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
Ghaziabad 201002 (U.P.), INDIA

डा. राजीव सिंह रघुवंशी
सचिव-सह-वैज्ञानिक निदेशक

Dr. Rajeev Singh Raghuvanshi
Secretary-cum-Scientific Director

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

Date: June 28, 2024

Subject: Amendment List 06 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 06 to IP 2022 is being issued containing such amendments and this shall become effective from July 1, 2024 except for amendment in Bisacodyl, Bisacodyl Suppositories, Bisacodyl Gastro-resistant Tablets, and Pregabalin Capsules for which effective date is mentioned along with the amendment issued.

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 06 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 IPC
5. Directors of the Drugs Testing Laboratories
6. IDMA/OPPI/BDMA/FOPE/FSSAI/Small Scale Industry Associations

4.2. General Reagents. Page 1066

Page 1077

Insert before **Cadmium Iodide**

Butyrolactone; Dihydro-2-(3*H*)-furanone, γ-butyrolactone

A clear, colourless to practically colourless, oily liquid. Miscible with *water*. Soluble in *methanol* and in *ether*; bp, between 193° and 208°; refractive index, about 1.435 at 20°; wt. per ml, between 1.128 and 1.135.

Page 1130

Insert before **Toluene**

Titanium Trichloride-Sulphuric Acid Solution. Mix carefully 20 ml of *titanium trichloride solution* in 13 ml of *sulphuric acid*. Add sufficient *hydrogen peroxide* (30 per cent) to produce a yellow colour. Heat until white fumes are evolved, allow to cool, and dilute with *water*, repeat the evaporation and addition of *water* until a colourless solution is obtained and dilute to 100 ml with *water*.

Page 1132

Insert before **2-Vinylpyridine**

1-Vinylpyrrolidin-2-one; Vinylpyrrolidinone; 1-Vinyl-2-pyrrolidinone; 1-Vinyl-2-pyrrolidone; *N*-Vinylpyrrolidinone; *N*-Vinylpyrrolidone: C_6H_9NO = 111.1

Colourless liquid.

Complies with the following test.

ASSAY — Determine by gas chromatography (2.4.13).

Chromatographic system
- a capillary column 30 m x 0.25 mm, packed with 100 per cent dimethylpolysilxane (film thickness 1 μm),
- temperature: injection port at 250°, detector at 300°, column at 100° and programmed to rise 10° per minute to 250°,
- flame ionisaiton detector,
- carrier gas: helium.

The area of the 1-Vinylpyrrolidin-2-one peak is not less than 99.0 per cent of the total peak area.

Water (2.3.43). Not more than 0.1 per cent, determined on 2.5 g, using a mixture of 50 ml of *anhydrous methanol* and 10 ml of *butyrolactone* as solvent.

Capsules. Page 1297

Prolonged-release Capsules

Dissolution. Change **to**:

Dissolution (2.5.2). Unless otherwise stated in the individual monograph, carry out the test as per the manufacturer's specification.

NOTE — The following recommendations to be considered for the development of dissolution specifications. Stakeholders can have different specifications depending on their dosage form design.

The dissolution test acceptance criteria for prolonged-release capsules is normally expected to consist of 3 or more points. The first specification point is intended to prevent unintended rapid release of the active substance ('dose dumping'). It is therefore set after a testing period corresponding to a dissolved amount typically of not more than 20 per cent to 30 per cent. The second specification point defines the dissolution pattern and so is set at a time point when 40 per cent to 60 per cent drug release has happened. The final specification point is intended to ensure almost complete release, which is generally understood as more than 80 per cent release.

Tablets. Page 1342

Prolonged-release Tablets

Dissolution. Change **to**:

Dissolution (2.5.2). Unless otherwise stated in the individual monograph, carry out the test as per the manufacturer's specification.

NOTE —The following recommendations to be considered for the development of dissolution specifications. Stakeholders can have different specifications depending on their dosage form design.

The dissolution test acceptance criteria for prolonged-release tablets is normally expected to consist of 3 or more points. The first specification point is intended to prevent unintended rapid release of the active substance ('dose dumping'). It is therefore set after a testing period corresponding to a dissolved amount typically of not more than 20 per cent to 30 per cent. The second specification point defines the dissolution pattern and so is set at a time point when 40 per cent to 60 per cent drug release has happened. The final specification point is intended to ensure almost complete release, which is generally understood as more than 80 per cent release.

Amlodipine and Olmesartan Medoxomil Tablets. Page 5128

Related substances. Chromatographic system, line 6

Change **from**: *sodium dihydrogen orthophosphate*

to:*sodium dihydrogen orthophosphate monohydrate*

After impurity table, para 4, line 6 and 7

Change from : As_2 = peak response of amlodipine from reference solution (d),

to: As_2 = peak response of amlodipine from reference solution (f),

Amoxycillin and Potassium Clavulanate Tablets. Page 1471

Assay. Chromatographic system

Insert before line 3

– sample temperature: 10º,

Artesunate. Page 1510

Para 2, line 2

Change **from**: on the dried basis.

to: on the anhydrous basis.

