European Directorate for the Quality of Medicines & HealthCare

COUNCIL OF EUROPE CONSEIL DE L'EUROPE

Certification of Substances Division

Certificate of suitability No. R1-CEP 1999-127-Rev 03

Name of the substance:
CISPLATIN

Name of holder:
OFICHEM BV
Heembadweg 5
The Netherlands-9561 CZ Ter Apel

Site(s) of production:
OFICHEM BV
Heembadweg 5
The Netherlands-9561 CZ Ter Apel

THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE
R1-CEP 1999-127-REV 02

After examination of the information provided on the manufacturing method and subsequent processes (including purification) for this substance on the site(s) of production mentioned above, we certify that the quality of the substance is suitably controlled by the current version of the monograph **CISPLATIN** no. 599 of the European Pharmacopoeia, current edition including supplements, only if it is supplemented by the test(s) mentioned below, based on the analytical procedure(s) given in annex.

— Test for residual solvents by gas chromatography (Annex 1)
Methanol not more than 3000 ppm

The test for silver described in the monograph is not necessary since this compound is not used in the synthesis.

The holder of the certificate has declared the absence of use of material of human or animal origin in the manufacture of the substance.

The submitted dossier must be updated after any significant change that may alter the quality, safety or efficacy of the substance.

Manufacture of the substance shall take place in accordance with the Good Manufacturing Practice and in accordance with the dossier submitted.

Address: 7, allée Kastner, CS 30026 - F - 67081 Strasbourg (France)
Telephone: 33 (0) 3 88 41 30 30 - Fax: 33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
Internet : http://www.edqm.eu

29 Failure to comply with these provisions will render this certificate void.

30 This certificate is renewed from **12 December 2005** according to the provisions of
31 Resolution AP-CSP (93) 5 as amended, and of Directive 2001/83/EC and Directive
32 2001/82/EC and any subsequent amendment, and the related guidelines.

33 This certificate has one annex of 2 pages.
34 This certificate has:
35 lines.

On behalf of the
Director of EDQM

Strasbourg, 9 March 2010

DECLARATION OF ACCESS *(to be filled in by the certificate holder under their own responsibility)*

Ofichem BV, as holder of the certificate of suitability

R1-CEP 1999-127-Rev 03 for CISPLATIN

hereby authorises .....
(name of the pharmaceutical company)

to use the above-mentioned certificate of suitability in support of their application(s) for the following Marketing Authorisation(s): *(name of product(s) and marketing number(s), if known)*

The holder also certifies that no significant changes to the operations as described in the CEP dossier have been made since the granting of this version of the certificate.

Date and Signature *(of the CEP holder)*:

Address: 7, allée Kastner, CS 30026 - F - 67081 Strasbourg (France)
Telephone: 33 (0) 3 88 41 30 30 - Fax: 33 (0) 3 88 41 27 71 - e-mail: cep@edqm.eu
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1. Assay of methanol

Class 2, 3000ppm

Chromatographic system (Ph Eur System A)

- stationairy phase: 30 m capillary column, i.d. 0.32 mm coated with cross-linked 6% polycyanopropylphenylsiloxane and 94% polydimethylsiloxane
- carrier gas: nitrogen with a velocity of 35 cm/s (undelayed ±85 s) (=10 lb/in^2).
- flame ionisation detector
- temperatures:
  column at 40°C, injection port 140 °C, detector 250 °C.
- sensitivity: RANGE = 1; ATTN = 1
- injection volume: 0,5 ml of the gaseous phase above the liquid in de head-space vial
- runtime = 3 min.

Sample solution:
Weigh accurately 200.0 mg of the substance to be examined and add 5.0 ml 1,3-dimethyl-2-imidazolidinone (DMI) and add 1 ml of the blank solution. Shake to dissolve and suspend the cisplatin.
Close the head-space vial with a crimp cap and heat for one hour at 80°C.
Inject 0,5 ml of the gaseous phase above the liquid in de head-space vial.

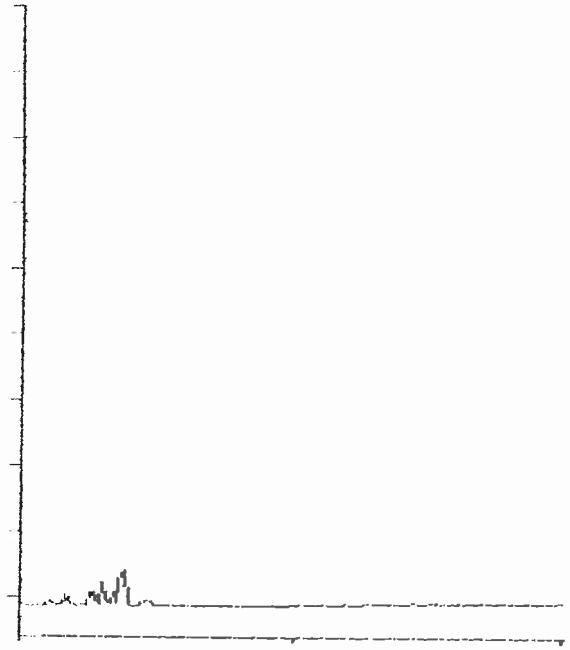
Stock and reference solutions:
Blank solution: Dissolve 10.0 ml Dimethylsulphoxide in water and dilute with water to 100.0 ml

Procedure: Introduce the reference solution and solvent and blank solution as mentioned below in a head-space vial. Close it with a crimp cap and heat for one hour at 80°C.
Inject 0,5 ml of the gaseous phase above the liquid in de head-space vial.

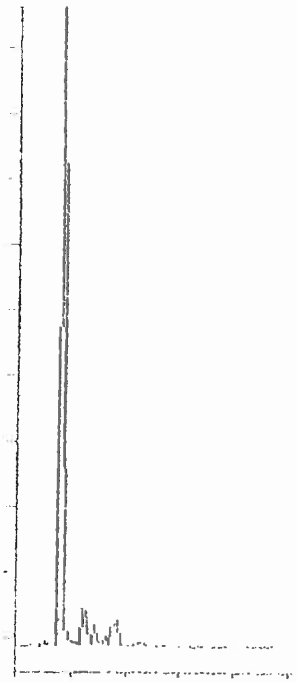
6000 ppm: Dilute 300 mg Methanol to 50.0 ml with water (stock solution).
600 ppm: Dilute 5.0 ml of stock solution to 50.0 ml with water (reference solution).

Concentration	Reference solution	Solvent	Blank	
750 ppm	0.25 ml	4.75 ml	1.0 ml	
1500 ppm	0.50 ml	4.50 ml	1.0 ml	
2250 ppm	0.75 ml	4.25 ml	1.0 ml	
3000 ppm	1.00 ml	4.00 ml	1.0 ml	Limit concentration
3750 ppm	1.25 ml	3.75 ml	1.0 ml	
4500 ppm	1.50 ml	3.50 ml	1.0 ml	

2. Typical chromatograms



Blank
Detected peak: retention time 1.806 min



Reference methanol 300 ppm.
Retention time 0.798 min