

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Chlorhexidine Acetate

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This draft proposal contains monograph 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. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. 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.

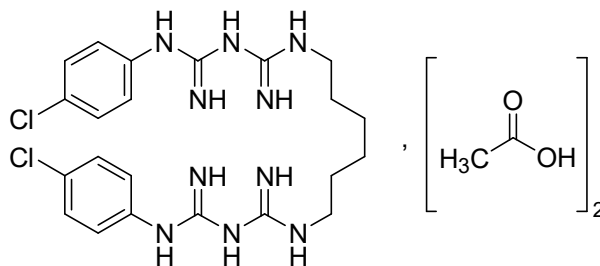
Document History and Schedule for the Adoption Process

Description	Details
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Monograph revisions proposed for inclusion in	IP 2026
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Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

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Change to: **Chlorhexidine Acetate**

Chlorhexidine Diacetate



$C_{22}H_{30}Cl_2N_{10}, 2C_2H_4O_2$

Mol. Wt. 625.6

Chlorhexidine Acetate is 1,1'-(hexane-1,6-diyl)bis[5-(4-chlorophenyl)biguanide] diacetate.

Chlorhexidine Acetate contains not less than 98.0 per cent and not more than 101.0 per cent of chlorhexidine diacetate, $C_{22}H_{30}Cl_2N_{10}, 2C_2H_4O_2$, calculated on the dried basis.

Category. Antiseptic.

Description. A white or almost white, microcrystalline powder.

Identification

A. Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *chlorhexidine acetate IPRS* or with the reference spectrum of chlorhexidine acetate.

B. In the Assay, the principal peak in the chromatogram obtained with test solution (b) corresponds to the peak in the chromatogram obtained with reference solution (b).

C. It gives reaction (A) of acetates (2.3.1).

Tests

***p*-Chloroaniline.** Not more than 500 PPM.

Determine by liquid chromatography (2.4.14).

Test solution (a). Dissolve 0.2 g of the substance under examination in mobile phase A and dilute to 100.0 ml with mobile phase A.

Test solution (b). Dilute 5.0 ml of test solution (a) to 200.0 ml with mobile phase A.

Reference solution (a). A 0.0001 per cent w/v solution of *p*-chloroaniline IPRS in mobile phase A.

Reference solution (b). A 0.005 per cent w/v solution of *chlorhexidine acetate IPRS* in mobile phase A.

Reference solution (c). A solution containing 0.005 per cent w/v of *chlorhexidine acetate IPRS* and 0.0001 per cent w/v of *p*-chloroaniline IPRS in mobile phase A.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with base-deactivated octadecylsilane bonded to porous silica (5 μ m) (Such as Luna C18),
- column temperature: 40°,
- mobile phase: A. a mixture of 70 volumes of a buffer solution prepared by dissolving 13.8 g of *sodium dihydrogen orthophosphate* and 5 ml of *triethylamine* in 750 ml of *water*, adjusted to pH 3.0 with *orthophosphoric acid*, dilute to 1000 ml with *water*, and 30 volumes of *acetonitrile*,
B. *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 239 nm,
- injection volume: 50 μ l.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
9	100	0
10	45	55
15	45	55
16	100	0
21	100	0

The relative retention time with reference to chlorhexidine for *p*-chloroaniline is about 1.3.

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to chlorhexidine and *p*-chloroaniline is not less than 3.0 and the relative standard deviation for replicate injections is not more than 1.0 per cent, for chlorhexidine peak and not more than 5.0 per cent, for *p*-chloroaniline peak.

Inject reference solution (a) and test solution (a).

Calculate the content of *p*-chloroaniline.

Related substances. Determine by liquid chromatography (2.4.14).

NOTE – Store the solutions at a temperature not more than 12°.

Test solution. Dissolve 0.14 g of the substance under examination in mobile phase A and dilute to 100.0 ml with mobile phase A.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with mobile phase A.

Reference solution (b). A 0.5 per cent w/v solution of chlorhexidine system suitability mixture IPRS in mobile phase A.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with base-deactivated octadecylsilane bonded to porous silica (5 µm) (Such as Luna C18(2)),
- sample temperature: 12°,
- mobile phase: A. a mixture of 20 volumes of a 0.1 per cent v/v solution of trifluoroacetic acid in acetonitrile and 80 volumes of a 0.1 per cent v/v solution of trifluoroacetic acid in water,
B. a mixture of 90 volumes of a 0.1 per cent v/v solution of trifluoroacetic acid in acetonitrile and 10 volumes of a 0.1 per cent v/v solution of trifluoroacetic acid in water,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
2	100	0
32	80	20
37	80	20
47	70	30
54	70	30
55	100	0
60	100	0

Name	Relative retention time
Chlorhexidine guanidine ¹	0.35
Chlorhexidine nitrile ²	0.6
Chlorhexidine dimer ³	0.85
<i>o</i> -Chlorhexidine ^{4*} and specified unidentified impurity 2 ^{5*}	0.90, 0.91
Chlorhexidine	1.0
Oxochlorhexidine ⁶	1.4

*If present, *o*-chlorhexidine and specified unidentified impurity 2 may not be completely resolved by the method. These peaks are integrated together to determine conformance

¹1-[6-(Carbamimidoylamino)hexyl]-5-(4-chlorophenyl)biguanide,

²1-(4-Chlorophenyl)-5-[6-[(cyanocarbamidoyl)amino]hexyl]biguanide,

³1,5-Bis[5-(4-chlorophenyl)biguanidylhexyl]biguanide,

⁴1-(2-Chlorophenyl)-5-[6-({[(4-chloro phenyl)carbamimidoyl]carbamimidoyl}amino) hexyl]biguanide,

⁵1-(4-Chlorophenyl)-5-[6-({4-[(4-chlorophenyl)amino]-6-[(1*S*,2*R*,3*R*,4*R*)-1,2,3,4,5-pentahydroxypentyl]-1,3,5-triazin-2-yl}amino)hexyl]biguanide,

⁶*N*-(4-Chlorophenyl)-*N'*-{[6-({[(4-chlorophenyl)carbamimidoyl]carbamimidoyl}amino)hexyl]carbamimidoyl}urea.

Inject reference solution (b). The test is not valid unless the peak-to-valley ratio is not less than 2.0 between the peaks due to chlorhexidine urea and chlorhexidine guanidine.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to chlorhexidine guanidine, chlorhexidine nitrile and chlorhexidine dimer, each of, is not more than 0.15 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.15 per cent), the area of the peaks corresponding to *o*-chlorhexidine + specified unidentified impurity 2 and oxochlorhexidine, each of, is not more than 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent), the area of any other secondary peak is not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 0.7 times the area of the principal peak in the chromatogram with reference solution (a) (0.7 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Loss on drying (2.4.19). Not more than 3.5 per cent, determined on 1.0 g by drying in an oven at 105°.

Sulphated ash (2.3.18). Not more than 0.15 per cent.

Assay. Determine by liquid chromatography (2.4.14), as described under *p*-chloroaniline with the following modification.

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to chlorhexidine and *p*-chloroaniline is not less than 3.0 and the relative standard deviation for replicate injections is not more than 1.0 per cent, for chlorhexidine peak and not more than 5.0 per cent, for *p*-chloroaniline peak.

Inject reference solution (b) and test solution (b).

Calculate the content of C₂₂H₃₀Cl₂N₁₀,2C₂H₄O₂.

Insert at the end

Storage. Store protected from light and moisture, at a temperature not exceeding 30°.