Carboprost Tromethamine

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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

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Further follow-up action as required.	

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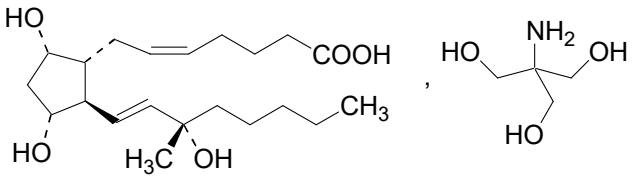
Change **to**: **Carboprost Tromethamine**



$C_{21}H_{36}O_5,C_4H_{11}NO_3$ Mol. Wt. 489.7

Carboprost Tromethamine is Prosta-5,13-dien-1-oic acid, 9,11,15-trihydroxy-15-methyl, (5Z, 9α,11α,13*E*,15*S*), compound with 2-amino-2-(hydroxymethyl)-1,3-propanediol (1:1).

Carboprost Tromethamine contains not less than 95.0 per cent and not more than 105.0 per cent of $C_{21}H_{36}O_5,C_4H_{11}NO_3$, calculated on the dried basis.

CAUTION- Great care should be taken to prevent inhaling particles of Carboprost Tromethamine and exposing the skin to it.

Category. Uterine stimulant; abortifacient.

Description. A white to off-white powder.

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

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

Tests
Specific optical rotation (2.4.22). + 18.0° to + 24.0°, determined in a 1.0 per cent w/v solution in *ethanol (95 per cent)*.

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 20 volumes of *acetonitrile*, 30 volumes of *methanol* and 50 volumes of *water*.

Test solution. Dissolve 25 mg of the substance under examination in the solvent mixture and dilute to 25.0 ml with the solvent mixture.

Reference solution (a). A 0.1 per cent w/v solution of *carboprost tromethamine IPRS* in the solvent mixture.

Reference solution (b). Dilute 5.0 ml of reference solution (a) to 20.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (c). A solution containing 0.1 per cent w/v of *carboprost tromethamine IPRS* and 0.01 per cent w/v of *15-epicarboprost IPRS* in the solvent mixture.

Reference solution (d). Dilute 1.0 ml of reference solution (b) to 25.0 ml with the solvent mixture.

Chromatographic system
- a stainless steel column 15 cm x 4.0 mm, packed with octadecylsilane bonded to porous silica (3 µm) (Such as Hypersil BDS C18),

- mobile phase: a mixture of 50 volumes of *0.02 M monobasic potassium phosphate*,30 volumes of *methanol* and 20 volumes of *acetonitrile*,
- flow rate: 0.8 ml per minute,
- spectrophotometer set at 200 nm,
- injection volume: 20 µl.

Name	Relative retention time
15-Epicarboprost[1]	0.9
trans-Carboprost[2]	0.94
Carboprost	1.0

[1](*Z*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-[(*E*)-(3*R*)-3-hydroxy-3-methyloct-1-enyl]cyclopentyl]-5-heptenoic acid,
[2](*E*)-7-[(1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-[(*E*)-(3*S*)-3-hydroxy-3-methyloct-1-enyl]cyclopentyl]-5-heptenoic acid.

Inject reference solution (b), (c) and (d). The test is not valid unless the resolution between the peaks due to 15-epicarboprost and trans-carboprost is not less than 1.0 and between the peaks due to trans-carboprost and carboprost is not less than 1.2 in the chromatogram obtained with reference solution (c), the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (b) and the signal-to-noise ratio is not less than 10 for carboprost peak in the chromatogram obtained with reference solution (d).

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to 15-Epicarboprost is not more than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (b) (2.0 per cent), the area of any peak corresponding to trans-Carboprost is not more than 1.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (3.0 per cent), the area of any other secondary peak is not more than 0.04 times 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 1.6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (4.0 per cent).

Heavy metals (2.3.13). 1.0 g complies with the limit test for heavy metals, Method B (20 ppm).

Sulphated ash (2.3.18). Not more than 0.5 per cent.

Loss on drying (2.4.19). Not more than 1.0 per cent, determined by drying in oven at 50° for 16 hours at a pressure not exceeding 0.7 kPa.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances using the following modifications.
- Injection volume: 10 µl.

Inject reference solution (a). The test is not valid unless the resolution between the peaks due to trans-carboprost and carboprost is not less than 1.2, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 1.0 per cent.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{21}H_{36}O_5$,$C_4H_{11}NO_3$.

Storage. Store protected from moisture, at a temperature between 2° to 8°.