Scheduling status: S4

Proprietary names and dosage forms:

Cisplatin 10 mg/20 ml Oethmaan solution for infusion
Cisplatin 50 mg/100 ml Oethmaan solution for infusion

Composition:
Cisplatin 10 mg/20 ml Oethmaan solution for infusion: Each 1,0 ml of solution for infusion contains 0,5 mg cisplatin.
Cisplatin 50 mg/100 ml Oethmaan solution for infusion: Each 1,0 ml of solution for infusion contains 0,5 mg cisplatin.
Other Excipients: Sodium chloride, hydrochloric acid, water for injection.

Pharmacological classification:
A 26 Cytostatic agents.

Pharmacological action:
Cisplatin is a platinum co-ordination compound with antitumour properties. The platinum complexes can react with DNA forming both interstrand and intrastrand DNA cross links. In addition to its reactivity with DNA, cisplatin can react with other nucleophiles, such as sulfhydryl groups of proteins.
There is no phase specificity in the action of cisplatin on the cell cycle. At rapid intravenous administration the medicine has an initial half-life in plasma of 25 to 50 minutes; concentrations decline subsequently with a half-life of 58 to 73 hours. More than 90 % of the platinum in the blood is bound to plasma proteins. High concentrations of cisplatin are found in the kidney, liver, intestine and testes, but there is poor penetration into the central nervous system.

Indications:
Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan are indicated for advanced, non-seminomatous testicular cancer in combination therapy with bleomycin and vinblastine.
Carcinoma of the ovary, particularly when used with cyclophosphamide or doxorubicin.
Cancers of the bladder, head and neck, endometrium, small cell carcinoma of the lung, lymphomas and some neoplasms of childhood.

Contraindications:
C**isplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** are contraindicated in patients with a history of allergic reactions to cisplastin or other platinum containing compounds, or any component of the formulation. **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** are contraindicated in patients with pre-existing renal impairment or hearing impairment or bone marrow depression.
Cisplatin is nephrotoxic and neurotoxic (in particular ototoxic). These toxicities may be cumulative if disorders of this type pre-exist. Patients receiving cisplatin should not breastfeed.
Concurrent administration of yellow fever vaccine is contraindicated.
Pregnancy and lactation, (see "Pregnancy and Lactation").

Warnings:
Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan should be administered under the supervision of a qualified medical practitioner experienced in the use of antineoplastic therapy. Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available.

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 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 (e.g., 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 50 mg/m^2, and is manifested by tinnitus and/or hearing loss in the high frequency range (4000 to 8000 Hz). 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 Side effects).

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 Contraindications and Side effects).
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.
Because of the possibility of carcinogenicity and mutagenicity **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan**, patients of child bearing age or conceiving potential must exercise non-hormonal conception control.

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 method of administration and Side effects).
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 (see Side effects).

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.

Interactions:
Combinations of the following medications may also interact **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan.**
The reaction is dose dependant: blood dyscrasia causing medications, bone marrow depressants (particularly adriamycin) or radio therapy, nephrotoxic medication (amino glycoside antibiotics), ototoxic medication, killed virus vaccines.

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 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** 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.

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.

Pregnancy and lactation:
Cisplatin is contraindicated in pregnancy and lactation.
During treatment with cisplatin and for a minimum of the following 6 months, appropriate measures must be taken to avoid pregnancy; this applies to patients of both genders.
Genetic counseling 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 cryo-conservation of their sperm prior to treatment.

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

Dosage and directions for use:
The medical practitioner should in all cases familiarize himself/herself with the current literature before **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** are given by intravenous infusion not more frequently than every 3 to 4 weeks. It is usually given as a single dose of 50 to 120 mg per m^2 daily for 5 days.
Subsequent doses should be adjusted according to the nadir of the white-blood cell and platelet counts or before renal function approaches normal. Auditory acuity must also be within normal limits.
Lower doses may be required when **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** are given as part of a combination regimen. Lower doses may be given ranging from 20 mg per m^2 upwards every 3 to 4 weeks.
In order to prevent renal toxicity, hydration of the patient is recommended by infusion of 1 to 2 litres of suitable fluid containing 37,5 g mannitol for intravenous infusion for 8 to 12 hours before administration of cisplatin.
Adequate hydration and urinary output must be maintained before and for 24 hours after administration. Concurrent furosemide may also be used provided that salt and water depletion are avoided.
Any solution not used must be discarded.
Dosage adjustments are needed in cases of impaired renal function, use in elderly patients or use in combination with other myelosuppressive agents.
Note: **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** are incompatible with aluminium, do not use needles, intravenous sets or equipment containing aluminium for administration since an interaction may occur and a black precipitate will form.
Guidelines for the handling of antineoplastic agents must be followed. Cautious and proper disposal of needles, syringes, containers and unused medication must be done.

