Summary of Product Characteristics

1. Name of the medicinal product
PLATIFIRST (Cisplatin 1mg/ml solution for Injection)

Cisplatin 1 mg/ml Concentrate for solution for infusion

2. Qualitative and quantitative composition
1 ml contains 1 mg cisplatin.
1 vial of 10 ml concentrate for solution for infusion contains 10 mg cisplatin.

Excipient(s) with known effect
NNN

For the full list of excipients, see section 6.1.

3. Pharmaceutical form
Concentrate for solution for infusion

A clear colourless to pale yellow solution

4. Clinical particulars
4.1 Therapeutic indications

To be used as mono-therapy, or as part of an existing chemotherapy for advanced or metastatic tumours: testicular carcinoma (palliative and curative poly-chemotherapy) and ovary carcinoma (stages III and IV), and head and neck squamous-cell epithelioma (palliative therapy).
In the treatment of small cell lung carcinoma.

In the treatment of advanced non-small cell lung carcinoma.

4.2 Posology and method of administration

Posology
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 a combination chemotherapy. The dosage directions are applicable for both adults and children. For recommendations on the dosage applicable, based on the diagnosis and the clinical condition, the current medical literature should be consulted.

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 unless in the combination therapy of small-cell and non-small-cell lung carcinoma, in which a typical dose of 80 mg/m² is administered.
Further dosage recommendations are to be based upon current medical insights, to be obtained from the literature or/and the appropriate working parties.

For warnings and precautions to be considered prior to the start of the next treatment cycle, see section 4.4.

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

Method of administration
Cisplatin 1mg/ml concentrate for solution for infusion is to be diluted before use (see section 6.6.). The diluted solution should be administered only intravenously by infusion (see below). For administration, any device containing aluminium that may come in contact with cisplatin (sets for intravenous infusion, needles, catheters, syringes) must be avoided (see section 6.2.).

The cisplatin solution for infusion prepared according to instructions (see section 6.6.) 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. Hydration 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.

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/m^2 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

- Hypersensitivity to the active substance or other platinum containing compounds, or to any of the excipients listed in section 6.1.
- in dehydrated condition (pre- and post-hydration is required to prevent serious renal dysfunction);
- with myelosuppression;
- pre-existing renal impairment or hearing impairment 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.
- breastfeeding (see section 4.6.)
- in combination with yellow fever vaccine and phenytoin in prophylactic use (See section 4.5)

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 must be administered under close supervision by a qualified doctor specialized in the use of chemotherapeutic agents.

Appropriate monitoring and management of the treatment and its complications are only possible if adequate diagnosis and exact treatment conditions are available.
Before, during and after administration of cisplatin, the following parameters resp. organ functions must be determined:

- renal function;
- hepatic function;
- haematopoiesis 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 resp. 1.5 mg/dl
- urea <25 mg/dl
- white blood cells >4.000/µl resp. >4.0 x 10^9/l
- blood platelets >100.000/µl resp. >100 x 10^9/l

- audiogram: results within the normal range.

Nephrotoxicity

Cisplatin causes severe cumulative nephrotoxicity which may be potentiated by other substances (please refer to section 4.5). A urine output of 100 mL/hour or greater will tend to minimize cisplatin nephrotoxicity. This can be accomplished by pre-hydration with 2 liters of an appropriate intravenous solution, and similar post cisplatin hydration (recommended 2,500 mL/m^2/24 hours). If vigorous hydration is insufficient to maintain adequate urinary output, an osmotic diuretic may be administered (eg, mannitol).

Neuropathies

Severe cases of neuropathies have been reported. These neuropathies may be irreversible and may manifest by paraesthesia, 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.

Ototoxicity

Ototoxicity has been observed in up to 31% of patients treated with a single dose of cisplatin 50mg/m^2, 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 (see section 4.8).

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 (see section 4.3 and section 4.8).

Hepatic function and hematological formula

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

Carcinogenic potential

In humans, in rare cases the appearance of acute leukemia has coincided with use of cisplatin, which was in general associated with other leukemogenic 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 teratogenic and embryotoxic in mice.

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 has 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 (see section 4.2 and section 4.8).

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

Prophylactic administration of an anti-emetic may be effective in alleviating or preventing nausea and vomiting.

The liquid loss caused by vomiting and diarrhoea must be compensated.

Close supervision must also be carried out with regard to ototoxicity, myelodepression and anaphylactic reactions (see section 4.8).

