भारतीय भेषज संहिता आयोग
स्वास्थ्य एवं परिवार कल्याण मंत्रालय, भारत सरकार
सैक्टर २३, राज नगर
गाज़ियाबाद २०१००२ (उ. प्र.), भारत

INDIAN PHARMACOPOEIA COMMISSION
Ministry of Health & Family Welfare, Government of India
Sector 23, Raj Nagar
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डा. राजीव सिंह रघुवंशी
सचिव-सह-वैज्ञानिक निदेशक

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Secretary-cum-Scientific Director

F. No. T.11015/01/2020-AR&D

Date: January 16, 2025

Subject: Amendment List 07 to IP 2022

The 9th Edition of Indian Pharmacopoeia (IP) 2022 has become effective from 1st December, 2022. Based on the scientific inputs, some monographs of the IP 2022 and IP Addendum 2024 need amendments for their effective implementation. Accordingly, Amendment List 07 to IP 2022 is being issued containing such amendments and this shall become official with immediate effect.

All concerned are requested to bring it to the notice of all authorities under their control for compliance with the IP 2022.

(Dr. Rajeev Singh Raghuvanshi)

Encl. Amendment List 07 to IP 2022

To,

1. The Drugs Controller General (India)
2. All State Drug Controllers
3. CDSCO Zonal Offices
4. Members of the Scientific Body of the IPC
5. Directors of the Drugs Testing Laboratories
6. IDMA/OPPI/BDMA/FOPE/FSSAI/Small Scale Industry Associations

4.5. Volumetric Reagents and Solutions

Page 1145

Disodium Edetate, 0.1 M. Para 2, last line

Change **from**: green.

to: blue.

6.2.2. Glass Containers. Page 1263

Hydrolytic resistance. **Test 1**

Para 4, line 6

Change **from**: Table 2

to: Table 4

Alprostadil Injection. Page 1407

Assay. *Internal standard solution.* Line 2

Change **from**: *ethylparaben*

to: *ethylparaben IPRS*

Amitriptyline Hydrochloride. Page 1443

Related substances. *Reference solution (a).* Line 1 to 3

Change **from**: Dissolve 5.0 mg each of *amitriptyline impurity A IPRS (dibenzosuberone IPRS)* and *amitriptyline impurity B IPRS (cyclobenzaprine hydrochloride IPRS)*

to: Dissolve 5.0 mg, each of, *dibenzosuberone IPRS* (amitriptyline impurity A) and *cyclobenzaprine hydrochloride IPRS* (amitriptyline impurity B)

Amitriptyline Tablets. Page 1445

Related substances. *Reference solution (b).* Line 3 and 4

Change **from**: *amitriptyline impurity A IPRS* and 0.001 per cent w/v of *amitriptyline impurity B IPRS*

to: *dibenzosuberone IPRS* (amitriptyline impurity A) and 0.001 per cent w/v of *cyclobenzaprine hydrochloride IPRS* (amitriptyline impurity B)

Amlodipine and Olmesartan Medoxomil Tablets. Page 5128

Related substances. *Reference solution (b)*. Line 1

Change **from**: 0.8 per cent

to: 0.4 per cent

Reference solution (c). Line 2

Change **from**: 1.0 ml of reference solution (b)

to: 2.0 ml of reference solution (b)

Atenolol. Page 5131

Related substances. *Buffer solution*, line 2 and 3

Change **from**: *water*, adjusted to pH 3.0 with *orthophosphoric acid*.

to: *water*.

Chromatographic system, line 8

Change **from**: the buffer solution,

to: the buffer solution. Adjust to pH 3.0 with *orthophosphoric acid*.