Side-effects and special precautions:
Side effects depend on the used dose and may have cumulative effects.
Many of the adverse effects of **Cisplatin 10 mg/20 ml Oethmaan and Cisplatin 50 mg/100 ml Oethmaan** are an extension of their therapeutic action, which is not selective for malignant cells, but affects all rapidly dividing cells. In consequence, adverse effects may be expected where normal cell division is fairly rapid, e.g. the bone marrow, lymphoreticular tissue, gastro-intestinal mucosa, skin and gonads, as well as in the foetus. Serious toxic effect, on the kidneys, bone-marrow depression and ears, occur. These effects are generally dose related and cumulative, and may require dosage adjustment.
Frequencies are defined using the following convention:
Frequent: (≥ 1/10); (≥ 1/100 to < 1/10);
Less Frequent: (≥ 1/1,000 to < 1/100); (≥ 1/10,000 to ≤ 1/1,000); (≤ 1/10,000), not known (cannot be estimated from the available data).
Adverse Drug Events reported during clinical or post-marketing experience (MedDRA terms)

Infections and infestations	
Frequent:	Sepsis
Not known:	Infection (infectious complications fatal in some patients)
Blood and lymphatic system disorders	
Frequent:	Bone marrow failure, thrombocytopenia, leukopenia, anemia
Not known:	Coombs positive hemolytic anemia
Neoplasm benign, malignant and unspecified	
Less frequent:	Acute leukemia
Immune system disorders	
Less frequent:	Anaphylactoid reactions (such as facial edema, wheezing, bronchospasm, tachycardia, hypotension)
Endocrine disorders	
Not known:	Blood amylase increased, inappropriate antidiurectic hormone secretion
Metabolism and nutrition disorders	
Frequent:	Hyponatremia
Less frequent:	Hypomagnesemia
Not known:	Dehydration, hypokalemia, hypophosphatemia, hyperuricemia, hypocalcemia, tetany
Nervous system disorders	
Less frequent:	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	
Less frequent:	Ototoxicity
Not known:	Tinnitus, deafness
Cardiac disorders	
Frequent:	Arrhythmia, bradycardia, tachycardia
Less frequent:	Myocardial infarction, Cardiac arrest
Not known:	Cardiac disorder
Vascular disorders	
Not known:	Thrombotic microangiopathy (hemolytic uremic syndrome), Raynaud's phenomenon
Gastrointestinal disorders	
Less frequent:	Stomatitis
Not known:	Vomiting, nausea, anorexia, hiccups, diarrhea
Hepatobiliary disorders	
Not known:	Hepatic enzymes increased, blood bilirubin increased
Respiratory, thoracic and mediastinal disorders	
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 failure (including elevations in BUN and creatinine, serum uric acid, and/or a decrease in creatinine clearance), renal tubular disorder
Reproductive system and breast disorders	
Less frequent:	Abnormal spermatogenesis
General disorders and administration site conditions	
Frequent:	Pyrexia
Not known:	Asthenia, malaise, injection site extravasation (with resulting local soft tissue toxicity including tissue cellulitis, fibrosis and necrosis, pain, edema and erythema)

Effects on ability to drive and use machines
No studies on the effects on ability to drive and use machines have been performed.
Nevertheless, the profile of undesirable effects (like nephrotoxicity) may influence the ability to drive vehicles and use machinery.

Known symptoms of over-dosage and particulars of its treatment:
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 should be symptomatic and supportive.

Identification:
Cisplatin 10 mg/ 20 ml Oethmaan Solution for infusion:
Clear, colourless to light-yellow solution, practically free from visible particles.
Cisplatin 50 mg/100 ml Oethmaan Solution for infusion:
Clear, colourless to light-yellow solution, practically free from visible particles.