Loss on drying

Change **to**: **Water** (2.3.43). Not more than 0.5 per cent, determined on 2.0 g.

Aspirin Gastro-resistant and Rosuvastatin Capsules. Page 1522

Related substances. After chromatographic system, table

Change **to**:

Name	Relative retention time	Correction factor
Aspirin	1.0	---
Salicylic acid	1.48	1.05

Atenolol. Page 1529

Para 2

Change **from**: Atenolol contains not less than 99.0 per cent and not more than 101.0 per cent of $C_{14}H_{22}N_2O_3$, calculated on the dried basis.

to: Atenolol contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{14}H_{22}N_2O_3$, calculated on the dried basis.

Atropine Ophthalmic Solution. Page 5133

Related substances. *Test solution*, line 3

Change **from**: 0.05 per cent

to: 0.005 per cent

Reference solution (a). Line 1

Change **from**: 0.05 per cent

to: 0.005 per cent

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

Reference solution (b). A solution containing 0.00005 per cent w/v of *atropic acid* and 0.005 per cent w/v of *atropine sulphate IPRS* in the solvent mixture.

Chromatographic system. Line 12

Change **from**: 20 µl.

to: 200 µl.

Azilsartan Kamedoxomil. Page 5136

Related substances. RRT table, last line, column 1

Change **from**: Dimer-3

to: Dimer-3[9]

Insert at the end of RRT table

[9](5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 2-ethoxy-1-((2'-(5-(2-ethoxy-1-((2'-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-yl)methyl)-1*H*-benzo[d]imidazol-7-yl)-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-yl) methyl)-1*H*-benzo[d]imidazole-7-carboxylate.

Betamethasone Valerate Cream. Page 1629

Assay. After chromatographic system, para 2

Change **from**: test solution (b).

to: test solution (a).

Last line

Change **from**: Calculate the content of $C_{22}H_{29}FO_5$ in the cream.

to: Calculate the content of $C_{22}H_{29}FO_5$ in the cream from the peak area ratio of the betamethasone valerate to the internal standard in the chromatograms obtained with the reference solution and test solution (a).

Bisacodyl. Page 1642 (*Effective from 1st August 2024*)

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 4 volumes of *glacial acetic acid*, 30 volumes of *acetonitrile* and 66 volumes of *water*.

Test solution. Dissolve 50 mg of the substance under examination in 25 ml of *acetonitrile* and dilute to 50.0 ml with the solvent mixture.

Reference solution (a). A 0.0001 per cent w/v solution of *bisacodyl IPRS* in the solvent mixture.

Reference solution (b). A solution containing 1.0 per cent w/v of *bisacodyl IPRS,* 0.001 per cent w/v, each of, *bisacodyl impurity A IPRS* and *bisacodyl impurity B IPRS,* 0.005 per cent w/v, each of, *bisacodyl impurity C IPRS* and *bisacodyl impurity E IPRS* and 0.002 per cent w/v of *bisacodyl impurity D IPRS* in *acetonitrile*. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (c). Dissolve 5 mg of *bisacodyl impurity F IPRS* in 2.5 ml of *acetonitrile* and dilute to 5.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm × 4.6 mm, packed with endcapped octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 45 volumes of *acetonitrile* and 55 volumes of 0.16 per cent w/v solution of *ammonium formate,* adjusted to pH 5.0 with *anhydrous formic acid,*
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 265 nm,
- injection volume: 20 µl.

Name	Relative retention time	Correction factor
Bisacodyl impurity D[1]	0.12	---
Bisacodyl impurity A[2]	0.2	0.7
Bisacodyl impurity B[3]	0.4	---
Bisacodyl impurity C[4]	0.45	---
Bisacodyl impurity E[5]	0.9	---
Bisacodyl (Retention time is about 13 minutes)	1.0	---
Bisacodyl impurity F[*]	2.6	---

[*]Unknown structure.

[1]Di-sodium (pyridin-2-ylmethylene)bis(4,1-phenylene) bis(sulphate),

[2]4,4'-(pyridine-2-ylmethylene) diphenol,

[3]2-((RS)-(4-hydroxyphenyl)(pyridine-2-yl)methyl)phenol,

[4]4-((RS)-(4-hydroxyphenyl) (pyridine-2-yl)methyl)phenyl acetate,

[5]2-((RS)-(4-acetyloxy)phenyl)(pyridine-2-yl)methyl)phenyl acetate.

Inject reference solution (b) and (c) to identify the peaks due to bisacodyl impurity A, B, C, D, E and bisacodyl impurity F, respectively.

Inject reference solution (b). The test is not valid unless the peak-to-valley ratio is not less than 1.5, where *Hp* = height above the baseline of the peak due to bisacodyl impurity E and *Hv* = height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to bisacodyl impurity A and B, each of, is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent), the area of any peak corresponding to bisacodyl impurity D is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent), the area of any peak corresponding to bisacodyl impurity C and E, each of, is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent), the area of any peak corresponding to bisacodyl impurity F is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 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 (a) (0.1 per cent) and the sum of the areas of all the secondary peaks is not more than 10 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 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 (a) (0.05 per cent).