Azacitidine for Injection. Page 5134

Related substances. Last para, line 1-7

Change **from**: In the chromatogram obtained with the test solution, the sum of the areas of the peaks corresponding to isomer-1, isomer-2, isomer-3 and isomer-4 (azacitidine related compound C) is not more than 2.4 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.2 per cent),

to: In the chromatogram obtained with the test solution, the sum of the areas of the peaks corresponding to isomer-1, isomer-2, isomer-3 and isomer-4 (azacitidine related compound C) is not more than 4.4 times the area of the principal peak in the chromatogram obtained with reference solution (b) (2.2 per cent),

Betahistine Hydrochloride. Page 1613

Related substances. *Reference solution (a).* Line 2

Change **from**: *2-vinylpyridine*

to: *2-vinylpyridine IPRS* (betahistine mesylate impurity A)

Betahistine Tablets. Page 1614

Related substances. *Reference solution (c).* Line 2

Change **from**: *betahistine impurity A IPRS (2-vinylpyridine)*

to: *2-vinylpyridine IPRS* (betahistine mesylate impurity A)

Betahistine Mesylate. Page 1615

Related substances. *Reference solution (a)*. Line 2 and 3

Change **from**: *2-vinylpyridine* (betahistine mesylate impurity A)

to: *2-vinylpyridine IPRS* (betahistine mesylate impurity A)

Calamine Lotion. Page 1716

Identification. A, line 3 and 4

Change **from**: a silver mirror is produced on the walls of the tube.

to: Heat on a water-bath at 70° for 5 minutes. A silver mirror is produced on the walls of the tube.

Carboxymethylcellulose Eye Drops. Page 5152

Identification. B, line 3 and 4

Change **from**: about 295 nm, 366 nm, 519 nm and 635 nm.

to: about 366 nm, 519 nm and 635 nm.

Cefuroxime Axetil Tablets. Page 1804

Assay.

Reference solution (c). Change **to**:

Reference solution (c). Dissolve a suitable quantity of *cefuroxime axetil IPRS* in *methanol* and dilute with *methanol* to obtain a solution containing 0.3 per cent w/v of Cefuroxime Axetil. Dilute 1.0 ml of the solution to 10.0 ml with the mobile phase.

Chlorcyclizine Hydrochloride. Page 1838

Related substances. *Reference solution (b)*. Line 2

Change **from**: *methylpiperazine IPRS*

to: *N-methylpiperazine IPRS*

Copovidone. Page 5161

Nitrogen. Para 2, line 13 and 14

Change **from**: *0.05 M sulphuric acid*

to: *0.025 M sulphuric acid*

Cyclizine Hydrochloride. Page 1970

Related substances. *Reference solution (b)*. Line 2 and 3

Change **from**: *cyclizine impurity A IPRS* and *cyclizine impurity B IPRS*

to: *N-methylpiperazine IPRS* (cyclizine impurity A) and *benzhydrol IPRS* (cyclizine impurity B)

After RRT table, line 1 and 2

Change **from**: [1]1-methylpiperazine,
[2]diphenylmethanol.

to: [1]*N*-methylpiperazine,
[2]diphenylmethanol; benzhydrol.

Cyclobenzaprine Tablets. Page 5166

Related substances. Last para, line 3-6

Change **from**: The area of any peak corresponding to cyclobenzaprine *N*-oxide is not more than 1.33 times the area of the principal peak in the chromatogram obtained with the reference solution (0.2 per cent),

to: The area of any peak corresponding to cyclobenzaprine *N*-oxide is not more than 3.33 times the area of the principal peak in the chromatogram obtained with the reference solution (0.5 per cent),

Cyclophosphamide Injection. Page 1980

Assay. *Reference solution (b)*. Line 3

Change **from**: *ethylparaben*

to: *ethylparaben IPRS*

Cyproheptadine Hydrochloride. Page 1989

Related substances. *Reference solution (b)*. Line 2

Change **from**: *cyproheptadine impurity B IPRS*

to: *dibenzosuberone IPRS* (cyproheptadine impurity B)

