

Draft Proposal for Comments and Inclusion in The Indian Pharmacopoeia

Edetate Calcium Disodium

Published on: 08.10.2024

Last date for comments: 22.11.2024

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.

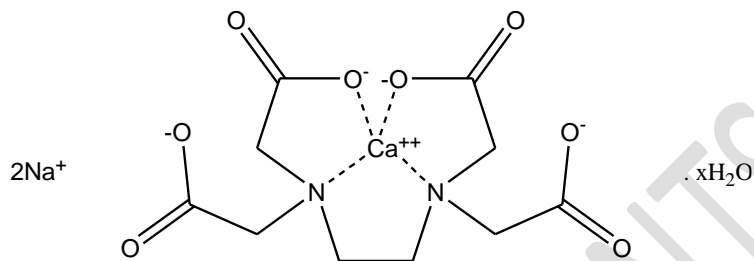
Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

Description	Details
Document version	2.0
Category	New Inclusion
Monograph proposed for inclusion	IP 2026
Tentative effective date of monograph	July, 2026
First draft published on IPC website for public comments	18.01.2024
Draft revision published on IPC website for public comments	08.10.2024
Further follow-up action as required.	

Edetate Calcium Disodium

This monograph has been harmonized with corresponding texts of the European Pharmacopoeia, the Japanese Pharmacopoeia and the United States Pharmacopoeia. Portions of the IP text that are not part of the PDG harmonized text, are marked with symbols (◆◆).



$C_{10}H_{12}CaN_2Na_2O_8 \cdot xH_2O$

Mol. Wt. 374.3

Edetate Calcium Disodium contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{10}H_{12}CaN_2Na_2O_8$, calculated on the anhydrous basis.

Category. Pharmaceutical aid.

Description. A white crystalline granules or powder.

Identification

- Determine by infrared absorption spectrophotometry (2.4.6). Compare the spectrum with that obtained with *edetate calcium disodium IPRS* or with the reference spectrum of edetate calcium disodium.
- Dissolve 2.0 g in 10 ml of *water*, add 6 ml 3.3 per cent w/v solution of *lead nitrate*, shake and add 3 ml of *potassium iodide* solution; no yellow precipitate is formed. Make alkaline by adding 50 per cent v/v solution of *ammonia* and add 3 ml of 4.0 per cent w/v solution of *ammonium oxalate*; a white precipitate is produced.
- Dissolve 0.5 g in 10 ml of *water*, and add 10 ml of 2.0 per cent w/v solution of *potassium pyroantimonate*; a white crystalline precipitate is formed. The formation of precipitate is accelerated by rubbing the inside wall of the test tube with a glass rod.

Tests

pH (2.4.24). 6.5 – 8.0, determined in 20.0 per cent w/v solution.

Disodium edetate. Not more than 1.0 per cent, determined by the following method.

Dissolve 1.0 g in 50 ml of *water*, add 5 ml of *strong ammonia-ammonium chloride solution* and 40 mg of *eriochrome black T mixture* and titrate with 0.01 M *magnesium chloride*, until the blue colour of the solution turns to red-violet, not more than 3.0 ml of 0.01 M *magnesium chloride* is consumed.

Limit of nitrilotriacetic acid. Determine by liquid chromatography (2.4.14).

Solvent mixture. 1.0 per cent w/v solution of *cupric nitrate* in *water*.

Test solution. Dissolve 100.0 mg of substance under examination in the solvent mixture, with the aid of ultrasound and dilute to 10.0 ml with the solvent mixture.

Reference solution (a). A 1.0 per cent w/v solution of *cupric nitrate* ($Cu(NO_3)_2$) in *water*.

Reference solution (b). Transfer 100 mg of *nitrilotriacetic acid* to a 10-ml volumetric flask, add 0.5 ml of *ammonium hydroxide* and mix, dilute to volume with *water*.

Reference solution (c). Transfer 1.0 g of *Edetate Calcium Disodium* to a 100-ml volumetric flask, add 100 μ l of reference solution (b) and dilute to volume with reference solution (a), Sonicate, if necessary to dissolve.

Reference solution (d). Transfer 10 mg of *Edetate Calcium Disodium* to a 100-ml volumetric flask, add 100 μ l of reference solution (b) and dilute to volume with reference solution (a), Sonicate, if necessary to dissolve.

Chromatographic system

- a stainless steel column 15 cm x 4.6 mm packed with octylsilane bonded to porous silica (5 µm) (Such as Zorbax C8),
- mobile phase: add 10 ml of 1 M tetrabutylammonium hydroxide in methanol to 200 ml with water, adjusted to pH 7.5 with 1 M phosphoric acid. Transfer the solution to a 1000-ml volumetric flask, add 90 ml of methanol and dilute to volume with water,
- flow rate: 2 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 50 µl.

The relative retention time with reference to edetate, for nitrilotriacetic acid and copper are 0.35 and 0.65, respectively.

Inject reference solution (c) and (d). The test is not valid unless the resolution between the peaks due to nitrilotriacetic acid and copper is not less than 3.0 in the chromatogram obtained with reference solution (d) and the relative standard deviation for replicate injection is not more than 2.0 per cent in the chromatogram obtained with reference solution (c).

Inject reference solution (c) and the test solution. In the chromatogram obtained with the test solution, the area of the any peak corresponding to nitrilotriacetic acid does not exceed the difference between the nitrilotriacetic acid peak area obtained from the reference solution (c) and the test solution (0.1 per cent).

Chlorides (2.3.12). Not more than 0.1 per cent.

Dissolve 0.7 g in water and dilute to 20 ml with water, add 30 ml of dilute nitric acid and allow to stand for 30 minutes, filter. Dilute 10 ml of the filtrate to 50 ml with water. Use this solution as test solution. Prepare the reference solution using 0.4 ml of 0.01 M hydrochloric acid, add 6 ml of dilute nitric acid and dilute to 50 ml with water. Filter both solutions if necessary. Add 1 ml of 0.1 M silver nitrate to, each of, the test solution and the reference solution, mix. After standing for 5 minutes protected from light, any opalescence in the test solution is not more than that in the reference solution.

Water (2.3.43). 5.0 to 13.0 per cent, determined on 0.2 g.

Assay. Dissolve 0.5 g of the substance under examination in 200 ml of water. Dilute 20.0 ml of the solution with 80 ml of water, adjusted to pH 2 - 3 with dilute nitric acid, add 0.2 ml of xylene orange solution and titrate with 0.01 M bismuth nitrate; the yellow colour of the solution turns to red.

1 ml of 0.01 M bismuth nitrate is equivalent to 0.0037432 g of C₁₀H₁₂CaN₂Na₂O₈.

Storage. Store protected from moisture.

Solubility. Freely soluble in water, practically insoluble in ethanol (95 per cent).