Bisacodyl Suppositories. Page 1643 (*Effective from 1st August 2024*)

Identification. Change **to**:

Identification

A. 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).

B. Extract a quantity of the suppositories containing 50 mg of Bisacodyl with 20 ml of *dichloromethane*, filter evaporate the filtrate to dryness and dissolve the residue in 10 ml of a 0.5 per cent v/v solution of *sulphuric acid*. To 2 ml of the solution, add *sulphuric acid*. A reddish-violet colour is produced on addition of the concentrated acid.

C. Boil 2 ml of the solution obtained in test B with a little *nitric acid*; a yellow colour is produced. Cool and add *5M sodium hydroxide*; the colour become yellowish brown.

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 4 volumes of *glacial acetic acid*, 30 volumes of *acetonitrile* and 66 volumes of *water*.

Test solution (a). Disperse a quantity of the suppositories containing 25 mg of Bisacodyl in the solvent mixture and dilute to 50.0 ml with the solvent mixture, centrifuge and filter.

Test solution (b). Dilute 2.0 ml of test solution (a) with 20.0 ml with the solvent mixture.

Reference solution (a). A 0.005 per cent w/v solution of *bisacodyl IPRS* in the solvent mixture.

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

Reference solution (c). A solution containing 0.5 per cent w/v of *bisacodyl IPRS,* 0.004 per cent w/v, each of, *bisacodyl impurity A IPRS* and *bisacodyl impurity B IPRS,* 0.0075 per cent w/v of *bisacodyl impurity C IPRS*, 0.0025 per cent w/v of *bisacodyl impurity E IPRS* and 0.001 per cent w/v of *bisacodyl impurity D IPRS* in *acetonitrile*. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (d). Dissolve 5 mg of *bisacodyl impurity F IPRS* in 2.5 ml of *acetonitrile* and dilute to 5.0 ml with the solvent mixture.

Reference solution (e). Dilute 1.0 ml of reference solution (b) with 10.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm × 4.6 mm, packed with endcapped octadecylsilane bonded to porous silica (Such as Symmetry C18) (5 µm),
- mobile phase: a mixture of 45 volumes of *acetonitrile* and 55 volumes of 0.16 per cent w/v solution of *ammonium formate,* adjusted to pH 5.0 with *anhydrous formic acid,*
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 265 nm,
- injection volume: 20 µl.

Name	Relative retention time	Correction factor
Bisacodyl impurity D[1]	0.12	---
Bisacodyl impurity A[2]	0.2	0.7
Bisacodyl impurity B[3]	0.4	---
Bisacodyl impurity C[4]	0.45	---
Bisacodyl impurity E[5]	0.9	---
Bisacodyl (Retention time is about 13 minutes)	1.0	---
Bisacodyl impurity F*	2.6	---

*Unknown structure.

[1]Di-sodium (pyridin-2-ylmethylene)bis(4,1-phenylene) bis(sulphate),

[2]4,4'-(pyridine-2-ylmethylene) diphenol,

[3]2-((RS)-(4-hydroxyphenyl)(pyridine-2-yl)methyl)phenol,

[4]4-((RS)-(4-hydroxyphenyl) (pyridine-2-yl)methyl)phenyl acetate,

[5]2-((RS)-(4-acetyloxy)phenyl)(pyridine-2-yl)methyl)phenyl acetate.

Inject reference solution (c) and (d) to identify the peaks due to bisacodyl impurity A, B, C, D, E and bisacodyl impurity F, respectively.

Inject reference solution (c). The test is not valid unless the peak-to-valley ratio is not less than 1.5, where *Hp* = height above the baseline of the peak due to bisacodyl impurity E and *Hv* = height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

Inject reference solution (b), (e) and test solution (a). In the chromatogram obtained with test solution (a), the area of any peak corresponding to bisacodyl impurity C is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent), the area of any peak corresponding to bisacodyl impurity A is not more than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.8 per cent), the area of any peak corresponding to bisacodyl impurity E is not more than 0.5 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 bisacodyl impurity F is not more than 0.3 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.3 per cent), the area of any peak corresponding to bisacodyl impurity D is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent), the area of any other secondary peak is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of the areas of all the secondary peaks other than bisacodyl impurity A,C,D,E and F, is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent). Ignore any peak with an area less than the area of the principal peak in the chromatogram obtained with reference solution (e) (0.1 per cent).

Assay. Change **to**:

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

Inject reference solution (c). The test is not valid unless the peak-to-valley ratio is not less than 1.5, where *Hp* = height above the baseline of the peak due to bisacodyl impurity E and *Hv* = height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

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

Calculate the content of bisacodyl, $C_{22}H_{19}NO_4$ in the suppositories.

Bisacodyl Gastro-resistant Tablets. Page 1644 (*Effective from 1st August 2024*)

Identification. Change **to**:

Identification

A. 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).

B. Extract a quantity of the powdered tablets containing 50 mg of Bisacodyl with 20 ml of *dichloromethane*, filter evaporate the filtrate to dryness and dissolve the residue in 10 ml of a 0.5 per cent v/v solution of *sulphuric acid*. To 2 ml of the solution, add *sulphuric acid*. A reddish-violet colour is produced on addition of the concentrated acid.

