European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

Certification of Substances Department

Certificate of suitability
No. R0-CEP 2020-114 - Rev 01

Name of the substance:
SODIUM NITROPRUSSIDE

Name of holder:
HAINAN POLY PHARMACEUTICAL COMPANY LIMITED
Guilinyang Economic Development Area
Meilan District
China-571 127 Haikou, Hainan Province

Site(s) of production:
SEE ANNEX 1

THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE
R0-CEP 2020-114 - REV 00

After examination of the information provided on the manufacturing method and subsequent processes (including purification) for this substance on the site(s) of production listed in annex, we certify that the quality of the substance is suitably controlled by the current version of the monograph **SODIUM NITROPRUSSIDE** no. 565 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 2)
Ethanol not more than 5000 ppm

In the last steps of the synthesis water is used as solvent.

A risk management summary for elemental impurities has been provided. (Annex 3)

The re-test period of the substance is 36 months if stored in two triple laminated bags (polyethylene terephthalate/aluminium/polyethylene), placed in a fibre box.

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.

Address: 7 Allée Kastner, CS 30026
F-67081 Strasbourg (France)
Tel: +33 (0) 3 88 41 30 30 – e-mail: cep@edqm.eu
Internet: http://www.edqm.eu

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

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

This certificate is granted within the framework of the procedure established by the European Pharmacopoeia Commission [Resolution AP-CSP (07) 1] for a period of five years starting from **12 April 2021**. Moreover, it is granted according to the provisions of Directive 2001/83/EC and Directive 2001/82/EC and any subsequent amendment, and the related guidelines.

This certificate has three annexes of 1 page each.
This certificate has:
lines.

On behalf of the
Director of EDQM

Strasbourg, 14 March 2022

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

HAINAN POLY PHARMACEUTICAL COMPANY LIMITED, as holder of the certificate of suitability

R0-CEP 2020-114 - Rev 01 for Sodium nitroprusside

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*):

European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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Annex 1: Site(s) of production for R0-CEP 2020-114 - Rev 01

Production of Sodium nitroprusside:

HAINAN POLY PHARMACEUTICAL COMPANY LIMITED
Guilinyang Economic Development Area
Meilan District
China-571 127 Haikou, Hainan Province

Test Items	Analytical procedure
Residual solvents	*Ph. Eur. 2.2.28*: By GC-headspace *Chromatographic condition* Column: Capillary column, 30 m × 0.320 mm, 1.80 μm Stationary phase: 6% cyanopropyl phenyl- 94% dimethyl polysiloxane Oven temperature: 40 °C for 8 min, heat to 90 °C with a speed of 10 °C/min, maintain for 2 min, then heat to 210 °C with a speed of 30 °C/min, maintain for 5 min. Injector temperature: 250 °C Detector temperature: 250 °C Split ratio: 10:1 Carrier gas: Nitrogen, flow rate: 1 mL/min Burn gas: hydrogen, flow rate: 30 mL/min Auxiliary gas: compressed air, 400 mL/min *Headspace condition that may be used:* Headspace equilibration temperature: 90 °C Loop temperature: 100 °C Transmission line temperature: 110 °C Headspace equilibration time: 30 min *Test solution*: accurately weigh 0.2 g of sample to be examined to a 20-mL of headspace vial, accurately add 2.0 mL of DMF to ultrasound dissolve, shake well. *Reference solution*: accurately weigh an appropriate amount of ethanol, add DMF dissolve and dilute to obtain a solution contains 0.5 mg of ethanol per 1 mL. Accurately transfer 2.0 ml of this solution to a 20-mL of headspace vial. *Procedure* Separately inject equal volumes of the *Reference solution* and *Test solution*, record the chromatograms. In the chromatograph obtained from *Reference solution*, resolution between deferent solvents peaks should be not less 1.5, RSD of peak area for six replicate injections should be not more than 15.0%. The content of ethanol should not more than 5000 ppm calculated by external standard method and the formula is shown as below. $$\text{Ethanol (\%)} = (As \times Cr) / (Ar \times Cs) \times 100\%$$ In which, As is the peak area of ethanol in chromatogram of the test solution, Cs is the concentration of the test solution, mg/ml; Ar is the peak area of ethanol in chromatogram of the reference solution, Cr is the concentration of the reference solution, mg/ml.

Risk Assessment Results of Elemental Impurities in Sodium Nitroprusside

Intended route of administration / Use of the substance: Parenteral				
Element	**Class**	**Intentionally added?**	**Considered in risk management?**	**Conclusion**
Cd	1	No	Yes	Absent
Pb	1	No	Yes	Absent
As	1	No	Yes	Absent
Hg	1	No	Yes	Absent
Co	2A	No	Yes	Absent
V	2A	No	Yes	Absent
Ni	2A	No	Yes	Absent
Tl	2B	No	No	N/A
Au	2B	No	No	N/A
Pd	2B	No	No	N/A
Ir	2B	No	No	N/A
Os	2B	No	No	N/A
Rh	2B	No	No	N/A
Ru	2B	No	No	N/A
Se	2B	No	No	N/A
Ag	2B	No	No	N/A
Pt	2B	No	No	N/A
Li	3	No	Yes	Absent
Sb	3	No	Yes	Absent
Ba	3	No	No	N/A
Mo	3	No	Yes	Absent
Cu	3	No	Yes	Absent
Sn	3	No	No	N/A
Cr	3	No	Yes	Absent

**Absent: less than 30% ICH Q3D Option 1 limit.*