Cyproterone Tablets. Page 1993

Dissolution

Insert at the end

Q. Not less than 70 per cent of the stated amount of $C_{24}H_{29}ClO_4$.

Diethylcarbamazine Citrate. Page 2100

***N,N'*-Dimethylpiperazine and *N*-methylpiperazine**. *Reference solution (c).* Line 2

Change **from**: *N-methylpiperazine*

to: *N-methylpiperazine IPRS*

Diethylcarbamazine Tablets. Page 2101

***N,N'*-Dimethylpiperazine and *N*-methylpiperazine**. *Reference solution (b).* Line 2

Change **from**: *N-methylpiperazine*

to: *N-methylpiperazine IPRS*

Diphenhydramine Capsules. Page 2127

Assay. *Test solution*

Change **to** : *Test solution*. Weigh and mix the contents of 20 capsules. Disperse a quantity of the mixed content containing 75 mg of Diphenhydramine Hydrochloride in *water* and dilute to 100.0 ml with *water*, mix and filter. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

OR

Weigh and transfer not less than 20 capsules to 200-ml volumetric flask, add 125 ml of *water* at 50º and shake to dissolve, dilute to volume with *water*. Dilute a suitable volume of the solution with the solvent mixture to obtain a solution containing 0.0075 per cent w/v of Diphenhydramine Hydrochloride.

Reference solution (b). Line 1

Change **from**: 0.007 per cent

to: 0.0075 per cent

After chromatographic system, para 2

Change **to** : Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to diphenhydramine and diphenhydramine related compound A is not less than 2.0 in the chromatogram obtained with reference solution (a) and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (b).

Dydrogesterone Tablets. Page 5178

Related substances. After chromatographic system, para 4, line 6-9

Change **from**: the area of any secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

to: the area of any secondary peak is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent).

Gemcitabine Hydrochloride. Page 2457

Insert before **Storage**

Gemcitabine Hydrochloride intended for use in the manufacture of parenteral preparations without a further sterilisation procedure complies with the following additional requirement.

Sterility (2.2.11). Complies with the test for sterility.

Gentamicin Sulphate. Page 2464

Identification. Change **to**:

Test A may be omitted if tests B and C are carried out. Test B may be omitted if tests A and C are carried out.

A. Determine by thin-layer chromatography (2.4.17), coating the plate with *silica gel G*.

Mobile phase. The lower layer obtained by shaking together equal volumes of *strong ammonia solution*, *chloroform* and *methanol* and allowing to separate.

Test solution. Dissolve 0.5 g of the substance under examination in 100 ml of *water*.

Reference solution. A 0.5 per cent w/v solution of *gentamicin sulphate IPRS* in *water*.

Apply to the plate 10 µl of each solution. After development, dry the plate in air, spray with *ethanolic ninhydrin solution* and heat at 110° for 5 minutes. The three principal spots in the chromatogram obtained with the test solution correspond to those in the chromatogram obtained with the reference solution.

B. In the test for Composition of gentamicin sulphate, the four principal peaks in the chromatogram obtained with the test solution correspond to the four peaks in the chromatogram obtained with the reference solution.

C. It gives the reaction (A) of sulphates (2.3.1).

Insert before **Sterility**

Gentamicin Sulphate intended for use in the manufacture of parenteral preparations without a further sterilisation procedure complies with the following additional requirement.

Indomethacin Suppositories. Page 2603

Related substances. *Reference solution (b).* Line 2

Change **from**: *4-chlorobenzoic acid*

to: *4-chlorobenzoic acid IPRS*

Magnesium Sulphate. Page 4098

Iron. Change **to**:

Iron (2.3.14). 20.0 ml of solution A complies with the limit test for iron (20 ppm).

Malic Acid. Page 2820

Related substances. *Reference solution (a).* Line 1

Change **from**: *fumaric acid*

to: *fumaric acid IPRS* (malic acid impurity A)

Line 2

Change **from**: *maleic acid*

to: *maleic acid IPRS*

Mefenamic Acid. Page 2836

Related substances. *Reference solution (b).* Line 2 and 3

Change **from**: *mefenamic acid impurity C* and *mefenamic acid impurity D*

to: *2-chlorobenzoic acid IPRS* (mefenamic acid impurity C) and *benzoic acid IPRS* (mefenamic acid impurity D)

Mercaptopurine. Page 5212

Related substances.

