Beclomethasone Dipropionate

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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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Draft revision published on IPC website for public comments	--
Further follow-up action as required.	

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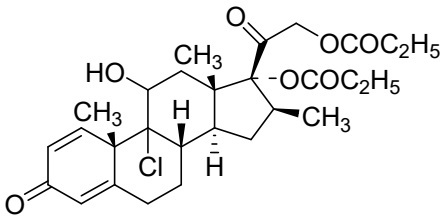
Change **to**: **Beclomethasone Dipropionate**



$C_{28}H_{37}ClO_7$ Mol. Wt. 521.0

$C_{28}H_{37}ClO_7 . H_2O$ Mol. Wt. 539.1

Beclomethasone Dipropionate is 9-chloro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropionate. Beclomethasone Dipropionate is anhydrous or monohydrate.

Beclomethasone Dipropionate contains not less than 96.0 per cent and not more than 103.0 per cent of $C_{28}H_{37}ClO_7$, calculated on the dried basis.

Category. Adrenocortical steroid.

Description. A white to creamy-white, crystalline powder.

Identification

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

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 (a).

Tests

Specific optical rotation (2.4.22). +88° to +94°, determined in a 1.0 per cent w/v solution in *dioxane.*

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 45 volumes of mobile phase A and 55 volumes of mobile phase B.

Test solution (a). Dissolve 50 mg of the substance under examination in 28 ml of mobile phase B and dilute to 50.0 ml with mobile phase A.

Test solution (b). Dilute 1.0 ml of test solution (a) to 50.0 ml with the solvent mixture.

Reference solution (a). Dissolve 10 mg of *beclomethasone dipropionate IPRS* in 2.8 ml of mobile phase A and dilute to 10.0 ml with mobile phase B. Dilute 1.0 ml of the solution to 50.0 with the solvent mixture.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 20.0 ml of the solvent mixture.

Reference solution (c). Dissolve 5 mg of *beclomethasone dipropionate for system suitability IPRS (containing impurity D)* in 3.0 ml of mobile phase B and dilute to 5.0 ml with mobile phase A.

Reference solution (d). Dissolve 5 mg of *beclomethasone dipropionate for peak identification IPRS (containing impurity A, B, C, L and M)* in 3.0 ml of mobile phase B and dilute to 5.0 ml with mobile phase A. Use 1.0 ml of the solution to dissolve the contents of a vial *of beclomethasone dipropionate impurities F and N IPRS.*

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with end-capped octadecylsilane bonded to porous silica (5 µm),
- column temperature: 50°,
- mobile phase: A. a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 2.35 with *orthophosphoric acid,*
  B. a mixture of 10 volumes of *tetrahydrofuran,* 46 volumes of *acetonitrile* and 50 volumes of *methanol,*
- a gradient programme using the conditions given below,

– flow rate: 1.4 ml per minute,
– spectrophotometer set at 254 nm,
– injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	40	60
4	40	60
12	45	55
59	45	55
60	40	60
65	40	60

Name	Relative retention time	Correction factor
Beclomethasone dipropionate impurity A[1]	0.3	---
Beclomethasone dipropionate impurity B[2]	0.6	---
Beclomethasone dipropionate (Retention time: about 25 minutes)	1.0	---
Beclomethasone dipropionate impurity D[3]	1.1	---
Beclomethasone dipropionate impurity M[4]	1.2	2.0
Beclomethasone dipropionate impurity L[5]	1.3	---
Beclomethasone dipropionate impurity C[6]	1.8	---
Beclomethasone dipropionate impurity N[7]	2.0	---
Beclomethasone dipropionate impurity F[8]	2.2	1.3

[1]9-chloro-11β,17-dihydroxy-16β-methyl-3,20-dioxopregna-1,4-dien-21-yl propanoate (beclomethasone 21-propionate),
[2]21-(acetyloxy)-9-chloro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-dien-17-yl propanoate (beclomethasone 21-acetate 17-propionate),
[3]9-bromo-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropanoate,
[4]9-chloro-11β-hydroxy-16β-methyl-3,20-dioxopregna-4,6-diene-17,21-diyl dipropanoate,
[5]9-chloro-11β-hydroxy-16β-methyl-3,20-dioxopregn-4-ene-17,21-diyl dipropanoate,
[6]9-chloro-11β-hydroxy-16β-methyl-3,20-dioxo-17-(propanoyloxy)-pregna-1,4-dien-21-yl butanoate (beclomethasone 21-butyrate 17-propionate),
[7]2-bromo-9-chloro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropanoate,
[8]6α-bromo-9-chloro-11β-hydroxy-16β-methyl-3,20-dioxopregna-1,4-diene-17,21-diyl dipropanoate.

Inject reference solution (c). The test is not valid unless the peak-to-valley ratio of H_p and H_v is not less than 1.5, where H_p = height above the baseline of the peak due to beclomethasone dipropionate impurity D and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to beclomethasone dipropionate.

Inject reference solution (d) to identify the peaks due to beclomethasone dipropionate impurity A, B, C, F, L, M and N.

Inject reference solution (b) and test solution (a). In the chromatogram obtained with test solution (a), the area of any peak corresponding to beclomethasone dipropionate impurity L is not more than 6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.6 per cent), the area of any peak corresponding to beclomethasone dipropionate impurity B, F and M, each of, is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent), the area of any peak corresponding to beclomethasone dipropionate impurity A, D and N, each of, is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent), the area of any peak corresponding to beclomethasone dipropionate impurity C is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.15 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 15 times the area of the principal peak in the chromatogram with reference solution (b) (1.5 per cent). Ignore any peak with an area less than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

Sulphated ash (2.3.18). Not more than 0.1 per cent.

Loss on drying (2.4.19). Not more than 0.5 per cent for anhydrous form; 2.8 per cent to 3.8 per cent for monohydrate form, determined on 1.0 g by drying in an oven at 105° for 3 hours.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances with the following modifications.

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

Calculate the content of $C_{28}H_{37}ClO_7$.

Storage. Store protected from light.