values are achieved for the following parameters:

Serum creatinine < 130 µmol/l rsp. 1.5 mg/dl

Urea < 25 mg/dl

White blood cells > 4.000/µl resp. > 4.0 x 109/l

Blood platelets > 100.000/µl resp. > 100 x 109/l

Audiogram: results within the normal range.

1. Nephrotoxicity

Cisplatin causes severe cumulative nephrotoxicity. A urine output of 100 mL/hour or greater will tend to minimize cisplatin nephrotoxicity. This can be accomplished by prehydration with 2 litres of an appropriate intravenous solution, and similar post cisplatin hydration (recommended 2,500 mL/m2/24 hours). If vigorous hydration is insufficient to maintain adequate urinary output, an osmotic diuretic may be administered (eg, mannitol). Hyperuricaemia and hyperalbuminaemia may predispose to cisplatin-induced nephrotoxicity.

2. Neuropathies

Severe cases of neuropathies have been reported.

These neuropathies may be irreversible and may manifest by paresthesia, areflexia and a proprioceptive loss and a sensation of vibrations. A loss of motor function has also been reported. A neurologic examination must be carried out at regular intervals.

Special caution must be exercised for patients with peripheral neuropathy not caused by cisplatin. Prior to each course, the absence of symptoms of peripheral neuropathy should be established.

3. Ototoxicity

Ototoxicity has been observed in up to 31% of patients treated with a single dose of cisplatin 50mg/m2, and is manifested by tinnitus and/or hearing loss in the high frequency range (4000 to 8000Hz). Decreased ability to hear conversational tones may occur occasionally. Ototoxic effect may be more

pronounced in children receiving cisplatin. Hearing loss can be unilateral or bilateral and tends to become more frequent and severe with repeated doses; however, deafness after initial dose of cisplatin has been reported rarely. Ototoxicity may be enhanced with prior simultaneous cranial irradiation and may be related to peak plasma concentration of cisplatin. It is unclear whether cisplatin induced ototoxicity is reversible. Careful monitoring by audiometry should be performed prior to initiation of therapy and prior to subsequent doses of cisplatin. Vestibular toxicity has also been reported

4. Allergic phenomena

As with other platinum-based products, hypersensitivity reactions appearing in most cases during perfusion may occur, and necessitate discontinuation of the perfusion and an appropriate symptomatic treatment. Cross reactions, sometimes fatal, have been reported with all the platinum compounds

Anaphylactic-like reactions to cisplatin have been observed. These reactions can be controlled by administration of antihistamines, adrenaline and/or glucocorticoids.

5. Hepatic function and haematological formula

The haematological formula and the hepatic function must be monitored at regular intervals.

6. Carcinogenic potential

In humans, in the rare cases the appearance of acute leukaemia has coincided with use of Cisplatin, which was in general associated with other leukaemogenic agents. Cisplatin is a bacterial mutagen and causes chromosome aberrations in cultures on animal cells. Carcinogenicity is possible but has not been demonstrated. Cisplatin is teratogenetic and embryo toxic in mice.

7. Injection site reactions

Injection site reactions may occur during the administration of cisplatin. Given the possibility of extravasation, it is recommended to closely monitor the infusion site for possible infiltration during drug administration. A specific treatment for extravasation reactions is unknown at this time.

WARNING

This cytostatic agent had a more marked toxicity than is usually found in antineoplastic chemotherapy.

Renal toxicity, which is above-all cumulative, is severe and requires particular precautions during administration.

Nausea and vomiting may be intense and require adequate antiemetic treatment.

Close supervision must also be carried out with regard to ototoxicity, myelodepression and anaphylactic reactions.

Preparation of the intravenous solution

Warning

As with all other potentially toxic products, precautions are essential when handling the cisplatin solution. Skin lesions are possible in the event of accidental exposure to the product. It is advisable to wear gloves. In the event the cisplatin solution comes into contact with the skin or mucous membranes, wash the skin or mucous membranes vigorously with soap and water.

Conforming to the procedures appropriate for the manipulation and elimination of cytostatic agents is recommended.
Before administering the solution to the patient, verify the clarity of the solution and the absence of particles.

Special care is required for patients with acute bacterial or viral infections.

Male and female patients have to use effective contraception during and for at least 6 months after the treatment with cisplatin.