C. Boil 2 ml of the solution obtained in test B with a little *nitric acid*; a yellow colour is produced. Cool and add *5M sodium hydroxide*; the colour become yellowish brown.

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

Solvent mixture. 4 volumes of *glacial acetic acid*, 30 volumes of *acetonitrile* and 66 volumes of *water*.

Test solution (a). Disperse a quantity of the powdered tablets containing 25 mg of Bisacodyl in the solvent mixture and dilute to 50.0 ml with the solvent mixture.

Test solution (b). Dilute 2.0 ml of test solution (a) with 20.0 ml with the solvent mixture.

Reference solution (a). A 0.005 per cent w/v solution of *bisacodyl IPRS* in the solvent mixture.

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

Reference solution (c). A solution containing 0.5 per cent w/v of *bisacodyl IPRS,* 0.004 per cent w/v, each of, *bisacodyl impurity A IPRS* and *bisacodyl impurity B IPRS,* 0.0075 per cent w/v of *bisacodyl impurity C IPRS*, 0.0025 per cent w/v of *bisacodyl impurity E IPRS* and 0.001 per cent w/v of *bisacodyl impurity D IPRS* in *acetonitrile*. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (d). Dissolve 5 mg of *bisacodyl impurity F IPRS* in 2.5 ml of *acetonitrile* and dilute to 5.0 ml with the solvent mixture.

Reference solution (e). Dilute 1.0 ml of reference solution (b) with 10.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm × 4.6 mm, packed with endcapped octadecylsilane bonded to porous silica (Such as Symmetry C18) (5 µm),
- mobile phase: a mixture of 45 volumes of *acetonitrile* and 55 volumes of 0.16 per cent w/v solution of *ammonium formate,* adjusted to pH 5.0 with *anhydrous formic acid,*
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 265 nm,
- injection volume: 20 µl.

Name	Relative retention time	Correction factor
Bisacodyl impurity D[1]	0.12	---
Bisacodyl impurity A[2]	0.2	0.7
Bisacodyl impurity B[3]	0.4	---
Bisacodyl impurity C[4]	0.45	---
Bisacodyl impurity E[5]	0.9	---
Bisacodyl (Retention time is about 13 minutes)	1.0	---
Bisacodyl impurity F[*]	2.6	---

[*]Unknown structure.

[1]Di-sodium (pyridin-2-ylmethylene)bis(4,1-phenylene) bis(sulphate),

[2]4,4'-(pyridine-2-ylmethylene) diphenol,

[3]2-((RS)-(4-hydroxyphenyl)(pyridine-2-yl)methyl)phenol,

[4]4-((RS)-(4-hydroxyphenyl) (pyridine-2-yl)methyl)phenyl acetate,

[5]2-((RS)-(4-acetyloxy)phenyl)(pyridine-2-yl)methyl)phenyl acetate.

Inject reference solution (c) and (d) to identify the peaks due to bisacodyl impurity A, B, C, D, E and bisacodyl impurity F, respectively.

Inject reference solution (c). The test is not valid unless the peak-to-valley ratio is not less than 1.5, where *Hp* = height above the baseline of the peak due to bisacodyl impurity E and *Hv* = height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

Inject reference solution (b), (e) and test solution (a). In the chromatogram obtained with test solution (a), the area of any peak corresponding to bisacodyl impurity C is not more than 1.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1.5 per cent), the area of any peak corresponding to bisacodyl impurity A is not more than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.8 per cent), the area of any peak corresponding to bisacodyl impurity E is not more than 0.5 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 bisacodyl impurity F is not more than 0.3 times the area of the principal peak in the chromatogram obtained with

reference solution (b) (0.3 per cent), the area of any peak corresponding to bisacodyl impurity D is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent), the area of any other secondary peak is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 per cent) and the sum of the areas of all the secondary peaks other than bisacodyl impurity A,C,D,E and F, is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent). Ignore any peak with an area less than the area of the principal peak in the chromatogram obtained with reference solution (e) (0.1 per cent).

Assay. Change **to**:

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

Inject reference solution (c). The test is not valid unless the peak-to-valley ratio is not less than 1.5, where *Hp* = height above the baseline of the peak due to bisacodyl impurity E and *Hv* = height above the baseline of the lowest point of the curve separating this peak from the peak due to bisacodyl.

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

Calculate the content of bisacodyl, $C_{22}H_{19}NO_4$ in the tablets.

Brivaracetam Oral Solution. Page 5146

Microbial contamination. Line 3

Change **from**: not more than 10^3 CFU per g.

to: not more than 10^1 CFU per ml.