Presentation:
Cisplatin 10 mg/ 20 ml Oethmaan solution for infusion:
Brown glass vials (20 ml) closed with a chlorobutyl rubber stopper. Cartons contain either 1 or 10 glass vials.
Cisplatin 50 mg/100 ml Oethmaan solution for infusion:
Brown glass vials (100 ml) closed with a chlorobutyl rubber stopper. Cartons contain either 1 or 10 glass vials.

Storage instructions:
Store below 25 °C.
Do not refrigerate.
Protect from light. Any unused portion must be discarded.
KEEP OUT OF THE REACH OF CHILDREN.

Registration numbers:
Cisplatin 10 mg/ 20 ml Oethmaan solution for infusion: 37/25/0523
Cisplatin 50 mg/ 100 ml Oethmaan solution for infusion: 37/25/0524

Name and business address of the holder of the certificates of registration:
Oethmaan Biosims (Pty) Ltd.
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Date of publication of this package insert:
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Skeduleringstatus: S4

Eiendomsname en doseervorms:

Cisplatin 10 mg/20 ml Oethmaan oplossing vir infusie
Cisplatin 50 mg/100 ml Oethmaan oplossing vir infusie

Samestelling:
Cisplatin 10 mg/20 ml Oethmaan oplossing vir infusie: elke 1 ml oplossing vir infusie bevat 0,5 mg sisplatien.
Cisplatin 50 mg/100 ml Oethmaan oplossing vir infusie: elke 1,0 ml oplossing vir infusie bevat 0,5 mg sisplatien.
Ander hulpstowwe: natriumchloried, soutsuur, water vir inspuiting.

Farmakologiese klassifikasie:
A 26 Sitostatiese middels

Farmakologiese werking:
Sisplatien is 'n platinum-koördinasieverbinding met aktiwiteit teen tumore. Die platinumkomplekse kan met DNA reageer om sowel interstring- as intrastringkruisbindings met DNA te vorm. Behalwe vir die aktiwiteit teenoor DNA kan sisplatien met ander nukleofiele, soos sulfhidrielgroepe van proteiene, reageer.
Sisplatien is nie in 'n sekere fase van die selsiklus aktief nie. Teen vinnige intraveneuse toediening het die medisyne 'n aanvanklike plasmahalfleeftyd van 25 tot 50 minute; konsentrasies neem daarna met 'n halfleeftyd van 58 tot 73 uur af. Meer as 90 % van die platinum in die bloed is aan plasmaproteiene gebind. Hoë konsentrasies sisplatien word in die niere, lewer, ingewande en testes gekry, maar daar is swak penetrasie in die sentrale senustelsel.

Indikasies:
Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan is aangedui vir
- gevorderde, nie-seminomateuse testikulêre kanker in kombinasieterapie saam met bleomisien en vinblastien.
- karsinoom van die ovaria veral as dit saam met siklofosfamied of doksorubisien gebruik word
- kanker van die blaas, kop en nek, endometrium, kleinselkanker van die long, limfome en sekere neoplasmas in kinders.

Kontra-indikasies:
Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan is teenaangedui vir pasiënte met 'n geskiedenis van allergiese reaksies op sisplastien of ander platinumbevattende verbindings, of op enige komponent van die formulering. **Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan** is teenaangedui vir pasiënte met bestaande nierversaking of gehoorgestremdheid of beenmurgonderdrukking.
Sisplatien is nefrotoksies en neurotoksies (veral ototoksies). Hierdie toksisiteite kan kumulatief wees as daar reeds sulke siektes bestaan. Pasiënte wat sisplatien kry, moet nie borsvoed nie.
Gelyktydige toediening van geelkoors-entstof is teenaangedui.
Swangerskap en borsvoeding (kyk "Swangerskap en borsvoeding").

Waarskuwings:
Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan moet onder die toesig van 'n gekwalifiseerde mediese praktisyn met ondervinding in die gebruik van antineoplastiese middels toegedien word. Behoorlike beheer van behandeling en komplikasies is slegs moontlik indien voldoende fasiliteite vir diagnose en behandeling geredelik beskikbaar is.

