Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

General Monograph on - Liquids for Cutaneous Application

Published on: 25.11.2024 **Last date for comments:** 09.01.2025

This draft proposal contains general chapter text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to revisions before publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	**Details**
Document version	1.0
Monograph proposed for inclusion	IP 2026
Tentative effective date of monograph	July, 2026
First draft published on IPC website for public comments	25.11.2024
Draft revision published on IPC website for public comments	
Further follow-up action as required.	

Liquids for Cutaneous Application

Liquid preparations for cutaneous application are intended for application to the skin to deliver active substances for local or systemic effect.

They are solutions, emulsions or suspensions of a variety of viscosities. They contain one or more active substances in a suitable vehicle. They may contain suitable excipients such as preservatives, antioxidants, stabilisers, emulsifiers and thickeners.

They are usually supplied in multidose containers.

Emulsions may show evidence of phase separation but are readily redispersed on shaking. Suspensions may show a sediment that is readily dispersed on shaking to give a suspension that is sufficiently stable to enable a homogeneous preparation to be delivered.

Where applicable, containers for liquid preparations for cutaneous application comply with the requirements for Materials used for the manufacture of containers *(IP General Chapter 6.2 Containers)*. When liquid preparations for cutaneous application are supplied in pressurised containers, the containers comply with the requirements of the Pressurised Metered-dose Preparations under monograph Inhalation Preparations.

Preparations specifically intended for use on severely injured skin are sterile.
Several categories of liquid preparations for cutaneous application may be distinguished;
-shampoos;
-cutaneous foams.

Production

During the development of liquid preparations for cutaneous application whose formulation contains a preservative, the need for and the efficacy of the chosen preservative shall be demonstrated to the satisfaction of the competent authority. A suitable test method together with criteria for judging the preservative properties of the formulation are provided in *General chapter 2.2.2. Effectiveness of Antimicrobial Preservatives.*

During the development of liquid preparations for cutaneous application supplied in single-dose containers, it must be demonstrated that the nominal content can be withdrawn from the container.

In the manufacture, packaging, storage and distribution of liquid preparations for cutaneous application, suitable measures are taken to ensure their microbial quality; recommendations on this aspect are provided in *General chapter 2.2.9 Microbial Contamination in Nonsterile Products*.

Sterile liquid preparations for cutaneous application are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this aspect are provided in *General chapter 5.3. Sterilisation.*

In the manufacture of liquid preparations for cutaneous application containing dispersed particles, measures are taken to ensure a suitable and controlled particle size with regard to the intended use.

In the manufacture of metered-dose liquid preparations for cutaneous application intended for systemic effect, uniformity of delivered dose must be ensured within a container (intra-container) and between containers (inter-container), unless otherwise justified and authorised.

For intra-container testing of the uniformity of delivered dose, a test is given in the Tests section.
For inter-container testing of the uniformity of delivered dose, see below.

Uniformity of delivered dose, inter-container testing

Prepare and use the container as directed in the instructions to the patient. An example of a suitable procedure is to take 10 containers and collect a single dose from each container, collecting the dose at the beginning (from 3 containers), middle (from 4 containers) and end (from 3 containers) of the number of doses stated on the label. Other inter-container testing procedures are possible, where justified.

Tests

Prepare and use the container as directed in the instructions to the patient.

Sterility(2.2.11). Where the label indicates that the preparation is sterile, it complies with the test for sterility

Uniformity of delivered dose, intra-container testing

Metered-dose liquid preparations for cutaneous application intended for systemic effect comply with the following test. If justified and authorised, for preparations that are solutions, the test for uniformity of delivered dose can be replaced by the test for uniformity of delivered mass.

Use an apparatus capable of quantitatively retaining the dose leaving the metered-dose container.

Take 1 container and discharge the contents into the apparatus until the number of deliveries that constitute the minimum recommended dose have been sampled. Quantitatively collect the contents of the apparatus and determine the amount of active substance. Repeat the procedure for a further 2 doses.

Discharge the container to waste until (n/2) + 1 deliveries remain, where n is the number of deliveries stated on the label. Collect 4 doses using the procedure described above.

Discharge the container to waste until 3 doses remain. Collect these 3 doses using the procedure described above.

For preparations containing more than 1 active substance, carry out the test for uniformity of delivered dose for each active substance.