Cisplatin has been shown to be mutagenic. It may also have an anti-fertility effect. Other anti-neoplastic substances have been shown to be carcinogenic and this possibility should be borne in mind in long term use of cisplatin.

Warning

Preparation of the intravenous solution

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.

Excipients with known effect;

NNN

4.5 Interaction with other medicinal products and other forms of interaction

Nephrotoxic substances

Concomitant administration of nephrotoxic (e.g. cephalosporins, aminoglycosides, 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.

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.

The occurrence of nephrotoxicity caused by cisplatin may be intensified by concomitant treatment with antihypertensives containing furosemide, hydralazine, diazoxide, and propranolol.

It may be required to adjust the dose of allopurinol, colchicine, probenecid, or sulfinpyrazone if used together with cisplatin, since cisplatin causes an increase in serum uric acid concentration. Simultaneous use of ifosfamide causes increased protein excretion.

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/m^2, 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.

Attenuated live vaccines
Yellow fever vaccine is strictly contraindicated because of the risk of fatal systemic vaccinal disease (see section 4.3). In view of the risk of generalized illness, it is advisable to use an inactivated vaccine if available.

Use of living virus vaccinations is not recommended given within three months following the end of cisplatin treatment.

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 sub-therapeutic 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 anticonvulsant treatment with phenytoin is strictly contraindicated (see section 4.3.).

Pyridoxine + altretamine combination
During a randomized study of the treatment of advanced ovarian cancer, the response time was unfavorably 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.

Other
Simultaneous use of myelosuppressives or radiation will boost the effects of cisplatin's myelosuppressive activity.

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 (dose-related and sensoric) than either medicinal product 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.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of cisplatin in pregnant women, but based on its pharmacological properties Cisplatin is suspected to cause serious birth defects. Studies in animals have shown reproductive toxicity and transplacental carcinogenicity (see section 5.3.). Cisplatin should not be used during pregnancy unless the clinical condition of the woman requires treatment with cisplatin.

Breast-feeding
Cisplatin is excreted in human milk. Breastfeeding during the therapy is contraindicated (see section 4.3).

Fertility

Both male and female patients must use effective contraceptive methods to prevent conception and/or reproduction during and for at least 6 months after the treatment with Cisplatin.

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 the treatment.

4.7 Effects on ability to drive and use machines

No studies on the effects on ability to drive and use machines have been performed.
Due to the possible side effects (like nephrotoxicity) cisplatin has minor or moderate influence on the ability to drive and use machines. Patients who suffer from these effects (eg feeling 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.

The list is presented by system organ class, MedDRA preferred term, and frequency using the following frequency categories:

very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥1/1000, < 1/100), rare (≥ 1/10000, < 1/1000), very rare (< 1/10000), and not known (cannot be estimated from the available data).
Table of Adverse Drug Events reported during clinical or post-marketing experience (MedDRA terms)

Infections and infestations	
Common	Sepsis
Not known	Infection[a]
Neoplasm benign, malignant, and unspecified	
Uncommon	Acute leukemia
Blood and lymphatic system disorders	
Very common	Bone marrow failure, thrombocytopenia, leukopenia, anemia

Not known	Coombs positive hemolytic anemia
Immune system disorders	
Uncommon	Anaphylactoid[b] reactions
Endocrine disorders	
Not known	Blood amylase increased, inappropriate antidiurectic hormone secretion
Metabolism and nutrition disorders	
Very common	Hyponatremia
Uncommon	Hypomagnesemia
Rare	Hypercholesterolaemia
Very rare	Increased blood iron
Not known	Dehydration, hypokalemia, hypophosphatemia, hyperuricemia, hypocalcemia, tetany
Nervous system disorders	
Rare	Convulsion, neuropathy peripheral, leukoencephalopathy, reversible posterior leukoencephalopathy syndrome
Not known	Cerebrovascular accident, hemorrhagic stroke, ischemic stroke, ageusia, cerebral arteritis, Lhermitte's sign, myelopathy, autonomic neuropathy
Eye disorders	
Not known	Vision blurred, color blindness acquired, blindness cortical, optic neuritis, papilledema, retinal pigmentation
Ear and labyrinth disorders	
Uncommon	Ototoxicity
Not known	Tinnitus, deafness
Cardiac disorders	
Common:	Arrhythmia, bradycardia, tachycardia
Rare	Myocardial infarction
Very rare	Cardiac arrest
Not known	Cardiac disorder
Vascular disorders	
Common	Venous thromboembolism
Not known	Thrombotic microangiopathy (hemolytic uremic syndrome), Raynaud's phenomenon
Respiratory, thoracic and mediastinal disorders	
Common	Dyspnoea, pneumonia and respiratory failure
Not known	Pulmonary embolism
Gastrointestinal disorders	