Nefrotoksisiteit:
Sisplatien veroorsaak erge kumulatiewe nefrotoksisiteit. 'n Urienuitset van 100 ml/uur of meer is geneig om die nefrotoksisiteit van sisplatien te verminder. Dit kan bereik word deur vooraf hidrasie met 2 liter geskikte binneaarse oplossing en soortgelyke hidrasie nadat sisplatien gegee is (2500 ml /m^2/24 uur word aanbeveel). As sterk hidrasie onvoldoende is om voldoende urienuitset te behou, kan 'n osmotiese diuretikum gegee word (bv. mannitol).

Neuropatie:
Erge gevalle van neuropatie is aangemeld. Hierdie neuropatie kan onomkeerbaar wees en kan manifesteer as parestesie, arefleksie en 'n verlies van propriosepsie en 'n gevoel van vibrasies. Verlies van motoriese funksie is ook aangemeld. 'n Neurologiese ondersoek moet gereeld gedoen word.

Ototoksisiteit:
Ototoksisiteit is waargeneem in tot 31 % van pasiënte wat behandel is met 'n enkele dosis van 50 mg/m^2 sisplatien en word gekenmerk deur tinnitus en/of gehoorverlies in die hoëfrekwensiegebied (4000-8000 Hz). Daar kan af en toe 'n swakker vermoë wees om gesprekstone te hoor. Ototoksiese effekte kan meer uitgesproke wees in kinders wat sisplatien kry. Gehoorverlies kan unilateraal of bilateraal wees en neig om meer gereeld en ernstiger met herhaalde dosisse te wees; doofheid na die eerste dosis sisplatien is egter selde aangemeld. Ototoksisiteit kan verbeter word deur voorafgaande gelyktydige kraniale bestraling en kan met die maksimum plasmakonsentrasie van sisplatien verband hou. Dit is onduidelik of sisplatien-geïnduseerde ototoksisiteit omkeerbaar is. Noukeurige monitering met oudiometrie moet voor aanvang van behandeling en voor die daaropvolgende dosisse sisplatien gedoen word.
Vestibulêre toksisiteit is ook aangemeld (kyk "Newe-effekte").

Allergiese verskynsels:
Soos met ander op platinumgebaseerde produkte, kan hipersensitiwiteitsreaksies in die meeste gevalle tydens perfusie voorkom, waarvoor staking van perfusie en gepaste simptomatiese behandeling nodig kan wees.
Kruisreaksies, soms dodelik, is met al die platinumverbindings aangemeld
(kyk "Kontra- indikasies" en "Newe-effekte").

Lewerfunksie en hematologiese formule:
Die hematologiese formule en die lewerfunksie moet gereeld gemonitor word.

Karsinogeenpotensiaal:
In mense het akute leukemie in seldsame gevalle met die gebruik van sisplatien voorgekom, wat oor die algemeen met ander leukemogene middels gepaardgegaan het.
Sisplatien is 'n bakteriese mutageen en veroorsaak chromosoomafwykings in kulture var dieresselle. Karsinogenisiteit is moontlik, maar dit is nie bewys nie. Sisplatien is teratogeen en embriotoksies vir muise.
Vanweë die moontlikheid van karsinogenisiteit en mutageniseit van **Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan** moet pasiënte wat kinders kan hê of swanger kan raak nie-hormonale voorbehoedmiddels gebruik.

Reaksies by die plek van inspuiting:
Reaksies kan tydens die toediening van sisplatien by die inspuitplek voorkom. Vanweë die moontlikheid van ekstravasasie word aanbeveel om die plek van infusie tydens toediening van die middel noukeurig vir moontlike infiltrasie te monitor. Spesifieke behandeling vir reaksies vanweë ekstravasasie is tans onbekend.

Waarskuwing:
Hierdie sitostatiese middel het 'n meer uitgesproke toksisiteit as wat gewoonlik met antineoplastiese chemoterapie voorkom.
Niertoksisiteit, wat veral kumulatief is, is erg en spesiale voorsorgmaatreëls moet tydens toediening getref word (kyk "Toedieningsmetode" en "Newe-effekte").
Naarheid en braking kan intens wees en voldoende anti-emetiese behandeling kan daarvoor nodig wees.
Daar moet ook noukeurig opgelet word vir ototoksisiteit, beenmurgonderdrukking en anafilaktiese reaksies (kyk "Newe-effekte").

