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 2013-267-Rev 02

Name of the substance:
IOPAMIDOL

Name of holder:
ZHEJIANG STARRY PHARMACEUTICAL CO., LTD.
No. 1 Starry Road of Xianju Modern Industrial Centralization Zone
China-317 300 Xianju, Zhejiang Province

Site(s) of production:
SEE ANNEX 1

THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE
R0-CEP 2013-267-REV 01

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 **IOPAMIDOL** no. 1115 of the European Pharmacopoeia, current edition including supplements.

Any unspecified impurity detected by the test for related substances of the monograph is limited to not more than 0.05%.

In the last steps of the synthesis ethanol is used as solvent. Its residual content is limited by the test for loss on drying described in the monograph with a limit of not more than 0.5%.

A risk management summary for elemental impurities has been provided. (Annex 2)

The substance is packed in a polyethylene bag in an aluminium foil bag placed in a plastic drum.

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)
Tel: +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

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 **18 November 2014**. 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 two annexes, the first of 1 page and the second of 3 pages.
This certificate has:
lines.

On behalf of the
Director of EDQM

Strasbourg, 20 September 2018

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

ZHEJIANG STARRY PHARMACEUTICAL CO., LTD., as holder of the certificate of suitability

R0-CEP 2013-267-Rev 02 for Iopamidol

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*):

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F-67081 Strasbourg (France)
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Annex 1: Site(s) of production for R0-CEP 2013-267-Rev 02

Production of intermediate(s):
JIANGXI STARRY PHARMACEUTICAL CO., LTD.
North of the Wuyi Road
Salt Chemical Base
China-331 200 Zhangshu, Jiangxi Province

Production of Iopamidol:
ZHEJIANG STARRY PHARMACEUTICAL CO., LTD.
No. 1 Starry Road of Xianju Modern Industrial Centralization Zone
China-317 300 Xianju, Zhejiang Province

IOPAMIDOL
Impurities

Risk Management Summary (RMS) for Iopamidol

Element	Class	Intentionally added (if used in the process)?	Considered in risk management?	Permitted parenteral concentrations for option 1, µg/g	Control threshold[1], µg/g	Data from three lots of representative production scale Iopamdiol µg/g	Conclusion	Action
Cd	1	No	Yes	0.2	0.06	<0.0065(LOD) <0.0065(LOD) <0.0065(LOD)	Absent[2]	no further controls required
Pb	1	No	Yes	0.5	0.15	<0.10(LOD) <0.10(LOD) <0.10(LOD)	Absent	no further controls required
As	1	No	Yes	1.5	0.45	<0.24(LOD) <0.24(LOD) <0.24(LOD)	Absent	no further controls required
Hg	1	No	Yes	0.3	0.09	<0.080(LOD) <0.080(LOD) <0.080(LOD)	Absent	no further controls required
Co	2A	No	Yes	0.5	0.15	<0.024(LOD) <0.024(LOD) <0.024(LOD)	Absent	no further controls required
V	2A	No	Yes	1	0.3	0.012 0.012 0.012	Absent	no further controls required
Ni	2A	No	Yes	2	0.6	<0.044(LOD) <0.044(LOD) <0.044(LOD)	Absent	no further controls required
Tl	2B	No	No	0.8	0.24	Not applicable[4]	Not applicable	no further controls

IOPAMIDOL
Impurities

								required
Au	2B	No	No	10	3	Not applicable	Not applicable	no further controls required
Pd	2B	Yes[3]	Yes	1	0.3	<0.05(LOD) <0.05(LOD) <0.05(LOD)	Absent	no further controls required
Ir	2B	No	No	1	0.3	Not applicable	Not applicable	no further controls required
Os	2B	No	No	1	0.3	Not applicable	Not applicable	no further controls required
Rh	2B	No	No	1	0.3	Not applicable	Not applicable	no further controls required
Ru	2B	No	No	1	0.3	Not applicable	Not applicable	no further controls required
Se	2B	No	No	8	2.4	Not applicable	Not applicable	no further controls required
Ag	2B	No	No	1	0.3	Not applicable	Not applicable	no further controls required
Pt	2B	No	No	1	0.3	Not applicable	Not applicable	no further controls required

IOPAMIDOL
Impurities

Li	3	No	Yes	25	7.5	0.18 0.14 0.15	Absent	no further controls required
Sb	3	No	Yes	9	2.7	<0.83(LOD) <0.83(LOD) <0.83(LOD)	Absent	no further controls required
Ba	3	No	No	70	21	Not applicable	Not applicable	no further controls required
Mo	3	No	No	150	45	Not applicable	Not applicable	no further controls required
Cu	3	No	Yes	30	9	<0.13(LOD) <0.13(LOD) <0.13(LOD)	Absent	no further controls required
Sn	3	No	No	60	18	Not applicable	Not applicable	no further controls required
Cr	3	No	No	110	33	Not applicable	Not applicable	no further controls required

1: Control threshold is about of 30% of ICH Q3D option 1 limit;
2: Absent means less than 30% of ICH Q3D option 1 limit;
3: Pd catalyst is used in step 1 of the synthesis of Iopamidol.
4: Not applicable means that the elemental impurity is excluded from the risk assessment for Iopamidol according to ICH Q3D guideline.