Calcium Carbonate. Page 4045

Magnesium and alkali metals. Line 5 to 8

Change **from**: To 50 ml of the filtrate add 1.5 ml of *dilute sulphuric acid*, evaporate to dryness on water-bath, heat the residue to redness, allow to cool and weigh. The residue weights not more than 5 mg (1.0 per cent).

to: To 50 ml of the clear filtrate, add 0.5 ml of *sulphuric acid* and evaporate the mixture on a steam bath to a small volume. Carefully heat over a free flame to dryness and continue heating to complete decomposition and volatilization of ammonium salts. Finally ignite the residue to constant weight at 600 ± 50°. The residue weight not more than 5 mg (1.0 per cent).

Calcium Chloride. Page 4046

Magnesium and alkali metals. Line 4 to 7

Change **from**: To 50 ml of the filtrate add 1.5 ml of *dilute sulphuric acid*, evaporate to dryness on water-bath, heat the residue to redness, allow to cool and weigh. The residue weights not more than 5 mg (1.0 per cent).

to: To 50 ml of the clear filtrate, add 0.5 ml of *sulphuric acid* and evaporate the mixture on a steam bath to a small volume. Carefully heat over a free flame to dryness and continue heating to complete decomposition and volatilization of ammonium salts. Finally ignite the residue to constant weight at 600 ± 50°. The residue weight not more than 5 mg (1.0 per cent).

Crospovidone. Page 5164

Vinylpyrrolidinone (Impurity A). *Reference solution (a)*, line 1

Change **from**: 0.05 per cent

to: 0.0005 per cent

Nitrogen. Line 5 and 6

Change **from**: 1 part of *cupric sulphate*; omit the use of *hydrogen peroxide*.

to: 1 part of *cupric sulphate*; add 3-4 glass beads. Wash any adhering particles from the neck into the flask with a small quantity of *water*. Add 7 ml of *sulphuric acid*, allowing it to run down the inside wall of the flask and mix the contents, omit the use of *hydrogen peroxide*.

Vinylpyrrolidinone (Impurity A). *Reference solution (a)*, line 2

Change **from**: *1-vinylpyrrolidin-2-one IPRS*

to: *1-vinylpyrrolidin-2-one*

Reference solution (b). Line 2

Change **from**: *1-vinylpyrrolidin-2-one IPRS*

to: *1-vinylpyrrolidin-2-one*

Desogestrel and Ethinyl Estradiol Tablets. Page 2042

Dissolution. Line 2

Change **from**: 0.05 per cent,

to: 0.3 per cent,

Line 4

Change **from**: 50 rpm

to:100 rpm

Dexamethasone Injection. Page 2049

Assay

Reference solution (a), line 1

Change **from**: 0.008 per cent

to:0.009 per cent

After chromatographic system, para 1

Change **to**: Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to dexamethasone sodium phosphate and betamethasone sodium phosphate is not less than 2.2 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 2.0 per cent in the chromatogram obtained with reference solution (a).

Dexamethasone Sodium Phosphate. Page 5170

Related substances. Chromatographic system, line 1

Change **form**:a stainless steel column 25 cm × 4.6 mm,

to:a stainless steel column 12.5 cm × 4.6 mm,

Ethanol. Chromatographic system, line 10 and 11

Change **from**:*hydrogen* as carrier gas.

to: *helium* as carrier gas.

Dolutegravir, Lamivudine and Tenofovir Disoproxil Fumarate Tablets. Page 2159

Dissolution. Line 4

Change **from**:2.5 g of *sodium dodecyl sulphate*

to:5 g of *sodium lauryl sulphate*

Line 7

Change **from**: 60 rpm

to: 75 rpm

Domperidone. Page 2162

Para 2, line 1 and 2

Change **from**:Domperidone contains not than 99.0 per cent and more than 101.0 per cent

to:Domperidone contains not less than 99.0 per cent and not more than 101.0 per cent

Esomeprazole Gastro-resistant Capsules. Page 2274

Related substances. Last para, line 4

Change **from**: 0.5 per cent

to:0.2 per cent

Esomeprazole Gastro-resistant Tablets. Page 2276 and 5179

Identification. Change **to**:

Identification

A. In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

B. Enantiomeric purity (see Tests).

Ethanol. Page 5180

Light absorption. Line 2

Change **from**:340 nm (2.4.7), it shows an absorption maximum

to: 340 nm (2.4.7), using 5 cm cell. It shows an absorption maximum

Related substances. Last para

Change **to**: The sum of areas of all other secondary peak obtained with test solution (b) is not more than the area of 4-methylpentan-2-ol peak in the chromatogram obtained with test solution (b) (300 ppm). Ignore any peak with an area less than 0.03 times the area of 4-methylpentan-2-ol peak in the chromatogram obtained with test solution (b) (9 ppm).

Fluphenazine Decanoate Injection. Page 5184

Assay. *Reference solution (c),* line 3

Change **from**:0.08 per cent

to:0.008 per cent

Gabapentin Capsules. Page 2446

Related substances.

Test solution. Change **to**:

Test solution. Disperse a quantity of mixed contents of the capsules containing 0.5 g of Gabapentin in diluent, with the aid of ultrasound and dilute to 25.0 ml with diluent, filter.

Gabapentin Tablets. Page 2447

Related substances.