Uncommon	Metallic setting on the gums
Rare	Stomatitis
Not known	Vomiting, nausea, anorexia, hiccups, diarrhea
Hepatobiliary disorders	
Not known	Hepatic enzymes increased, blood bilirubin increased
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 failure[c], renal tubular disorder
Reproductive system and breast disorders	
Uncommon	Abnormal spermatogenesis and ovulation, and painful gynaecomastia
General disorders and administration site conditions	
Very common	Pyrexia
Not known	Asthenia, malaise, injection site extravasation[d]

a: Infectious complications have led to death in some patients.
b: Symptoms reported for anaphylactoid reaction included amongst others facial oedema, wheezing, bronchospasm, tachycardia, and hypotension 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 of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Health care providers are asked to report any suspected adverse reactions to the marketing authorisation holder, or, if available, via the national reporting system (see details below).

Paper based reporting: TMDA yellow card
Online reporting: https://sqrt.tmda.go.tz/
USSD reporting: send a simple short text message to report any suspected Adverse Drug Reaction by dialing *152*00# and follow the instructions

4.9 Overdose

CAUTION IS ESSENTIAL IN ORDER TO PREVENT AN INADVERTENT OVERDOSE.

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 a cisplatin overdose. Even if hemodialysis is initiated 4 hours after the overdose it has little effect on the elimination of cisplatin from the body due to a strong and rapid fixation of cisplatin to proteins.

Treatment in the event of an overdose consists of general supportive measures.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agent's / Platinum compounds ATC code: L01XA01

Mechanism of action

Cisplatin is an anorganic substance containing a heavy metal [cis-diamminedichloroplatinum(II)]. This substance inhibits the DNA synthesis by realising transverse connections within and between the DNA strings. The protein and RNA synthesis is inhibited to a lesser extent.

Pharmacodynamic effects

Although the primary activity of cisplatin seems to be the inhibition of DNA synthesis, the antineoplastic process includes other activities, such as enlargement of the tumour immunogenicity. Cisplatin's oncolytic functions can be compared to the functions of alkylating substances. Cisplatin also offers immunosuppressive, radiosensitising and antibacterial features. Cisplatin does not seem to be cell cycle specific.

The cytotoxic activities of cisplatin are caused by binding all DNA bases, with a preference for the N-7 position of guanine and adenosine.

5.2 Pharmacokinetic properties

Distribution

After intravenous administration, cisplatin is rapidly distributed among all tissues. Following cisplatin doses of 20 to 120 mg/m², the concentrations of platinum are highest in liver, prostate and kidney, somewhat lower in bladder, muscles, testicle, pancreas and spleen and lowest in bowel, adrenal, heart, lung, cerebrum and cerebellum.

Biotransformation

Over 90% of the total plasma cisplatin is bounded with protein after two hours following the administration. This process may be irreversible. The protein-bounded part is not antineoplastic active. Cisplatin is non-linearly pharmacokinetic. Cisplatin is converted by a non-enzymatic process into one or more metabolites.

Elimination

Elimination from the plasma is realised in two phases after intravenous bolus injection of 50-100 mg/m^2 of cisplatin. The following half-life period have been registered for humans:
t ½ (distribution): 10-60 minutes
t ½ (terminal): approximately 2-5 days

The considerable protein binding of the total platinum contents results in an extended or incomplete excretion phase with cumulative urine secretion ranging from 27 to 45% of the administered dose in a period from 84 to 120 hours. An extended infusion results in the urine secretion of a larger part of the dose. The faecal secretion is minimal, and small amounts of platinum can be traced in the gallbladder and the large intestine. Dysfunctional kidneys increase the plasma half-life period, which may also increase theoretically in the presence of ascites caused by the highly protein binding activities of cisplatin.

5.3 Preclinical safety data

Chronic toxicity:
Chronic toxicity models indicate kidney damage, bone marrow depression, gastro-intestine disorders and ototoxicity.

