Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cisplatin Teva 0.5 mg/ml, Concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Cisplatin Teva 0.5 mg/ml concentrate for solution for infusion contains 0.5 mg/ml of cisplatin.

Each ml of solution contains 3.5 mg of sodium.

For a complete list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion.
Clear, light yellow solution free from visible particles

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Cisplatin Teva 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 combination with radiotherapy in the treatment of cervical carcinoma.

Cisplatin can be used as monotherapy and in combination therapy.

4.2 Posology and method of administration

Cisplatin Teva 0.5 mg/ml concentrate for solution for infusion is to be diluted before administration. For instructions on dilution of the product before administration 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.).

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 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/m^2 weekly for 6 weeks.
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.

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 200 ml/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/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

Cisplatin is contraindicated in patients
- with hypersensitivity to cisplatin or other platinum compounds or to any of the excipients;
- with renal dysfunction **(**creatinine clearance < 60 ml/min**)**;
- in dehydrated condition (pre- and post-hydration is required to prevent serious renal dysfunction);
- with myelosuppression;
- with a hearing impairment;
- with neuropathy caused by cisplatin
- who are 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 may only be administered under the supervision of a physician qualified in oncology with experience in the use of antineoplastic chemotherapy.

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.

Audiograms must be made before starting treatment with cisplatin and always before starting another treatment cycle (see section 4.8).

Nephrotoxicity can be prevented by maintaining adequate hydration before, during and after the intravenous infusion of cisplatin.

Forced diuresis by hydration or by hydration and suitable diuretics before and after the cisplatin administration decreases the risk of nephrotoxicity. Hyperuricaemia and hyperalbuminaemia may predispose to cisplatin-induced nephrotoxicity.

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 $\leq$ 130 µmol/l rsp. 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.

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

Neurotoxicity secondary to **c***isplatin administration has been reported and therefore neurological examinations are recommended.*

Special caution must be exercised for patients with peripheral neuropathy not caused by cisplatin.

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

In cases of extravasation:
- immediately end the infusion of cisplatin;
- do not move the needle, aspirate the extravasate from the tissue, and rinse with sodium chloride solution 0.9% (if solutions with cisplatin concentrations higher than recommended were used; see section 6.6.).

Nausea, vomiting and diarrhoea often occur after administration of cisplatin (see section 4.8). These symptoms disappear in most patients after 24 hours. Less serious nausea and anorexia may continue up to seven days after the 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.

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.

Male and female patients during and for at least 6 months after the treatment with cisplatin: see section 4.6.

4.5 Interaction with other medicinal products and other forms of interaction

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

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 these organs. 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.

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.

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.

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

Simultaneous use of ifosphamide causes increased protein excretion.
The ototoxicity of cisplatin was reportedly enhanced by concomitant use of ifosfamide, an agent which is not ototoxic when given alone.

In a randomised trial in patients with advanced ovarian carcinoma the response to therapy was influenced negatively by concomitant administration of pyridoxine and hexamethylmelamine.

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

Evidence has been established that the treatment with cisplatin prior to an infusion with paclitaxel may reduce the clearance of paclitaxel by 70-75% and therefore can intensify neurotoxicity (in 70% of patients or more).

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 drug as a single agent in similar doses.

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.

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 (see section 4.3).

Chelating agents like penicillamine may diminish the effectiveness of cisplatin.

The high intra-individual variability of the coagulability during diseases, and the possibility of interaction between oral anticoagulants and anticancer chemotherapy requires an increased frequency of the INR (prothrombin time) monitoring.

In concomitant use of cisplatin and ciclosporin the excessive immunosuppression with risk of lymphoproliferation is to be taken into consideration.

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

Yellow fever vaccine are strictly contra-indicated because of the risk of fatal systemic vaccinal disease (see section 4.3.).

4.6 Fertility, pregnancy and lactation

Pregnancy
There is insufficient data about the use of cisplatin in pregnant women. However, based on the pharmacological properties, cisplatin is suspected to cause serious birth defects. Animal studies have shown reproductive toxicity and transplacental carcinogenity (see section 5.3). Cisplatin should not be used during pregnancy unless clearly necessary.

Women of childbearing potential and male patients have to use effective contraception during and up to 6 months after treatment.
A preconceptual consult is recommended when patients wish to have children after treatment with cisplatin. Cisplatin can cause temporary or permanent infertility. Sperm cryopreservation can be considered (see also section 4.4).

Lactation
Cisplatin is excreted in breast milk. Breastfeeding is contra-indicated during treatment with cisplatin.