Bereiding van die oplossing vir infusie:
Soos met alle ander potensieel giftige produkte, is voorsorgmaatreëls noodsaaklik tydens die hantering van die sisplatienoplossing. Velletsels is moontlik in geval van toevallige blootstelling aan die produk. Dit is raadsaam om handskoene te dra. Was die vel of slymvliese heftig met seep en water as die sisplatienoplossing met die vel of slymvliese in aanraking kom.
Dit word aanbeveel om te voldoen aan die toepaslike prosedures vir die manipulasie en eliminasie van sitostatiese middels.
Voordat u die oplossing aan die pasiënt toedien, moet u die duidelikheid van die oplossing en die afwesigheid van deeltjies verifieer.

Interaksies
Kombinasies van die volgende medisyne kan ook wisselwerking met **Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan** hê.
Die reaksie is dosis afhanklik: medisyne wat bloeddiskrasie veroorsaak, beenmurgonderdrukkers (veral adriamisien) of radioterapie, nefrotoksiese medikasie (aminoglikosiedantibiotika), ototoksiese medikasie, dooievirusentstof.

Nefrotoksiese stowwe:
Gelyktydige toediening van nefrotoksiese middels (bv. kefalosporiene, aminoglikosiede, amfoterisien B of kontrasmedia) of ototoksiese medisyne (bv. aminoglikosiede) kan die toksiese effek van sisplatien op die niere versterk. Wees tydens of na behandeling met **Cisplatin 10 mg/20 ml Oethmaan of Cisplatin 50 mg/100 ml Oethmaan** versigtig met middels wat oorwegend deur die niere uitgeskei word, bv. sitostatiese middels soos bleomisien en mitotreksaat, vanweë moontlike minder nieruitskeiding. Die niertoksisiteit van ifosfamied kan sterker wees as dit saam met sisplatien gebruik word of vir pasiënte wat voorheen sisplatien gekry het. Verlaging in die litiumvlakke in die bloed is in enkele gevalle opgemerk na behandeling met sisplatien gekombineer met bleomisien en etoposied. Dit word dus aanbeveel om die litiumwaardes te monitor.

Ototoksiese stowwe:
Gelyktydige toediening van ototoksiese middels (bv. aminoglikosiede, lusdiuretika) sal die toksiese effek van sisplatien op gehoorfunksie versterk. Behalwe vir pasiënte wat dosisse sisplatien van meer as 60 mg/m^2 kry wie se urienuitskeiding minder as 1000 ml per 24 uur is, moet geen gedwonge diurese met lusdiuretika toegepas word nie in die lig van moontlike skade aan die niere en ototoksisiteit.
Ifosfamied kan gehoorverlies vanweë sisplatien verhoog.

Swangerskap en borsvoeding
Sisplatien is teenaangedui tydens swangerskap en borsvoeding.
Tydens behandeling met sisplatien en vir 'n minimum van die daaropvolgende 6 maande, moet gepaste maatreëls getref word om swangerskap te vermy; dit geld vir pasiënte van beide geslagte. Genetiese berading word aanbeveel as die pasiënt kinders wil hê nadat die behandeling beëindig is. Aangesien behandeling met sisplatien onomkeerbare onvrugbaarheid kan veroorsaak, word aanbeveel dat mans wat in die toekoms vaders wil word, voor behandeling advies oor die bewaring van hul sperms vra.

Borsvoeding:
Sisplatien word in borsmelk uitgeskei. Pasiënte wat met sisplatien behandel word, moet nie borsvoed nie.

