

Certification of Substances Division

Certificate of suitability
No. R0-CEP 2002-104-Rev 02

1 *Name of the substance:*

2 **ISOSORBIDE MONONITRATE, DILUTED**

3 *Name of holder:*

4 **J P LABORATORIES PRIVATE LTD**
5 Midc, Block A-76
6 Chemical Zone Kurkumbh
7 India-413801 Daund

8 *Site(s) of production:*

9 **J P LABORATORIES PRIVATE LTD**
10 Midc, Block A-76
11 Chemical Zone Kurkumbh
12 India-413801 Daund

13 **THIS CERTIFICATE SUPERSEDES THE PREVIOUS CERTIFICATE**
14 **R0-CEP 2002-104-REV 01**

15 After examination of the information provided on the manufacturing method and
16 subsequent processes (including purification) for this substance on the site(s) of
17 production mentioned above, we certify that the quality of the substance is suitably
18 controlled by the current version of the monograph **ISOSORBIDE MONONITRATE,**
19 **DILUTED** no. 1118 of the European Pharmacopoeia, current edition including
20 supplements, only if it is supplemented by the test(s) mentioned below, based on the
21 analytical procedure(s) given in annex.

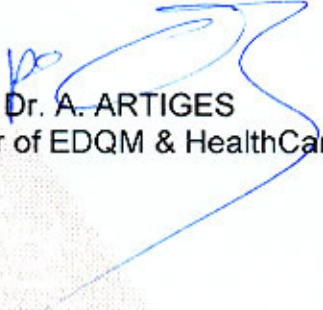
22 – Test for related substances by thin layer chromatography (Annex 1)
23 Any other detectable impurity * not more than 0.1%
24 * Other than those already mentioned in the monograph

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

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

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

- 30 Manufacture of the substance shall take place in accordance with the Good
31 Manufacturing Practice and in accordance with the dossier submitted.
- 32 Failure to comply with these provisions will render this certificate void.
- 33 This certificate is granted within the framework of the procedure established by the
34 European Pharmacopoeia Commission [Resolution AP-CSP (93) 5 as amended] for a
35 period of five years starting from **20 May 2003**. Moreover, it is granted according to the
36 provisions of Directive 2001/83/EC and Directive 2001/82/EC and any subsequent
37 amendment, and the related guidelines.
- 38 This certificate has one annex of 1 page.
39 This certificate has:
40 lines.


Dr. A. ARTIGES
Director of EDQM & HealthCare

Strasbourg, 30 May 2007

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

J P Laboratories Private Ltd, as holder of the certificate of suitability
R0-CEP 2002-104-Rev 02 for ISOSORBIDE MONONITRATE, DILUTED

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)*:

1.6.5.2 Limit test for isosorbide in Isosorbide mononitrate, diluted by TLC

Introduction:

The TLC method for the quantification of isosorbide in isosorbide mononitrate, diluted is an in-house method developed by J. P. Fine Chemicals. The test is a limit test with the limit for isosorbide set at Not More Than 0.1%.

Apparatus

A chromatographic tank with a flat bottom made of inert, transparent material and of a size suitable for the plates or sheets used and provided with a tightly fitting lid.

Micro pipettes, micro syringes, calibrated disposable capillaries or other application devices suitable for the proper application of the solutions.

Plates – use ready made plates, E Merck TLC plates (Silica Gel GF 254).

Mobile Phase – chloroform 90 ml, methanol 10 ml.

Developing Spray – ethanol 90 ml + sulphuric acid 10 ml.

Standard Sample

Dissolve 1 mg of isosorbide in 2 ml acetone.

Test Solution

Dissolve/disperse 1 g of ISMN, diluted from the batch to be tested in 2 ml of acetone. Filter off the lactose or mannitol with which the ISMN is diluted and use the filtrate for the test solution.

Application volume on TLC plate: 20 microlitres.

Retention Factor (R_f): Isosorbide: 0.07 to 0.18.

Procedure

Apply 20 μ l from the test and the standard solution to the base line of the plate and dry the plate under current of warm air. Develop over a path of 10 cm using the mobile phase. Dry the plate in a current of warm air and spray with ethanol and sulphuric acid (90:10), dry and develop spot at 100°C under IR for 30 minutes. The isosorbide spot in the chromatograph obtained in the test sample should not be more intense than that obtained with the standard sample solution.

EUROPEAN PHARMACOPOEIA
CERTIFICATION OF SUITABILITY

CEP FILE No. R0-CEP *Pool-104* - Rev 0 *2*
APPENDIX No. *1*
NUMBER OF PAGES *111*