4.5 Interaction with other medicinal products and other form of interactions

Simultaneous use of myelosuppressives or radiation will boost the effects of cisplatin's myelosuppressiveactivity.The occurrence of nephrotoxicity caused by cisplatin may be intensified by concomitant treatment with antihypertensives containing furosemide, hydralazine, diazoxide, and propranolol.

Nephrotoxic substances:

Concomitant administration of nephrotoxic (e.g. cephalosporins, aminoglycosides or Amphotericin B or contrast media) or ototoxic (e.g. aminoglycosides) medicinal products will potentiate the toxic effect of cisplatin on the kidneys. During or after treatment with cisplatin caution is advised with predominantly renally eliminated substances, e.g. cytostatic agents such as bleomycin and methotrexate, because of potentially reduced renal elimination. Cisplatin given in combination with bleomycin and vinblastin can lead to a Raynaud-phenomenon.

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

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

It may be required to adjust the dosage of allopurinol, colchicine, probenecid, or sulfinpyrazone if used together with cisplatin, since cisplatin causes an increase in serum uric acid concentration.

Cisplatin given in combination with bleomycin and vinblastin can lead to a Raynaud-phenomenon.

In a study of cancer patients with metastatic or advanced tumors, docetaxel in combination with cisplatin induced more severe neurotoxic effects (doserelated and sensoric) than either drug as a single agent in similar doses.

Chelating agents like penicillamine may diminish the effectiveness of cisplatin.
In concomitant use of cisplatin and ciclosporin the excessive immunosuppression with risk of lymphoproliferation is to be taken into consideration.

Ototoxic substances:

Concomitant administration of ototoxic (e.g. aminoglycosides, loop diuretics) medicinal products will potentiate the toxic effect of cisplatin on auditory function. Except for patients receiving doses of cisplatin exceeding 60 mg/m2, whose urine secretion is less than 1000 ml per 24 hours, no forced diuresis with loop diuretics should be applied in view of possible damage to the kidney tract and ototoxicity.

Ifosfamide may increase hearing loss due to cisplatin.

Weakened live vaccines:

Yellow fever vaccine is strictly contraindicated because of the risk of fatal systemic vaccinaldisease . In view of the risk of generalised illness, it is advisable to use an inactive vaccine if available.

Oral anticoagulants:

In the event of simultaneous use of oral anticoagulants, it is advisable regularly to check the INR.
Antihistamines, Phenothiazines and others:

Simultaneous use of antihistamines, buclizine, cyclizine, loxapine, meclozine, phenothiazines, thioxanthenes or trimethobenzamides may mask ototoxicity symptoms (such as dizziness and tinnitus).
Anticonvulsive substances:

Serum concentrations of anticonvulsive medicines may remain at subtherapeutic levels during treatment with cisplatin. Cisplatin may reduce the absorption of phenytoin resulting in reduced epilepsy control when phenytoin is given as current treatment. During cisplatin therapy starting a new anticonvulsivant treatment with phenytoin is strictly contraindicated.

Pyroxidine + altretamine combination:

During a randomised study of the treatment of advanced ovarian cancer, the response time was unfavourably affected when pyridoxine was used in combination with altretamine (hexamethylmelamine) and Cisplatin.

Paclitaxel:

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

4.6 Pregnancy and lactation

Pregnancy

Cisplatin may be toxic to the foetus when administered to a pregnant woman. Animal studies have shown reproductive toxicity and transplacentalcarcinogenity. Cisplatin should not be used during pregnancy unless the clinician considers the risk in an individual patient to be clinically justified.

During treatment with Cisplatin and for a minimum of the following 6 months, appropriate measures must be taken to avoid pregnancy;

Breast-feeding

Cisplatin is excreted in breast milk. Patients treated with cisplatin must not breastfeed.

Fertility

Genetic consultation is recommended if the patient wishes to have children after ending the treatment.

Since a treatment with cisplatin may cause irreversible infertility, it is recommended that men, who wish to become fathers in the future, ask for advice regarding cryoconservation of their sperm prior to treatment.

Contraception in males and females

Male and female patients have to use effective contraception during and for at least 6 months after the treatment with cisplatin.

