भारतीय भैषजसंहिता 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 201 002 (U.P.), INDIA

डा. राजीव सिंह रघुवंशी
सचिव-सह-वैज्ञानिक निदेशक

Dr. Rajeev Singh Raghuvanshi
Secretary-cum-Scientific Director

F. No. T.11013/02/2018-AR&D

Date: 30th December 2021

To,

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

Subject: Amendment List 09 to IP 2018

The 8th Edition of Indian Pharmacopoeia (IP) 2018 has become effective from 1st January, 2018. Based on scientific inputs, some IP monographs needed up-gradation and accordingly Amendment List 09 to IP 2018 is issued containing such amendments. The same shall be effective from **31st December 2021**.

This is for notice and compliance with the IP 2018.

(Dr. Rajeev Singh Raghuvanshi)
Secretary-cum-Scientific Director

Encl. Amendment List 09 to IP 2018

Amendment List 09 to IP-2018

2.4.26. Solubility. Page 220

Dapoxetine Hydrochloride. Page 228

Change **to**: Soluble in *methanol, acetonitrile, dichloromethane* and *water;* sparingly soluble in *isopropyl alcohol.*

Enoxaparin Sodium. Page 231

Change **from**: Soluble in *ethanol*; sparingly soluble in *dichloromethane*; practically insoluble in *water*.

to: Freely soluble in *water.*

Imatinib mesylate. Page 235

Change **from**: Soluble in *water.*

to: Freely soluble in *water,* slightly soluble in *ethanol,* practically insoluble in *methylene chloride.*

Neotame. Line 2

Change **from**: soluble in *water.*

to: sparingly soluble in *water.*

Parenteral Preparations. Page 1113

Powders for injection. Page 1116

Uniformity of content. Line 4

Change **from**: 50 mg

to: 40 mg

Amphotericin B Injection. Page 1237

Insert before **Tests**

Identification

Dissolve a quantity of powder for injection containing 25 mg of Amphotericin B in 5 ml of *dimethyl sulphoxide*, add sufficient *methanol* to produce 50 ml, and dilute 2 ml to 200 ml with *methanol*. When examined in the range 300 nm to 450 nm (2.4.7), the resulting solution shows absorption maxima at about 362 nm, 381 nm, and 405 nm. The ratio of the absorbance at the maximum at about 362 nm to the absorbance at the maximum at about 381 nm, 0.5 to 0.6; the ratio of the absorbance at the maximum at about 381nm to the absorbance at the maximum at about 405 nm, about 0.9.

Assay. Para 2, line 1 and 2

Change **from**: *dimethylformamide*

to: *dimethylsulphoxide*

Ammonium Chloride. Page 1225

Identification

Change **from**: It gives the reactions of ammonium salts and of chlorides (2.3.1).

to: It gives the reactions of chlorides (2.3.1) and 10 ml of a 10 per cent w/v solution in *carbon dioxide-free water* gives reaction of ammonia salts (2.3.1).

Aspartame. Page 1273

pH. Line 1

Change **from**: About 5.0, determine in a 0.8 per cent w/v solution.

to: 4.0 to 6.0, determine in a 0.8 per cent w/v solution.

Artemether and Lumefantrine Tablets.

Page 4612

Identification. Change **to**:

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.

Dissolution. Change **to**:

Dissolution (2.5.2)

For Artemether —

Apparatus No. 2 (Paddle),
Medium. 1000 ml of a buffer solution prepared by dissolving 1.4 g of *disodium hydrogen phosphate anhydrous* in 1000 ml of *water*, add 10 g of *sodium lauryl sulphate* and adjust the pH to 7.2 with *dilute hydrochloric acid*,
Speed and time.100 rpm and 60 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 20 mg of *artemether IPRS* in 2 ml of *acetonitrile*, with the aid of ultrasound and dilute to 100.0 ml with the dissolution medium. Dilute 1.0 ml of the solution to 10.0 ml with the dissolution medium.

Chromatographic system

– a stainless steel column 25 cm x 4.6 mm packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil ODS-3V),

- column temperatue: 40°,
- sample temperature: 10°,
- mobile phase: A. a buffer solution prepared by mixing 12 ml of *triethylamine* with 1000 ml of *water*, adjusted to pH 2.3 with *orthophosphoric acid*,
  B. a mixture of 95 volumes of *acetonitrile* and 5 volumes of *water*,
- a gradient programme using the conditions given below,
- flow rate: 2.0 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 100 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	27	73
9	30	70
9.5	27	73
12	27	73

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 3.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{16}H_{26}O_5$ in the medium.

