

# Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

## Aceclofenac and Paracetamol Tablets

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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](mailto:lab.ipc@gov.in), with a copy to Dr. Gaurav Pratap Singh (email: [gpsingh.ipc@gov.in](mailto:gpsingh.ipc@gov.in)) before the last date for comments.

### Document History and Schedule for the Adoption Process

Description	Details
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Further follow-up action as required.	

## Aceclofenac and Paracetamol Tablets

Aceclofenac and Paracetamol Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of aceclofenac,  $C_{16}H_{13}C_{12}NO_4$  and paracetamol,  $C_8H_9NO_2$ .

**Usual strength.** Aceclofenac 100 mg and Paracetamol 325 mg.

### Identification

In the Assay, the principal peaks in the chromatogram obtained with the test solution correspond to the principal peaks in the chromatogram obtained with the reference solution (c).

### Tests

#### Dissolution (2.5.2).

Apparatus No. 2 (Paddle),

Medium. 900 ml of phosphate buffer pH 6.8, prepared by dissolving 6.8 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 6.8 with *dilute sodium hydroxide*,

Speed and time. 75 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

*Test solution.* Use the filtrate, dilute if necessary, with the dissolution medium.

*Reference solution.* Dissolve 11 mg of *aceclofenac IPRS* and 36 mg *paracetamol IPRS* in 5 ml of *acetonitrile* and dilute to 100.0 ml with the dissolution medium.

#### Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5  $\mu$ m), (Such as X-Terra RP 18),
- mobile phase: A. a mixture of 90 volumes of 0.005 M *disodium hydrogen phosphate*, adjusted to pH 8.0 with *dilute orthophosphoric acid*, 9 volumes of *acetonitrile* and 1 volume of *methanol*,  
B. a mixture of 90 volumes of *acetonitrile* and 10 volumes of *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 10  $\mu$ l.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
10	35	65
11	95	5
15	95	5

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent, for both the peaks.

Inject the reference solution and the test solution.

Calculate the content of  $C_{16}H_{13}C_{12}NO_4$  and  $C_8H_9NO_2$  in the medium.

Q. Not less than 70 per cent of the stated amount of  $C_{16}H_{13}C_{12}NO_4$  and  $C_8H_9NO_2$ .

**Related substances.** Determine by liquid chromatography (2.4.14).

*Solvent mixture.* Equal volumes of *acetonitrile* and *water*.

*Test solution.* Disperse a quantity of the powdered tablets containing 325 mg of Paracetamol in the solvent mixture, with the aid of ultrasound for 10 minutes with intermittent shaking and dilute to 100.0 ml with the solvent mixture, filter.

*Reference solution.* A solution containing 0.01624 per cent w/v of *paracetamol IPRS* and 0.005 per cent w/v of *aceclofenac IPRS* in the solvent mixture. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

#### Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm), (Such as Symmetry C 18),
- column temperature: 40°,
- mobile phase: A. a buffer solution prepared by dissolving 1 g of *1-octane sulphonic acid sodium salt anhydrous* and 2 g of *sodium dihydrogen orthophosphate anhydrous* in 1000 ml of *water*, adjusted to pH 3.5 with *dilute orthophosphoric acid*,  
B. a mixture of 90 volumes of *acetonitrile* and 10 volumes of *water*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 220 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
3	95	5
8	80	20
42	20	80
50	20	80
52	95	5
60	95	5

Name	Relative retention time	Correction factor
Paracetamol	0.27	---
4-aminophenol	0.43	0.62
4-chloroacetanilide	0.69	1.52
Aceclofenac (Retention time: about 31 minutes)	1.0	---
Aceclofenac impurity A <sup>1</sup>	1.1	0.89

<sup>1</sup>[(2-[(2,6-dichlorophenyl)amino] phenyl)acetic acid

Inject the reference solution. The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent for both the peaks.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to aceclofenac impurity A is not more than 10 times the area of the aceclofenac peak in the chromatogram obtained with the reference solution (5.0 per cent), the area of any peak corresponding to 4-aminophenol is not more than 0.2 times the area of the paracetamol peak in the chromatogram obtained with the reference solution (0.1 per cent), the area of any peak corresponding to 4-chloroacetanilide is not more than 0.1 times the area of the paracetamol peak in the chromatogram obtained with the reference solution (0.05 per cent), the area of any other secondary peak is not more than the area of the aceclofenac peak in the chromatogram obtained with the reference solution (0.5 per cent) and the sum of areas of all the secondary peaks, excluding aceclofenac impurity A is not more than 4 times the area of the aceclofenac peak in the chromatogram obtained with the reference solution (2.0 per cent).

**Other tests.** Comply with the tests stated under Tablets.

**Assay.** Determine by liquid chromatography (2.4.14).

*NOTE* — Use freshly prepared solutions.

*Solvent mixture.* 40 volumes of *acetonitrile* and 60 volumes of *water*.

**Test solution.** Weigh and powder 20 tablets. Disperse a quantity of the powder containing 325 mg of Paracetamol in 40 ml of *acetonitrile*, with the aid of ultrasound with intermittent shaking. Add 100 ml of the solvent mixture and sonicate for 15 minutes with intermittent shaking, dilute to 200.0 ml with the solvent mixture. Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

**Reference solution (a).** Dissolve 32.5 mg of *paracetamol IPRS* in 5 ml of *acetonitrile*, with the aid of ultrasound for 5 minutes and dilute to 20.0 ml with the solvent mixture.

**Reference solution (b).** Dissolve 25 mg of *aceclofenac IPRS* in 10 ml of *acetonitrile*, with the aid of ultrasound for 5 minutes and dilute to 50.0 ml with the solvent mixture.

**Reference solution (c).** Transfer 5.0 ml, each of, reference solution (a) and reference solution (b) to a 50- ml volumetric flask. Add 10 ml of *acetonitrile* and dilute to 50.0 ml with the solvent mixture.

#### Chromatographic system

- a stainless steel column 15 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm), (Such as X-Terra RP 18),
- mobile phase: A. a mixture of 90 volumes of 0.005 M disodium hydrogen phosphate, adjusted to pH 8.0 with dilute orthophosphoric acid, 9 volumes of *acetonitrile* and 1 volume of *methanol*,  
B. a mixture of 90 volumes of *acetonitrile* and 10 volumes of *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	95	5
10	35	65
11	95	5
15	95	5

The elution order is paracetamol followed by aceclofenac peak.

Inject reference solution (c). The test is not valid unless the column efficiency is not less than 1500 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent, for both the peaks.

Inject reference solution (c) and the test solution.

Calculate the content of  $C_{16}H_{13}C_{12}NO_4$  and  $C_8H_9NO_2$  in the tablets.

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