4.7 Effects on ability to drive and use machine

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

However, the profiles of undesirable effects (central nervous system and special senses) may lead to minor or moderate influence on the ability to drive and use machines. Patients who suffer from these effects (e.g. sleepy or vomiting) must avoid driving and operating machinery.

4.8 Undesirable effects

Undesirable effects depend on the used dose and may have cumulative effects.

The most frequently reported adverse events (>10%) of cisplatin were haematological (leukopenia, thrombocytopenia and anaemia), gastrointestinal (anorexia, nausea, vomiting and diarrhoea), ear disorders (hearing impairment), renal disorders (renal failure, nephrotoxicity, hyperuricaemia) and fever.

Serious toxic effects on the kidneys, bone marrow and ears have been reported in up to about one third of patients given a single dose of cisplatin; the effects are generally dose-related and cumulative. Ototoxicity may be more severe in children.

Frequencies are defined using the following convention:

Very common (<1/10); common (<1/100 to <1/10); uncommon (<1/1,000 to <1/100); rare (<1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Hypersensitivity may present as rash, urticaria, erythema, or pruritus allergic.

Table of Adverse Drug Events Reported During Clinical or Postmarketing Experience (MedDRA terms).

System Organ Class	Frequency	MedDRA Term
Infections and infestations	Not Known	Infection a
	Common	Sepsis
Blood and lymphatic system disorders	Very common	Bone marrow failure, thrombocytopenia, leukopenia, anaemia
	Not known	Coombs positive haemolyticanaemia
Neoplasm benign, malignant, and unspecified	Rare	Acute leukaemia
Immune system disorders	Uncommon	Anaphylactoidb reaction Hypersensitivity may present as rash, urticaria, erythema, or pruritus allergic.
Endocrine disorders	Not known	Blood amylase increased, inappropriate antidiurectic hormone secretion
Metabolism and nutrition disorders	Not known	Dehydration, ,hypokalaemia, hypophosphataemia, hypocalcaemia, tetany, muscle spasms and/or electrocardiogram changes occur as a result of damage to the kidney caused by cisplatin, thus reducing the tubular resorption of cations. Hypercholesterolemia. Increased blood amylase
	Uncommon	Hypomagnesaemia
	Very rare	Increased blood iron
	Very common	Hyponatraemia
Nervous system disorders	Not known	Cerebrovascular accident, haemorrhagic stroke, ischaemic stroke ageusia, cerebral arteritis, Lhermitte's sign, myelopathy, autonomic neuropathy
	Rare	Convulsion, neuropathy peripheral, leukoencephalopathy, reversible posterior leukoencephalopathy syndrome
Eye disorders	Not known	Vision blurred, colour blindness acquired, blindness cortical, optic neuritis, papilloedema, retinal pigmentation
Ear and labyrinth disorders	Uncommon	Ototoxicity

	Not known	Tinnitus, deafness
	Rare	Patients may lose the ability to conduct a normal conversation. Cisplatin- induced hearing impairment may be serious for children and elderly patients. (See section 4.4.)
Cardiac disorders	Not known	Cardiac disorder
	Common	Arrhythmia, bradycardia, tachycardia
	Rare	Myocardial infarction
	Very rare	Cardiac arrest
Vascular disorders	Not known	Thrombotic microangiopathy (haemolyticuraemic syndrome), Raynaud's phenomenon
	Common	Phlebitis at injection site
Gastrointestinal disorders	Not known	Vomiting, nausea, anorexia, hiccups, diarrhoea
	Uncommon	Metallic setting on the gums
	Rare	Stomatitis
Hepatobiliary disorders	Not known	Hepatic enzymes increased, blood bilirubin increased
	Rare	Reduced blood albumin levels
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea, pneumonia, respiratory failure,
	Not known	Pulmonary embolism
Skin and subcutaneous tissue disorders	Not known	Rash, alopecia
Musculoskeletal, connective tissue and bone disorders	Not known	Muscle spasms
Renal and urinary disorders	Not known	Renal failure acute, renal failurec, renal tubular disorder
	Very common	Hyperuricaemia,
Reproductive system and breast disorders	Uncommon	Abnormal spermatogenesis and ovulation, and painful gynaecomastia
General disorders and administration site condition	Not known	Pyrexia (very common) , asthenia, malaise, injection site extravasationd