Mutagenity and carcinogenity:
Cisplatin is mutagenic in numerous *in vitro* and *in vivo* tests (bacterial test systems and chromosome defects in animal cells and tissue cultures). Long term studies of cisplatin on mice and rats evidenced the carcinogenic effects.

Reproductive toxicity:
Fertility: Gonadal suppression resulting in amenorrhoea or azoospermia may be irreversible and cause definitive infertility.

Studies in rats showed that exposure during pregnancy produces tumours in the adult offspring.
Pregnancy and lactation: Cisplatin is embryotoxic and teratogenic for mice and rats, and defects have been reported for both species. Cisplatin was found in the milk.

6. Pharmaceutical particulars

6.1 List of excipients

NNN

6.2 Incompatibilities

Cisplatin reacts with aluminium which results in production of a black platinum precipitate. Therefore, any device containing aluminium that may come in contact with cisplatin (sets for intravenous infusion, needles, catheters, syringes) must be avoided.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

The cisplatin 1 mg/ml concentrate must not be diluted with glucose solution 5% alone or mannitol solution 5% alone, but only with the mixtures containing additionally sodium chloride as stated in section 6.6.

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

6.3 Shelf life

Medicinal product as packaged for sale:
24 months

Solution for infusion after dilution (see section 6.6):
Chemical and physical in-use stability has been demonstrated for *48* hours *at* 2 to *8°C* when protected from light for solutions with a final cisplatin concentration of 0.1 mg/ml after dilution of the cisplatin 1mg/ml concentrate with one of the following solutions:
- sodium chloride solution 0.9%;
- mixture of sodium chloride solution 0.9% and glucose solution 5% (1:1);
- mixture of sodium chloride solution 0.9% and mannitol solution 5% (1:1).

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution / dilution (etc) has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Medicinal product as packaged for sale:
Store below 30°C.

For storage conditions of the diluted medicinal product, see section 6.3.

6.5 Nature and contents of container

Type I glass vial of 1 x 10 ml.

6.6 Special precautions for disposal and other handling

Cisplatin 1 mg/ml concentrate for solution for infusion is to be diluted before use. For preparation of solution for infusion, any device containing aluminium that may come in contact with cisplatin (sets for intravenous infusion, needles, catheters, syringes) must be avoided (see section 6.2.). Preparation of solution for infusion must take place in aseptic conditions.

For dilution of the concentrate, one of the following solutions should be used:
- sodium chloride solution 0.9%;

- mixture of sodium chloride solution 0.9% and glucose solution 5% (1:1) (resulting final concentrations: sodium chloride 0.45%, glucose 2.5%).
- Should hydration prior to the treatment with cisplatin be impossible, the concentrate may be diluted with:
- mixture of sodium chloride solution 0.9% and mannitol solution 5% (1:1) (resulting final concentrations: sodium chloride 0.45%, mannitol 2.5%).
Preparation of cisplatin solution for infusion:
The required amount (dose) of the cisplatin concentrate 1 mg/ml calculated according to the instructions in section 4.2. should be diluted in 1-2 litres of one of the above mentioned solutions. The diluted solution should be administered only by intravenous infusion (see section 4.2.).
Only clear and colourless to yellowish solutions without visible particles should be used.
For single use only.

Cytotoxic agents should be prepared for administration only by personnel who have been trained in the safe handling of the preparation.

Refer to local cytotoxic handling guidelines.
As any other cytotoxic agent, cisplatin should be used with extreme caution: gloves, face masks and protective clothing are required and vital. Cisplatin should be processed under a protective hood, if possible. Contact with skin and/or mucous membranes must be avoided. Pregnant hospital employees should not work with cisplatin.

Skin contact: Rinse with large quantities of water. Apply an ointment if you have a temporary burning feeling. (Note: Some persons are sensitive to platinum and may experience a skin reaction).

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 seal it. In the case of spillage all items coming into contact with Cisplatin should be handled and disposed in accordance to local cytotoxic guidelines.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder
VHB MEDI SCIENCES LIMITED
UTTARAKHAND-263145
PLOT NO: 20-22 & 49-51, INTEGRATED INDUSTRIAL ESTATE,
SECTOR-5, SIDCUL, PANT NAGAR, RUDRAPUR
UTTARAKHAND
INDIA

8. Marketing authorisation number(s)
TZ 19 H 0232

9. Date of first authorisation/renewal of the authorisation
August 02, 2019

10. Date of revision of the text
October 12, 2023