Test solution. Change **to**:

Test solution. Disperse a quantity of powdered tablets containing 0.5 g of Gabapentin in diluent, with the aid of ultrasound and dilute to 25.0 ml with diluent, filter.

Gliclazide Prolonged-release Tablets. Page 5190

Related substances. Last para, line 8 and 9

Change **from**: 0.5 per cent

to: 0.2 per cent

Hydroxyprogesterone Hexanoate. Page 2546

Para 2, line 3

Change **from**: calculated on the dried basis.

to: calculated on anhydrous basis.

Hydroxypropylmethylcellulose. Page 5191

Viscosity. B. Para 2, Table, line 3

Change **from**: 500 to less than 9500

to: 3500 to less than 9500

Assay. Chromatographic system, temperature, line 2

Change **from**: 50-110

to: 50-100

Lactulose Solution. Page 5202

Para 1, line 2

Change **from**: Lactose Concentrate

to: Lactulose Concentrate.

Light Magnesium Carbonate. Page 5308

Identification. Line 5

Change **from**: not less than 0.15 g per ml.

to: not more than 0.15 g per ml.

Light Magnesium Oxide. Page 5308

Identification. Line 4

Change **from**: not less than 0.15 g per ml.

to: not more than 0.15 g per ml.

Metoprolol Tartrate. Page 2916

Identification. B, line 1

Change **from**: reaction (C)

to: reaction (B)

Metronidazole Benzoate. Page 2923

Identification. Change **to**:

Identification

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

B. When examined in the range 230 nm to 360 nm (2.4.7), a 0.001 per cent w/v solution in *ethanol* shows an absorption maximum only at about 309 nm; absorbance at about 309 nm, about 0.3.

C. It gives reaction (B) of benzoates (2.3.1).

Assay. Change **to**:

Assay. Dissolve 0.25 g in 50 ml of *anhydrous acetic acid*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (2.4.25). Carry out a blank titration.

1 ml of *0.1 M perchloric acid* is equivalent to 0.02753 g of $C_{13}H_{13}N_3O_4$.

Metronidazole Gel. Page 5222

Related substances. After chromatographic system, para 2, line 1 and 2

Change **from**: *the test solution*

to: *test solution (a)*

Assay

Test solution. Delete the requirement.

Miltefosine. Page 5226

Related substances. A

After RRT table, line 6 and 7

Change **from**: [6]octadecyl(2-(trimethylammonio)ethyl)phosphate,

[7]hexadecyl dihydrogen phosphate.

to: [6]hexadecyl dihydrogen phosphate,

[7]octadecyl(2-(trimethylammonio)ethyl)phosphate.

B. *Reference solution (a)*. Line 2 and 3

Change **from**: *miltefosine impurity F IPRS* (octadecyl(2-(trimethylammonio)ethyl)phosphate)

to: *miltefosine impurity F IPRS*

Reference solution (c). Line 2 and 3

Change **from**: *miltefosine impurity A IPRS* (dodecyl(2-(trimethylammonio)ethyl)phosphate)

to: *miltefosine impurity A IPRS*

Miltefosine Capsules. Page 5229

Dissolution. Line 2

Change **from**: *0.01 M hydrochloric acid*

to: *0.1 M hydrochloric acid*

Related substances. Chromatographic system, line 6

Change **from**: 45 volumes

to: 40 volumes

After RRT table, line 8

Change **from**: [6]hexadecyl dihydrogen phosphate.

to: [6]octadecyl(2-(trimethylammonio)ethyl)phosphate.

Morphine Sulphate. Page 2965

Para 2, line 2 and 3

Change **from**: calculated on the dried basis.

to: calculated on the anhydrous basis.

Moxifloxacin Tablets. Page 5233

Related substances. Chromatographic system

Insert before line 3,

– column temperature: 50°,

Mustine Hydrochloride. Page 5235

Chloride content. Line 4 and 7

Change **from**: *0.2 M silver nitrate*

to: *0.02 M silver nitrate*

Nepafenac Ophthalmic Suspension. Page 5238

Stabilized Oxychloro Complex. Delete the requirement.

Nimodipine. Page 3068

Assay. Line 5

Change **from**: determining the end-point potentiometrically (2.4.25).

to: titrate slowly towards the end of the titration.

Ofloxacin. Page 5240

Methanol and Ethanol. Delete the requirement.

Olmesartan Medoxomil. Page 3109

Assay. Change **to**:

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

Test solution. Dissolve 25 mg of the substance under examination in *acetonitrile* and dilute to 50.0 ml with *acetonitrile*.

Reference solution. A 0.05 per cent w/v solution of *olmesartan medoxomil IPRS* in *acetonitrile.*

Chromatographic system

– mobile phase. a mixture of 75 volumes of mobile phase A and 25 volumes of mobile phase B.

Inject the reference solution. The test is not valid unless 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 $C_{29}H_{30}N_6O_6$.