4.7 Effects on ability to drive and use machines

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).

Infections and infestations
Common:
Infections. Sepsis.

Neoplasms benign, malignant and unspecified (incl cysts and polyps)
Rare:
Cisplatin increases the risk of secondary leukaemia. The risk of secondary leukaemia is dose-dependent and not age- and sex-related.
Carcinogenicity is theoretically possible (based on cisplatin's mechanism of action).

Blood and lymphatic system disorders
Very common:
Dose dependent, cumulative and mostly reversible leukopenia, thrombocytopenia and anaemia are observed in 25-30% of patients treated with cisplatin.

Common:
A considerable decrease in the number of white blood cells often occurs approximately 14 days after the use (less than 1.5×10^9/l in 5% of the patients). A decrease of the number of platelets is observed after approximately 21 days (less than 10% of the patients showed a total less than 50×10^9/l) (the recovery period is approximately 39 days). Anaemia (decreases of greater than 2g haemoglobin) occurs at approximately the same frequency, but generally with a later onset than leukopenia and thrombocytopenia.
Rare:
Coombs positive haemolytic anaemia was reported and was reversible if the use of cisplatin was terminated. Literature has been published regarding hemolysis possibly caused by cisplatin. Serious bone marrow failure (including agranulocytosis and/or aplastic anaemia) may occur after high doses of cisplatin.
Very rare:
Thrombotic microangiopathy combined with haemolytic uraemic syndrome.

Immune system disorders
Uncommon:
Hypersensitivity may present as rash, urticaria, erythema, or pruritus allergic.
Rare:
Anaphylactic reactions have been reported; hypotension, tachycardia, dyspnoea, bronchospasm, face oedema and fever have been reported.
Treatment with antihistamines, epinephrine (adrenaline) and steroids may be required.
Immunosuppression has been documented.

Endocrine disorders
Very rare:
Syndrome of inappropriate antiduretic hormone secretion.

Metabolism and nutrition disorders
Rare:
Hypomagnaesaemia, hypocalcaemia, hyponatraemia, hypophosphataemia and hypokalaemia with 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.
Very rare:
Increased blood iron.

Nervous system disorders
Common:
Neurotoxicity caused by cisplatin is characterised by peripheral neuropathy (typically bilateral and sensory), and rarely by the loss of taste or tactile function, or by optic retrobulbar neuritis with reduced visual acuity and cerebral dysfunction (confusion, disarthria, individual cases of cortical blindness, loss of memory, paralysis). Lhermitte's sign, autonomous neuropathy and myelopathy of the spinal cord have been reported.
Rare:
Cerebral disorders (including acute cerebrovascular complications, cerebral arteritis, occlusion of the carotic artery, and encephalopathy).
Very rare:
Seizures.

The use of cisplatin must be terminated immediately if one of the above mentioned cerebral symptoms occurs. Neurotoxicity caused by cisplatin may be reversible. However, the process is irreversible for 30-50% of the patients, even after discontinuation of the treatment. Neurotoxicity may occur after the first dose of cisplatin, or after a long-term therapy. Severe neurotoxicity may occur in patients who have received cisplatin at high concentrations or for a prolonged period.

Eye disorders
Rare:
Blindness during a combination treatment with cisplatin. Following high-dose cisplatin application impairment of colour vision and eye movement has been reported.
Very rare:
Papilloedema, optic neuritis and cortical blindness have been reported following treatment with cisplatin. One case of unilateral optic neuritis retrobulbar with reduced visual acuity has been reported after combination chemotherapy followed by cisplatin treatment.

Ear and labyrinth disorders
Very common:
Hearing impairment has been documented in approximately 31% of patients treated with 50 mg/m^2 cisplatin. The defect is cumulative, may be irreversible, and is sometimes limited to one ear. Ototoxicity manifests itself as tinnitus and/or hearing impairment at higher frequencies (4,000-8,000 Hz). Hearing impairment at frequencies of 250-2000Hz (normal hearing range) was noticed for 10 to 15% of the patients.
Common:
Deafness and vestibular toxicity combined with vertigo may occur. Prior or simultaneous cranial radiation increases the risk of hearing loss.
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
Common:
Arrythmia including bradycardia, tachycardia and other electrocardiogram changes e.g. ST-segment changes, signs of myocardial ischemia have been observed particularly in combination with other cytotoxics.
Rare:
Hypertension and myocardial infarction may occur, even some years after chemotherapy. Severe coronary artery disease.
Very rare:
Cardiac arrest has been reported after treatment with cisplatin combined with other cytotoxics.