Dosis en gebruiksaanwysings:
Die geneesheer moet in alle gevalle vertroud wees met die huidige literatuur voordat **Cisplatin 10 mg/20 ml Oethmaan of Cisplatin 50 mg/100 ml Oethmaan** nie meer dikwels nie as elke 3 tot 4 weke intraveneus toegedien word. Dit word gewoonlik as 'n enkele dosis van 50 tot 120 mg per m^2 daagliks vir 5 dae gegee.
Daaropvolgende dosis moet volgens die nadir van die witbloedsel- en plaatjietellings aangepas word of voor nierfunksie normale vlakke bereik. Die gehoor moet ook binne normale limiete wees.
Laer dosisse kan nodig wees as **Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan** as deel van 'n kombinasieregimen gegee word. Laer dosisse kan van 20 mg per m^2 en hoër elke 3 tot 4 weke wissel.
Om niertoksisiteit te voorkom, word hidrering van die pasiënt deur infusie van 1 tot 2 liter geskikte vloeistof wat 375 g mannitol vir intraveneuse infusie bevat 8 tot 12 uur voor toediening van sisplatien aanbeveel.
Voldoende hidrering en urienuitset moet voor en vir 24 uur na toediening volgehou word.
Furosemied kan saam gebruik word op voorwaarde dat sout- en watteruitputting vermy word.
Die oplossing wat nie gebruik is nie, moet weggegooi word.
Aanpassings in die dosis is nodig ingeval van swak nierfunksie, gebruik in bejaarde pasiënte of gebruik in kombinasie met ander beenmurgonderdrukkende middels.
Let wel: **Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan** is onverenigbaar met aluminium en naalde, intraveneuse stelle of toestelle wat aluminium vir toediening bevat, moet nie gebruik word nie omdat 'n interaksie kan voorkom en 'n swart presipitaat sal vorm. Riglyne vir die handeling van antineoplastiese middels moet gevolg word. Naalde, spuite, houers en ongebruikte medikasie moet versigtig en behoorlik weggedoen word.

Newe-effekte en spesiale voorsorgmaatreëls:
Newe-effekte hang af van die gebruikte dosis en kan kumulatiewe effekte hê.
Baie van die nadelige effekte van **Cisplatin 10 mg/20 ml Oethmaan en Cisplatin 50 mg/100 ml Oethmaan** is 'n voortsetting van die terapeutiese werking daarvan wat nie selektief vir kwaadaardige selle is nie, maar alle vinnig verdelende selle aantas. As gevolg hiervan kan nadelige effekte verwag word waar normale selverdeling redelik vinnig is, bv. die beenmurg, limforetikulêre weefsel, gastro-intestinale slymvlies, vel en gonades asook in die fetus. Ernstige toksiese effekte op die niere, beenmurg en ore kan voorkom. Hierdie effekte hou gewoonlik met die dosis verband en is kumulatief en kan maak dat aanpassing in die dosis nodig is.

Frekwensies word volgens die onderstaande konvensie gedefinieer:
Dikwels: (≥ 1/10); (≥ 1/100 tot < 1/10);
Minder dikwels: (≥ 1/1,000 tot < 1/100); (≥ 1/10,000 tot ≤ 1/1,000); (≤ 1/10,000), nie bekend nie (kan nie uit beskikbare data beraam word nie).
Nadelige geneesmiddeleffekte tydens kliniese toetse of na bemarking aangemeld (MedDRA-terme)

Infeksies en infestasies	
Dikwels:	Sepsis
Nie bekend nie:	Infeksie (aansteeklike komplikasies dodelik vir sommige pasiënte)
Versteurings van die bloed en limfstelsel	
Dikwels:	Beenmurgversaking, trombositopenie, leukopenie, bloedarmoede
Nie bekend nie:	Coombs-positiewe hemolitiese anemie
Goedaardige, kwaadaardige en ongespesifiseerde neoplasmas	
Minder dikwels:	Akute leukemie
Versteurings van die immuunstelsel	
Minder dikwels:	Anafilaktoïede reaksies (soos gesigsedeem, hyg, brongospasma, tagikardie, hipotensie)
Versteurings van endokrienstelsel	
Nie bekend nie:	Hoër vlakke amilase in die bloed, onvanpaste afskeiding van antidiuretiese hormoon
Versteurings in metabolisme en voeding	
Dikwels:	Hiponatremie
Minder dikwels:	Hipomagnesemie
Nie bekend nie:	Dehidrasie, hipokalemie, hipofosfatemie, hiperurisemie, hipokalsemie,tetanie
Versteurings van die senustelsel	
Minder dikwels:	Krampe, perifere neuropatie, leuko-enkefalopatie, sindroom van omkeerbare posterior leuko-enkefalopatie
Nie bekend nie:	Serebrovaskulêre ongeluk, hemorragiese beroerte, iskemiese beroerte, ageusie, serebrale arteritis, Lhermitte se teken, mielopatie, outonome neuropatie
Oogversteurings	
Nie bekend nie:	Dowwe visie, verkreë kleurblindheid, kortikale blindheid, optiese neuritis, papiledeem, retinale pigmentasie
Versteurings van die ore en labirint	
Minder dikwels:	Ototoksisiteit
Nie bekend nie:	Tinnitus, doofheid
Hartversteurings	
Dikwels:	Aritmie, bradikardie, tagikardie
Minder dikwels:	Miokardiale infarksie, hartarres.
Nie bekend nie:	Hartversteurings
Vaskulêre versteurings	
Nie bekend nie:	Trombotiese mikroangiopatie (hemolitiese uremiese sindroom), Raynaud se verskynsel
Gastro-intestinale versteurings	
Minder dikwels:	Stomatitis
Nie bekend nie:	Braking, naarheid, anoreksie, hik, diarree
Hepatobilière versteurings	
Nie bekend nie:	Hoër vlakke lewerensieme en bilirubien in die bloed
Respiratoriese, toragiese en mediastinale versteurings	
Nie bekend nie:	Pulmonêre embolisme
Versteurings van die vel en subkutane weefsel	
Nie bekend nie:	Veluitslag, alopesie
Versteurings van die muskuloskeletale stelsel, bindweefsel en skeletbene	
Nie bekend nie:	Spierspasma
Versteurings van die niere en urienweg	
Nie bekend nie:	Akute nierversaking, nierversaking (waaronder hoër BUS en kreatinien, urienuur in die serum en/of 'n afname in kreatinienopruiming), nierbuisversteuring
Versteurings in die voortplantingstelsel en borste	
Minder dikwels:	Abnormale spermatogenese
Algemene versteurings en effekte by die plek van toediening	
Dikwels:	Pireksie
Nie bekend nie:	Astenie, ongesteldheid, ekstravasasie by die inspuitplek (met gevolglike plaaslike sagteweefstoksisiteit, waaronder weefselsellulitis, fibrose en nekrose, pyn, edeem en eriteem)