Ondansetron Tablets. Page 5249

Assay. *Reference solution*, line 4

Change **from**: 0.0005 per cent

to: 0.005 per cent

Pantoprazole Sodium. Page 5249

Related substances. B. Chromatographic system, line 5

Change **from**: *potassium dihydrogen phosphate*

to: *dipotassium hydrogen orthophosphate*

Related substances. B. After chromatographic system, para 2, line 1

Change **from**: Inject reference solution (a) and the test solution at 305 nm.

to: Inject reference solution (a) at 290 nm and the test solution at 305 nm.

Pantoprazole for Injection. Page 5251

Para 2, line 2 and 3

Change **from**: sterile Water for Injections,

to: sterile 0.9 per cent w/v sodium chloride injection,

Paroxetine Hydrochloride Hemihydrate. Page 3207

Related substances. Chromatographic system, mobile phase A, line 1

Change **from**: 5 volumes of *trifluoroacetic acid*,

to: 0.5 volume of *trifluoroacetic acid*,

mobile phase B, line 1

Change **from**: 5 volumes of *trifluoroacetic acid*,

to: 0.5 volume of *trifluoroacetic acid*,

Pioglitazone Hydrochloride. Page 5259

Assay

Change **from**: Use the chromatographic system as described under Related substances.

to: Use the chromatographic system as described under Related substances with the following modification.

Chromatographic system

- injection volume: 20 µl.

Pregabalin Capsules. Page 3344 (*Effective from 1st August 2024*)

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Disperse a quantity of the mixed contents of capsules containing 0.3 g of Pregabalin in *water*, with the aid of ultrasound with intermittent shaking and dilute to 25.0 ml with *water*, filter.

Reference solution (a). A 0.0024 per cent w/v solution of *pregabalin IPRS* in *water*.

Reference solution (b). A 0.0024 per cent w/v solution of *pregabalin impurity A IPRS* (pregabalin lactam impurity*)* in *water*.

Reference solution (c). A solution containing 1.2 per cent w/v of *pregabalin IPRS,* 0.0024 per cent w/v, each of, *pregabalin impurity 1 IPRS* (pregabalin carbonyl impurity/ isobutylglutarmonamide (R-isomer)), *pregabalin impurity D IPRS* (Isopropyl mandelate) and *pregabalin impurity C IPRS* (mandelic acid) in *water.*

Chromatographic system

- a stainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS-3V),
- column temperature: 40º,
- mobile phase: A. a mixture of 100 volumes of a buffer solution prepared by dissolving 2.72 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 5.9 with *1M sodium hydroxide* and 2 volumes of *acetonitrile,*

  B. *acetonitrile*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 50 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	98	2
3	98	2
31	75	25
43	45	55
48	45	55
50	98	2
60	98	2

Name	Relative retention time	Correction factor
Pregabalin impurity C[1]	0.6	0.01
Pregabalin (Retention time about 12 minutes)	1.0	---
Pregabalin impurity 1[2]	1.4	0.3
Pregabalin impurity A[3]	3.1	---
Pregabalin impurity D[4]	3.5	0.01

[1](2*RS*)-2-hydroxy-2-phenylacetic acid,

[2]*rac*-3-(carbamoylmethyl)-5-methylhexanoic acid (isobutylglutarmonoamide),

[3](4*S*)-4-(2-methylpropyl)pyrrolidin-2-one,

[4]1-methylethyl (2*RS*)-2-hydroxy-2-phenylacetate.

Inject reference solution (c) to identify the peaks due to pregabalin impurity 1, pregabalin impurity C and pregabalin impurity D.

Inject reference solution (c). The test is not valid unless the resolution between the peaks due to pregabalin impurity 1 and pregabalin is not less than 13.

Inject reference solution (a), (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to pregabalin impurity A is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.2 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 (a) (0.2 per cent) and the sum of the areas of all the secondary peaks is not more than 5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 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 (a) (0.1 per cent).

Rabeprazole Sodium. Page 5268

Related substances. Para after RRT Table

Change **to**:

[1]Sodium 1-(1*H*-benzimidazol-2-yl)-3-methyl-4-oxo-1,4-dihydropyridine-2-carboxylate,

[2]1*H*-Benzimidazol-2-ol,

[3]1*H*-Benzimidazole-2-thiol,

[4]2-{[(1*H*-Benzimidazol-2-yl)sulphonyl]methyl}-4-(3-methoxypropoxy)-3-methylpyridine1-oxide,

[5]2-{[(1*H*-Benzimidazol-2-yl)sulphinyl]methyl}-4-(3-methoxypropoxy)-3-methylpyridine 1-oxide,

[6]2-{[(4-Methoxy-3-methylpyridin-2-yl)methyl]sulfinyl}benzimidazole,

[7]2-({[4-(3-Methoxypropoxy)-3-methyl-2-pyridyl]methyl}sulphonyl) benzimidazole,

[8]2-{[(4-Chloro-3-methyl-2-pyridyl)methyl]sulphinyl}benzimidazole,

[9]2-{[(4-Methoxy-3-methylpyridin-2-yl)methyl]thio}benzimidazole,

[10]2-{[4-(3-Methoxypropoxy)-3-methyl-2-pyridyl]methylthio} benzimidazole.