Vascular disorders
Common:
Phlebitis may occur in the area of the injection after intravenous administration.
Very rare:
Vascular disorders (cerebral or myocardial ischaemia, impairment of the peripheral circulation related to the Raynaud's syndrome) were linked to cisplatin chemotherapy.

Respiratory, thoracic and mediastinal disorders
Common:
Dyspnoea, pneumonia and respiratory failure.

Gastrointestinal disorders
Very common:
Anorexia, nausea, vomiting and diarrhoea occur between 1 and 4 hours after the use of cisplatin. (See section 4.4.)
Uncommon:
Metallic setting on the gums.
Rare:
Stomatitis, diarrhoea.

Hepatobiliary disorders
Common:
Abnormal hepatic function with increased transaminases and blood bilirubin are reversible.
Rare:
Reduced blood albumin levels were noticed and may be linked to the treatment with cisplatin.

Skin and subcutaneous tissue disorders
Common:
Erythema and skin ulcer may occur in the area of the injection after intravenous administration.
Uncommon:
Alopecia.

Renal and urinary disorders
Very common:
Renal failure after single or multiple doses of cisplatin. A mild, reversible renal dysfunction may be observed after a single intermediary dose of cisplatin (20 mg/m^2 to < 50 mg/m^2). The use of a single high dose (50-120 mg/m^2), or repeated daily use of cisplatin, may cause renal failure with tubular renal necrosis presenting as uraemia or anuria. Renal failure may be irreversible.
The nephrotoxicity is cumulative and may occur 2-3 days, or two weeks after the first dose of cisplatin. Serum creatinine and urea concentrations may increase. Nephrotoxicity was observed in 28-36% of patients without sufficient hydration after a single dose of 50 mg/m^2 of cisplatin. (See section 4.4.)
Hyperuricaemia occurs asymptomatically or as gout. Hyperuricaemia has been reported in 25-30% of patients in conjunction with nephrotoxicity. Hyperuricaemia and hyperalbuminaemia may predispose to cisplatin-induced nephrotoxicity.

Reproductive system and breast disorders
Uncommon:
Abnormal spermatogenesis and ovulation, and painful gynaecomastia.

General disorders and administration site conditions
Very common:
Fever.
Common:
Localised oedema and pain may occur in the area of the injection after intravenous administration.
Uncommon:
Hiccups, asthenia, malaise

4.9 Overdose

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/m^2), 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other antineoplastic agents, 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 Pharmacokinetic 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 and carcinogenity
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

Water for injections
Sodium chloride
Hydrochloric acid 1N for pH adjustment
Sodium hydroxide 1N for pH adjustment

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

Before opening
- 20 ml: 2 years
- 50 ml: 2 years
- 100 ml: 3 years

After dilution
After dilution in infusion fluids described in section 6.6, the product can be stored for at most 14 days at room temperature (15–25 °C) under protection from light.
Exposure to ambient light must be limited to at most 6 hours. If exceeding 6 hours, the bags must be thoroughly wrapped in aluminium foil in order to protect the contents from ambient light.

From a microbiological point of view, the diluted solution 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 dilution has taken place in controlled and validated aseptic conditions

6.4 Special precautions for storage

Undiluted solution: Store below 25°C. Do not refrigerate or freeze. Keep container in the outer carton in order to protect from light.

For the storage conditions of the diluted medicinal product: see section 6.3.
Do not store diluted solutions in the refrigerator or freezer.

6.5 Nature and contents of container

Brown, type I glass vials of 20, 50 and 100 ml with butyl rubber stop, aluminium closing and plastic snap-cap.

Not all pack sizes may be marketed.

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. 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 “Waste”.

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. Only a clear solution, free from particles should be administered.

DO NOT bring in contact with injection material that contains aluminium
DO NOT administer undiluted

With respect to microbiological, chemical and physical stability with use of the undiluted solutions, see section 6.3.

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. Remnants of the medicinal products as well as all materials that have been used for dilution and administration must be destroyed according to hospital standard procedures applicable to cytotoxic agents and in accordance with local requirements related to the disposal of hazardous waste.

7 MARKETING AUTHORISATION HOLDER

Teva Pharma B.V.
Computerweg 10
3542 DR Utrecht
The Netherlands

8 MARKETING AUTHORISATION NUMBER

PA 0749/119/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 30th January 2009

Date of last renewal: 31st August 2010

10 DATE OF REVISION OF THE TEXT

December 2010