Effek op vermoë om 'n voertuig te bestuur en masjiene te gebruik:
Geen studies van die effek op die vermoë om 'n voertuig te bestuur of masjiene te gebruik is gedoen nie. Nogtans kan die profiel van ongewenste effekte (soos nefrotoksisiteit) die vermoë om voertuie te bestuur en masjinerie te hanteer, beïnvloed.

Bekende simptome van oordosering en besonderhede vir die behandeling daarvan:
Wees versigtig om 'n onbedoelde oordosis te voorkom.
'n Akute oordosis sisplatien kan lei tot nierversaking, lewerversaking, doofheid, okulêre toksisiteit (waaronder loslating van die retina), beduidende beenmurgonderdrukking, onbehandelbare naarheid en braking en/of neuritis. 'n Oordosis kan dodelik wees.
Daar is geen spesifieke teenmiddel in geval van oordosering met sisplatien nie. Vanweë die sterk en vinnige binding van sisplatien aan proteïene het hemodialise selfs as dit 4 uur na die oordosis begin, min uitwerking op die uitskakeling van sisplatien uit die liggaam.
Behandeling is simptomaties en ondersteunend.

Identifikasie:
Cisplatin 10 mg/20 ml Oethmaan oplossing vir infusie:
Helder, kleurlose tot liggeel oplossing prakties sonder sigbare deeltjies.
Cisplatin 50 mg/100 ml Oethmaan oplossing vir infusie:
Helder, kleurlose tot liggeel oplossing prakties sonder sigbare deeltjies.

Aanbieding:
Cisplatin 10 mg/20 ml Oethmaan oplossing vir infusie:
Bruin glasflessies (20 ml) verseël met 'n chloorbutielrubberprop. Kartonne bevat óf 1 óf 10 glasflessies.
Cisplatin 50 mg/100 ml Oethmaan oplossing vir infusie:
Bruin glasflessies (100 ml) verseël met 'n chloorbutielrubberprop. Kartonne bevat óf 1 óf 10 glasflessies.

Bewaringsinstruksies:
Bêre onder 25 °C.
Moenie verkoel nie.
Beskerm teen lig. Gooi ongebruikte gedeelte weg.
HOU BUITE DIE BEREIK VAN KINDERS.

Registrasienommers:
Cisplatin 10 mg/20 ml Oethmaan oplossing vir infusie: 37/25/0523
Cisplatin 50 mg/50 ml Oethmaan oplossing vir infusie: 37/25/0524

Naam en besigheidsadres van die houer van die registrasiesertifikaat:
Oethmaan Biosims (Edms) Bpk.
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