Remogliflozin Etabonate. Page 5271

Assay. Last line

Change **from**: $C_{26}H_{38}N_2O_9O$

to: $C_{26}H_{38}N_2O_9$

Assay. Line 4 and 5

Delete the following requirement.

Chromatographic system

– spectrophotometer set at 278 nm,

Saline Nasal Solution. Page 5277

pH

Change **from**: 6.5 to 7.5.

to: 4.5 to 7.5.

Microbial contamination. Line 4 and 5

Change **from**: *Pseudomonas aeruginosa, Staphylococcus aureus* and *Burkholderia cepacia*.

to: *Pseudomonas aeruginosa* and *Staphylococcus aureus*.

Sodium Benzoate. Page 5278

Assay. Insert before last line.

1 mg of benzoic acid, C_6H_5COOH is equivalent to 1.18 mg of sodium benzoate, $C_7H_5NaO_2$.

Sofosbuvir and Velpatasvir Tablets. Page 5281

Related substances

For Velpatasvir —

Impurity table, line 5 and 6

Change **from**: *S*-Moc Phenyl glycine isomer or Diastereomer impurity[4]

to: *S*-Moc Phenyl glycine isomer or Diastereomer impurity[4*]

After impurity table, para 2, line 4

Change **from**: twice

to: 4 times

Line 7

Change **from**: not more than

to: not more than twice

Line 9

Change **from**: not less than

to: not less than twice

Spironolactone. Page 5284

Specific optical rotation. Line 4

Change **from**: *ethanol*.

to: *ethanol (95 per cent)*.

Tartaric Acid. Page 3719

Identification. C

Change **from**: It gives reactions (A) and (B) of tartrates (2.3.1).

to: It gives reaction (A) of tartrates (2.3.1).

Velpatasvir. Page 5297

Related substances.

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

Reference solution (b). A solution containing 0.25 per cent w/v of *velpatasvir IPRS*, 0.00125 per cent w/v, each of, *velpatasvir impurity A IPRS*, *velpatasvir impurity B IPRS*, *velpatasvir impurity C IPRS*, *velpatasvir impurity D IPRS*, *velpatasvir impurity E IPRS*, *velpatasvir impurity F IPRS* and *velpatasvir impurity G IPRS* in *acetonitrile*. Dilute 1.0 ml of the solution to 10.0 ml with the solvent mixture.

Reference solution (c). Delete the requirement.

After chromatographic system, para 1

Change **to**: Inject reference solution (b) to identify the peaks due to velpatasvir impurity A, B, C, D, E, F and G.

Zoledronic Acid. Page 3998 and 5301

Identification. B, line 2

Change **from**: the test solution

to: test solution (b)

Line 3

Change **from**: the reference solution.

to: reference solution (a).

Related substances. After impurity table, para 2, line 1

Change **from**: the test solution.

to: test solution (a).

HERBS AND HERBAL PRODUCTS

Arachis Oil. Page 4171

Refractive index

Change **from**: 1.467 to 1.470.

to: 1.462 to 1.464 at 40°.

Coconut Oil. Page 4207

Iodine value

Change **from**: 82 to 90.

to: 7.5 to 10.

Dill Seed Oil. Page 4214

Assay. *Reference solution (a)*

Change **from**: A 2.0 per cent w/v solution of *cis-dihydrocarvone IPRS* in *ethanol (95 per cent)*.

to: A 2.0 per cent w/v solution of *d-limonene IPRS* in *ethanol (95 per cent)*.

After chromatographic system, para 2

Change **from**: Calculate the cis-dihydrocarvone, and L-carvone contents in the oil under examination using the ratios.

to: Calculate the limonene, and L-carvone contents in the oil under examination using the ratios.

BIOTECHNOLOGY DERIVED THERAPEUTIC PRODUCTS

Follicle Stimulating Hormone Injection. Page 4623

Identification

Insert before Identification A

NOTE — Identification B. Determine by Isoelectric focusing (2.4.33) may be omitted if the recombinant Follicle Stimulating

Hormone injection is prepared from recombinant Follicle Stimulating Hormone/recombinant Follicle Stimulating Hormone Concentrated Solution complied as per monograph in current edition of IP.

Biphasic Insulin Lispro Injection. Page 4638

Related Proteins. *Reference solution*, line 3 and 4

Change **from**: 0.8 per cent and 11 per cent w/v of A21 desamido Insulin.

to: a concentration between 0.8 per cent and 11 per cent w/v of A21 desamido Insulin.

Pegfilgrastim Injection. Page 5336

Impurities with charges differing from that of Pegfilgrastim

Method A. Last para, line 4 and 5

Change **from**: the pI of the principal band is 7.4 to 7.8.

to: the pI of the principal band is 5.7 - 6.3.

Method B. After chromatographic system, para 1, line 4

Change **from**: not less than >8.

to: not less than 8.

Bacterial endotoxin. Line 1 and 2

Change **from**: Not more than 33.3 EU per mg dose of Pegfilgrastim.

to: Not more than 33.33 EU per mg of Pegfilgrastim.