For preparations supplied in pressurised metered-dose containers, prevent excessive cooling by waiting not less than 5 s between each actuation.
Unless otherwise justified and authorised, the preparation complies with the test if 9 out of 10 results lie between 75 per cent and 125 per cent of the mean value and all lie between 65 per cent and 135 per cent. If 2 or 3 values lie outside the limits of 75 per cent to 125 per cent but within the limits of 65 per cent to 135 per cent, repeat the test for 2 more containers. Not more than 3 of the 30 values lie outside the limits of 75 per cent to 125 per cent and no value lies outside the limits of 65 per cent to 135 per cent. Unless otherwise authorised, the mean value must be between 85 per cent and 115 per cent of the label claim for delivered dose.

Uniformity of delivered weight

Metered-dose liquid preparations for cutaneous application that are solutions comply with the following test.
Take 1 container and weigh. Discharge the contents to waste until the number of deliveries that constitute the minimum recommended dose has been attained. Weigh the container again. Calculate the difference between the 2 masses. Repeat the procedure for a further 2 doses.

Discharge the container to waste until (n/2) + 1 deliveries remain, where n is the number of deliveries stated on the label. Determine the mass of 4 doses using the procedure described above.

Discharge the container to waste until 3 doses remain. Determine the mass of these 3 doses using the procedure described above.

Unless otherwise justified and authorised, the preparation complies with the test if 9 out of 10 results lie between 75 per cent and 125 per cent of the mean value and all lie between 65 per cent and 135 per cent. If 2 or 3 values lie outside the limits of 75 per cent to 125 per cent but within the limits of 65 per cent to 135 per cent, repeat the test for 2 more containers. Not more than 3 of the 30 values lie outside the limits of 75 per cent to 125 per cent and no value

lies outside the limits of 65 per cent to 135 per cent. Unless otherwise authorised, the mean value must be between 85 per cent and 115 per cent of the target delivered mass.

Number of deliveries per container

Metered-dose liquid preparations for cutaneous application comply with the following test.

Take 1 container and discharge the contents to waste until empty. Record the deliveries discharged. The total number of deliveries so discharged from the container is not less than the number stated on the label.

Uniformity of dosage units (2.5.4). Unless otherwise prescribed or justified and authorised, liquid preparations for cutaneous application that are intended for systemic effect and supplied in single-dose containers representing 1 dose of medicinal product comply with the test. Where justified and authorised, the test may be replaced with the test for uniformity of mass or uniformity of content shown below. Herbal drugs and herbal drug preparations present in the dosage form are not subject to the provisions of this paragraph.

Uniformity of content (2.5.4). Liquid preparations for cutaneous application that are intended for systemic effect and supplied in single-dose containers representing 1 dose of medicinal product comply with the test. Carry out the assay on the amount of well-mixed material that is removed from an individual container under conditions of normal use. Express the results as delivered dose. They comply with the requirements under Test B.

Uniformity of weight (2.5.3). Liquid preparations for cutaneous application that are intended for systemic effect and supplied in single-dose containers representing 1 dose of medicinal product comply with the following test.

Weigh individually the amount that is removed from 10 individual containers in conditions of normal use, and determine the average mass. Not more than 2 of the individual masses deviate by more than 10 per cent from the average mass, and none deviate by more than 20 per cent.

Storage. If the preparation is sterile, store in a sterile, airtight, tamper-evident container.

Labelling. The label states (1) the name of any added preservative; (2) where applicable, that the preparation is sterile; (3) for multidose containers: (4) where applicable, the number of deliveries per container; (5) where applicable, the delivered dose.

Shampoos

Shampoos are liquid or, occasionally, semi-solid preparations intended for application to the scalp and subsequent washing away with water. When rubbed with water they usually form a foam.
They are emulsions, suspensions or solutions. Shampoos normally contain surface active agents.

Cutaneous foams

Cutaneous foams are liquid preparations intended for application to the skin, containing active substance(s), usually supplied in pressurised containers equipped with an applicator suitable for delivery of a foam.

They are usually supplied in multidose containers.

Cutaneous foams comply with the requirements of the monograph *Medicated foams.*

Medicated Foams

Medicated Foams comply with the requirements of the Indian Pharmacopoeia. These requirements are reproduced below.