Reference solution (a). Change **to**:

Reference solution (a). A 0.006 per cent w/v solution of *mercaptopurine IPRS* in solution A. *(NOTE — Use methanol equivalent to 2.5 per cent of the final volume to dissolve)*. Dilute 1.0 ml of the solution to 50.0 ml with mobile phase A.

Metoprolol Injection. Page 2918

Identification. C. *Reference solution (b).* Line 3

Change **from**: *fumaric acid*

to: *fumaric acid IPRS*

Metronidazole. Page 5220

Related substances. *Reference solution.* Line 2 and 3

Change **from**: *tinidazole related compound A IPRS*

to: *2-methyl-5-nitroimidazole IPRS* (tinidazole related compound A)

Metronidazole Injection. Page 5221

Related substances. *Reference solution (a).* Line 2 and 3

Change **from**: *tinidazole related compound A IPRS*

to: *2-methyl-5-nitroimidazole IPRS* (tinidazole related compound A)

Reference solution (b). Line 3

Change **from**: *tinidazole related compound A IPRS*

to: *2-methyl-5-nitroimidazole IPRS* (tinidazole related compound A)

Assay. *Reference solution (b).* Line 3

Change **from**: *tinidazole related compound A IPRS*

to: *2-methyl-5-nitroimidazole IPRS* (tinidazole related compound A)

Metronidazole Gel. Page 5222

Related substances. *Reference solution (b).* Line 2 and 3

Change **from**: *tinidazole related compound A IPRS*

to: *2-methyl-5-nitroimidazole IPRS* (tinidazole related compound A)

Metronidazole Tablets. Page 5222

Related substances. *Reference solution.* Line 2 and 3

Change **from**: *tinidazole related compound A IPRS*

to: *2-methyl-5-nitroimidazole IPRS* (tinidazole related compound A)

Nortriptyline Hydrochloride. Page 5239

Related substances. *Reference solution (b).* Line 2

Change **from**: *nortriptyline impurity A IPRS*

to: *dibenzosuberone IPRS* (nortriptyline impurity A)

Oleic Acid. Page 5243

Loss on ignition. Line 1

Change **from**: **Loss on ignition** (2.4.20).

to: **Sulphated ash** (2.3.18).

Olmesartan Medoxomil and Hydrochlorothiazide Tablets. Page 5245

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

NOTE — Prepare the solutions immediately before use.

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

Test solution. Disperse a quantity of powdered tablets containing 50 mg of Olmesartan Medoxomil in the solvent mixture, with the aid of ultrasound with intermittent shaking and dilute to 50.0 ml with the solvent mixture. Centrifuge a portion of the solution, filter.

Reference solution. A 0.001 per cent w/v solution of *olmesartan medoxomil IPRS* in the solvent mixture.

Chromatographic system

- a stainless steel column 10 cm x 4.6 mm, packed with octylsilane bonded to porous silica (3.5 µm) (Such as Symmetry C8),
- column temperature: 40°,
- mobile phase: A. a buffer solution prepared by dissolving 4.08 g of *potassium dihydrogen orthophosphate* in 850 ml of *water*, adjusted to pH 2.5 with *orthophosphoric acid* and dilute to 1000 ml with *water*,

  B. *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 250 nm,
- injection volume: 10 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	85	15
6	85	15
8	83	17
20	83	17
30	40	60
35	85	15
40	85	15

The relative retention time with reference to olmesartan medoxomil for olmesartan impurity (1-{[2′-(1*H*-Tetrazol-5-yl)biphenyl-4-yl]methyl}-4-(2-hydroxypropan-2-yl)-2-propyl-1*H*-imidazole-5-carboxylic acid) is about 0.65.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation of replicate injections is not more than 5.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to olmesartan is not more than 2.5 times the area of the principal peak in the chromatogram obtained with the reference solution (2.5 per cent), the area of any other secondary peak is not more than 0.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than 4.1 times the area of the principal peak in the chromatogram obtained with the reference solution (4.1 per cent). Ignore any peak with an area less than 0.1 times the area of the principal peak in the chromatogram obtained with the reference solution (0.1 per cent).