*** Source of frequencies: Cisplatin Injection Company Core Data Sheet (CCDS), BMS Pharmacovigilance & Epidemiology, 02 August 2010. Frequencies not reported in the CCDS, have been added from the assessment report**
a: Infectious complications have led to death in some patients.
b: Symptoms reported for anaphylactoid reaction such as facial edema (PT-face oedema), wheezing, bronchospasm, tachycardia, and hypotension will be included in the parentheses for anaphylactoid reaction in the AE frequency table.
c: Elevations in BUN and creatinine, serum uric acid, and/or a decrease in creatinine clearance are subsumed under renal insufficiency/failure.
d: Local soft tissue toxicity including tissue cellulitis, fibrosis, and necrosis (common) pain (common), oedema (common) and erythema (common) as the result of extravasation.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA)

4.9 Overdosage

Symptoms of overdose involve above mentioned side effects in an excessive manner. Efficient hydration and osmotic diuresis can aid in reduction of toxicity, provided this is applied immediately after overdose.
In case of overdose (> 200 mg/m2), direct effects on the respiratory centre are possible, which might result in life threatening respiratory disorders and acid base equilibrium disturbance due to passage of the blood brain barrier.

An acute overdose of Cisplatin may result in renal failure, liver failure, deafness, ocular toxicity (including detachment of the retina), significant myelosuppression, untreatable nausea and vomiting and/or neuritis. An overdose may be fatal.

There is no specific antidote in the event of an overdose of Cisplatin. Even if haemodialysis is initiated 4 hours after the overdose it has little effect on the elimination of cisplatin from the body following a strong and rapid fixation of Cisplatin to proteins.
Treatment in the event of an overdose consists of general support measures.

5. Pharmacological properties

5.1 Pharmacodynamics Properties

Pharmacotherapeuticgroup: Platinum compounds, **ATC code:** L01XA01

Cisplatin is an inorganic compound which contains a heavy metal [cis- diamminedichloridoplatinum (II)]. It inhibits DNA-synthesis by the formation of DNA cross- links. Protein and RNA synthesis are inhibited to a lesser extent.

Although the most important mechanism of action seems to be inhibition of DNA synthesis, other mechanisms can also contribute to the antineoplastic activity of cisplatin, including the increase of tumour immunogenicity. The oncolytic properties of cisplatin are comparable to the alkylating agents. Cisplatin also has immunosuppressive, radiosensitising, and antibacterial properties. Cisplatin seems to be cell-cycle non-specific. The cytotoxic action of cisplatin is caused by binding to all DNA-bases, with a preference for the N-7 position of guanine and adenosine.

5.2 Pharmacokinetics Properties

After intravenous administration cisplatin quickly distributes across all tissues; cisplatin badly penetrates in the central nervous system. The highest concentrations are reached in the liver, kidneys, bladder, muscle tissue, skin, testes, prostate, pancreas and spleen.

After intravenous administration the elimination of filterable, non-protein bound cisplatin runs biphasic, with an initial and terminal half life of 10-20 minutes and 32-53 minutes, respectively. The elimination of the total quantity of platinum runs triphasic with half lives of 14 minutes, and 274 minute and 53 days respectively.

Cisplatin is bound to plasma proteins for 90%.

The excretion primarily takes place via the urine: 27-43% of the administered dose is recovered in the urine in the first five days after the treatment. Platinum is also excreted in the bile.

5.3 Preclinical safety data

Chronic toxicity

In chronic toxicity models indications for renal damage, bone marrow depression, gastro- intestinal disorders and ototoxicity have been observed.

Mutagenicity encarcinogenity

Cisplatin is mutagenic in numerous in vitro and in vivo tests (bacterial test systems, chromosomal disorders in animal cells and in tissue cultures). In long-term studies it has been shown that cisplatin is carcinogenic in mice and rats.

Reproductive toxicity

In mice, gonadal suppression, resulting in amenorrhoea or azoospermia has been observed, which can be irreversible and result in infertility. In female rats cisplatin induced morphological changes in the ovaries, causing partial and reversible infertility.

Studies in rats have shown that exposure during pregnancy can cause tumours in adult offspring.

Cisplatin is embryotoxic in mice and rats, and in both species deformities have been reported. Cisplatin is excreted in the breast milk.