Medicated foams are preparations usually intended for application to the skin or mucous membranes. They are formed, typically at the time of administration, by dispersion of a large volume of gas in a liquid. This liquid contains one or more active substances and generally a surfactant to help create the foam, together with various other excipients.

The preparation is usually supplied in a pressurised multidose container equipped with a device consisting of a valve and a push button suitable for the delivery of the foam.

Medicated foams intended for application to severely injured skin and to large open wounds are sterile.

Production

Sterile medicated foams are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this aspect are provided in *General chapter 5.1.1. Methods of preparation of sterile products.*

Tests

Relative foam density

Maintain the pressurised container at about 25 °C for at least 24 h before the test. Taking care not to warm the container, fit a rigid tube 70-100 mm long and about 1 mm in internal diameter onto the push button. Shake the container to homogenise the liquid phase of the contents and discharge 5-10 mL of foam to waste. Tare a flat-bottomed dish with a capacity of about 60 mL and a height of about 35 mm. Place the end of the rigid tube at the base of the wall of the dish, press the push button and fill the dish uniformly, using a circular motion. After the foam has completely expanded, level it off by removing the excess with a slide. Weigh. Determine the mass of the same volume of water R by filling the same dish with water R.
The relative foam density is calculated from the ratio:

$$m/e$$

m	=	mass of the foam, in grams;
e	=	mass of the same volume of water R, in grams.

Carry out 3 measurements. None of the individual values deviates by more than 20 per cent from the mean value.

Duration of expansion

The apparatus (Figure 19) consists of a 50 mL burette, 15 mm in internal diameter, with 0.1 mL graduations and fitted with a 4 mm single bore stopcock. The graduation corresponding to 30 mL is at least 210 mm from the axis of the stopcock. The lower part of the burette is connected to the pressurised container by a plastic tube 4 mm in internal diameter and not more than 50 mm in length.

Maintain the pressurised container at about 25 °C for at least 24 h before the test. Shake the container, taking care not to warm it, to homogenize the liquid phase of the contents and discharge 5-10 mL of the foam to waste. Connect the push button to the outlet of the burette. Press the button and introduce about 30 mL of foam in a single delivery. Close the stopcock, at the same time start the chronometer, and read the volume of foam in the burette. Every 10 s read the growing volume until the maximum volume is reached.

Carry out 3 measurements. The time required to obtain the maximum volume is not more than 5 min in all cases.

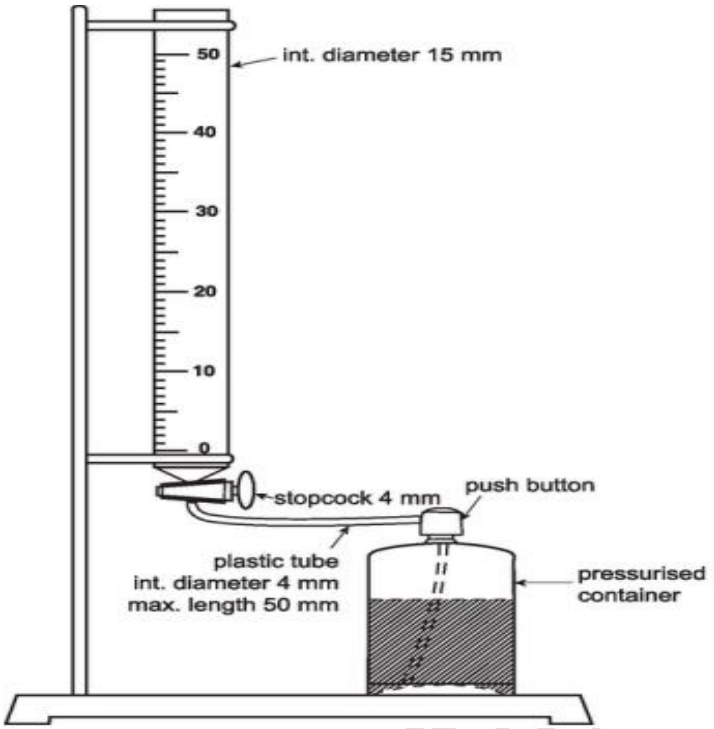

Figure 19. – *Apparatus for the determination of the duration of expansion*