Ondansetron Tablets. Page 3126

Identification. Line 3

Change **from**: chromatogram obt d with the reference solution (a).

to: chromatogram obtained with the reference solution.

Pantoprazole Sodium. Page 5249

Related substances. B, impurity table, line 15 and 16

Change **from**: Pantoprazole dimer (pantoprazole related compound B)

to: Pantoprazole sulphide (pantoprazole related compound B)

Paroxetine Prolonged-release Tablets. Page 3208

Assay. Chromatographic system, lines 1 to 3

Change **from**: a stainless steel column 25 cm x 4.6 mm packed with octadecylsilane bonded to porous silica (5 µm) (Such as Zorbax TMS),

to: a stainless steel column 25 cm x 4.6 mm, packed with trimethylsilane bonded to porous silica (5 µm) (Such as Zorbax TMS),

Pitavastatin Calcium. Page 3298

Related substances. Chromatographic system, line 5 to 6

Change **from**: 1.54 per cent w/v solution of *ammonium acetate* in 1000 ml of *water*,

to: 1.54 g of *ammonium acetate* in 1000 ml of *water*,

Pravastatin Sodium. Page 3326

Assay. Para 3 and 4

Change **from**: Calculate the content of $C_{23}H_{35}NaO_7$ from the declared content of pravastatin in *pravastatin 1,1,3,3-tetramethylbutylamine IPRS*.

1 mg of pravastatin is equivalent to 1.052 mg of pravastatin sodium.

to: Calculate the content of $C_{23}H_{35}NaO_7$ taking into account the assigned content of *pravastatin 1,1,3,3-tetramethylbutylamine IPRS* and using a conversion factor of 0.806.

Pravastatin Tablets. Page 3328

Assay. Last para

Change **from**: Calculate the content of $C_{23}H_{35}NaO_7$ in the tablets using the declared content of pravastatin in *pravastatin 1,1,3,3-tetramethylbutylamine IPRS*.

1 mg of $C_{23}H_{36}O_7$ is equivalent to 1.052 mg of $C_{23}H_{35}NaO_7$.

to: Calculate the content of $C_{23}H_{35}NaO_7$ in the tablets taking into account the assigned content of *pravastatin 1,1,3,3-tetramethylbutylamine IPRS* and using a conversion factor of 0.806.

Pregabalin. Page 5262

Enantiomeric purity. Chromatographic system

Insert before mobile phase

– sample temperature: 10º,

Related substances. A. *Reference solution (c).* Line 2

Change **from**: *pregabalin impurity C IPRS (mandelic acid)*

to: *mandelic acid IPRS* (pregabalin impurity C)

Salicylic Acid. Page 3555

Related substances. *Reference solution (c).* Line 1 and 2

Change **from**: *salicylic acid impurity A*

to: *4-hydroxybenzoic acid IPRS* (salicylic acid impurity A)

Sertraline Hydrochloride. Page 3574

Impurity E. *Reference solution (a).* Line 2

Change **from**: *sertraline impurity E (mandelic acid)*

to: *mandelic acid IPRS* (sertraline impurity E)

Reference solution (b). Line 2 and 3

Change **from**: *mandelic acid* (sertraline impurity E)

to: *mandelic acid IPRS* (sertraline impurity E)

Sertraline Tablets. Page 3576

Related substances. *Reference solution (b).* Line 2

Change **from**: *(R)-mandelic acid (sertraline impurity E)*

to: *mandelic acid IPRS* (sertraline impurity E)

Sitagliptin Tablets. Page 5278

Dissolution. After chromatographic system, para 1, line 2

Change **from**: not more than

to: not less than

Sodium Propylparaben. Page 3623

Related substances. *Reference solution (a).* Line 2 and 3

Change **from**: *ethyl parahydroxybenzoate IPRS (propylparaben impurity C IPRS)*

to : *ethylparaben IPRS* (propylparaben impurity C)