6. Pharmaceutical Particulars

6.1 List of excipients

Sodium chloride,

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH adjustment)

Water for injection

6.2 Incompatibilities

Do not bring in contact with aluminium. Cisplatin reacts with metal aluminium to form a black precipitate of platinum. All aluminium-containing IV sets, needles, catheters and syringes should be avoided. Cisplatin decomposes with solution in media with low chloride content; the chloride concentration should at least be equivalent to 0.45% of sodium chloride.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Antioxidants (such as sodium metabisulphite), bicarbonates (sodium bicarbonate), sulfates, fluorouracil and paclitaxel may inactivate cisplatin in infusion systems.

6.3 Shelf life

24 months from the date of manufacturing, when retained in the original carton.

6.4 Special precautions for storage

Proposed Shelf life (after reconstitution or dilution)

Cisplatin Injection remains stable for 24 hours at 20 - 25 °C room temperature. The diluted solution should be protected from light. Do not store diluted solutions in the refrigerator or freezer. The aqueous solution should be used intravenously only and should be administered by IV infusion over a 6- to 8-hour period

Proposed Shelf Life (After first opening containers)

As the finished product is sterile formulation, from the microbiological point of view, the product should be used immediately otherwise should be administered by IV infusion over a 6- to 8-hour period

Proposed Storage Conditions

Store at a temperature not more than 25º (77°F), excursions permitted between 15º and 30º (59º F and 86º F).Protect from light. Do not refrigerate.

Special precautions for storage

Undiluted solution:

Keep container in the outer carton in order to protect from light. Do not refrigerate or freeze.

Store protected from light at a temperature not more than 25º (77°F), excursion permitted between 15º and 30º (59º F and 86º F). Do not refrigerate.

6.5. Nature and contents of container

50 mL Amber Glass Vial USP Type I

20 mm Bromo butyl rubber plug

20 mm Aluminium flip off seal

6.6 Special precautions for disposal and other handling

Preparation and handling of the product

Like with all anti-neoplastic products caution is needed with the processing of cisplatin. Must be diluted beforeuse. Dilution should take place under aseptic conditions by trained personnel in an area specifically intended for this. Protective gloves should be worn for this. Precautions should be taken to avoid contact with the skin and mucous membranes. If skin contact did occur anyway, the skin should be washed with soap and water immediately. With skin contact tingling, burns and redness have been observed. In case of contact with the mucous membranes they should be copiously rinsed with water. After inhalation dyspnoea, pain in the chest, throat irritation and nausea have been reported.

Pregnant women must avoid contact with cytostatic drugs.

Bodily waste matter and vomit should be disposed with care.

If the solution is cloudy or a deposit that does not dissolve is noticed, the bottle should be discarded.

A damaged bottle must be regarded and treated with the same precautions as contaminated waste. Contaminated waste must be stored in waste containers specifically marked for this. See section "Disposal".

Preparation of the intravenous administration

Take the quantity of the solution that is needed from the bottle and dilute with at least 1 litre of the following solutions:

Sodium chloride 0.9%, - mixture of sodium chloride 0.9% / glucose 5% (1:1), (resulting final concentrations:

Sodium chloride 0.45%, glucose 2.5%)

Sodium chloride 0.9% and 1.875% mannitol, for injection

Sodium chloride 0.45%, glucose 2.5% and 1.875% mannitol for injection

Always look at the injection before use. If the solution is not clear or an undissolvable precipitate is formed the solution must not be used. Only a clear solution, free from particles should be administered.

DO NOT bring in contact with injection material that contains aluminium, DO NOT administer undilutedWith respect to microbiological, chemical and physical stability with use of the undiluted solutions.

Disposal

All materials that have been used for the preparation and administration, or which have been in contact with cisplatin in any way, must be disposed of according to local cytotoxic guidelines. Medicines should not be disposed of via wastewater or household waste.

7. Marketing authorisation holder

Beta Drugs Limited
Kharuni-Lodhimajra Road,
Vill: Nandpur, Baddi, Distt. Solan,
Himachal Pradesh, 173205 INDIA

8. Marketing authorisation number(s)

07484/08126/NMR/2020

9. Date of first authorisation

31 May 2022

10. Date of revision of the text

July 2024