Telmisartan Tablets. Page 5287

Related substances. *Test solution*

Change **to**: *Test solution*. Transfer a suitable quantity of intact tablets (not less than 20 tablets) to a suitable volumetric flask, add about 80 per cent of the volume of the solvent mixture. Swirl to disperse and sonicate for 10 minutes, allow to cool to room temperature and dilute to volume with the solvent mixture and filter. Dilute a suitable volume of the filtrate with the mobile phase to obtain a solution having concentration 0.011 per cent w/v of Telmisartan.

Tenofovir Disoproxil Fumarate. Page 3745

Insert before **Water**

Sulphated ash (2.3.18). Not more than 0.2 per cent.

Tenofovir and Emtricitabine Tablets. Page 3748

Related substances. *For Tenofovir Disoproxil Fumarate — Reference solution (c).* Line 1

Change **from**: *fumaric acid*

to: *fumaric acid IPRS*

Travoprost Eye Drops. Page 3850

pH. Change **to**:

pH (2.4.24). 5.5 to 6.5; If labelled to contain polyquarternium-1 as a preservative, 6.4 to 7.0; and if labelled to contain zinc chloride as an ingredient, 5.5 to 5.9.

Insert at the end

Labelling. If the eye drops are formulated with polyquarternium-1 as a preservative, it is so labelled. If the eye drops are formulated with zinc chloride as an ingredient, it is so labelled

Vildagliptin Prolonged-release Tablets. Page 5299

Dissolution. Insert before line 2

Test-1

Insert at the end

Test-2

Apparatus No. 2 (Paddle),
Medium. 900 ml of *0.1 M hydrochloric acid,*
Speed and time. 50 rpm and 30 minutes, 2 hours, 4 hours and 12 hours,

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Solvent mixture. 85 volumes of *water* and 15 volumes of *acetonitrile.*

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

Reference solution. A 0.055 per cent w/v solution of *vildagliptin IPRS* in the solvent mixture. Dilute 5.0 ml of the solution to 25.0 ml with the dissolution medium.

Chromatographic system
- a stainless steel column 15 cm x 4.6 mm, packed with octylsilane bonded to porous silica (5 µm) (Such as Waters X-Bridge C8),
- mobile phase: a mixture of 80 volumes of a buffer solution prepared by dissolving 2 g of *sodium-1-heptanesulphonate* in 1000 ml of *water,* adjusted to pH 3.0 with 10 per cent v/v solution of *orthophosphoric acid*,19 volumes of *acetonitrile* and 1 volume of *methanol*,
- flow rate: 1.2 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 10 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 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.

Inject the reference solution and the test solution.

Calculate the content of $C_{17}H_{25}N_3O_2$ in the medium.

The percentages of the labelled amount of vildagliptin, $C_{17}H_{25}N_3O_2$ dissolved at the times specified conform to 2.5.2 Dissolution test, Acceptance Table 2.

At 30 minutes, not less than 20 per cent and not more than 35 per cent; at 2 hours, not less than 35 per cent and not more than 55 per cent; at 4 hours, not less than 55 per cent and not more than 75 per cent and at 12 hours, not less than 80 per cent.

Insert at the end

Labelling. The label states the dissolution test used only if dissolution Test-1 is not used.

Zidovudine. Page 3985

Related substances. B. *Reference solution (b).* Line 2 and 3

Change **from**: *zidovudine impurity B IPRS, zidovudine impurity C IPRS*

to : *3'-chloro-3'-deoxythymidine IPRS* (zidovudine impurity B), *thymine IPRS* (zidovudine impurity C)

Zidovudine Injection. Page 3987

Related substances. *Reference solution (b).* Line 2 and 3

Change **from**: *zidovudine impurity C (thymine)*

to: *thymine IPRS* (zidovudine impurity C)