Q. Not less than 60 per cent of the stated amount of $C_{16}H_{26}O_5$.

For Lumefantrine —

Apparatus No. 2 (Paddle),
Medium. 1000 ml of 2 per cent w/v solution of *benzalkonium chloride* in *0.1M hydrochloric acid*,
Speed and time. 100 rpm and 60 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. A 0.12 per cent w/v solution of *lumefantrine IPRS* in the mobile phase. Dilute 1.0 ml of the solution to 10.0 ml with the dissolution medium.

Chromatographic system

- a stainless steel column 15 cm x 3.9 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Waters symmetry),
- sample temperature: 10°,
- mobile phase: a mixture of 25 volumes of a buffer solution prepared by dissolving 5.65 g of *sodium-1-hexane sulphonate* and 2.75 g of *sodium dihydrogen phosphate monohydrate* in 800 ml of *water*, add 5.0 ml of *triethylamine* and adjust to pH 2.3 with *dilute orthophosphoric acid*, dilute to 1000 ml with *water* and 75 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 380 nm,
- injection volume: 10 µl.

Inject the reference solution. The test is not valid unless he 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 $C_{30}H_{32}Cl_3NO$ in the medium.

Q. Not less than 60 per cent of the stated amount of $C_{30}H_{32}Cl_3NO$.

Assay. Change **to**:

Assay. Determine by liquid chromatography (2.4.14).

Buffer solution. Mix 12 ml of *triethylamine* with 1000 ml of *water*, adjusted to pH 2.3 with *orthophosphoric acid*.

Solvent mixture. Dilute 20 ml of the buffer solution, 6 ml of *water*, 20 ml of *isopropyl alcohol* to 100.0 ml with *acetonitrile.*

Test solution. Transfer 5 intact tablets into 1000-ml volumetric flask, add 60 ml of *water*, 200 ml of *isopropyl alcohol* and dissolve with the aid of ultrasound for 15 minutes, add 200 ml of buffer solution and 400 ml of *acetonitrile*, dissolve with the aid of ultrasound for 45 minutes by maintaining water temperature of sonicator at 15° and dilute to volume with *accetonitrile*. Dilute a suitable volume of the solution with the solvent mixture to obtain the concentration similar to the reference solution.

Reference solution. A solution containing 0.01 per cent w/v of *artemether IPRS* and 0.06 per cent w/v of *lumefantrine IPRS* in 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 Inertsil ODS-3V),
- column temperatue: 40°,
- sample temperature: 10°,
- mobile phase: A. buffer solution,
  B. a mixture of 95 volumes of *acetonitrile* and 5 volumes of *water*,
- a gradient programme using the conditions given below,
- flow rate: 2 ml per minute,
- spectrophotometer set at 210 nm for artemether and 380 nm for lumefantrine,
- injection volume: 30 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	27	73
9	30	70
9.5	27	73
12	27	73

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent for lumefantrine and not more than 3.0 per cent for artemether.

Inject the reference solution and the test solution.

Calculate the content of $C_{16}H_{26}O_5$ and $C_{30}H_{32}Cl_3NO$ in the tablets.

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

Aspirin Gastro-resistant and Atorvastatin Capsules.Page 4614

Dissolution. *For Aspirin —*

A. Chromatographic system

Insert after line 2

– sample temperature: 15º,

B. Line 2

Change **from** : 1000 ml of *phosphate buffer pH 6.8*,

to : 1000 ml of *mixed phosphate buffer pH 6.8*,

Line 3

Change **from** : Speed and time. 75 rpm and 30 minutes.

to : Speed and time. 100 rpm and 45 minutes.

Aspirin Gastro-resistant and Rosuvastatin Capsules. Page 4617

Dissolution. *For Aspirin —*

A. Chromatographic system

Insert after line 2

– sample temperature: 15º,

Atomoxetine Hydrochloride. Page 1284

Change **from** : Atomoxetine Hydrochloride contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{11}H_{12}I_3NO_2$, calculated on the anhydrous basis.

to : Atomoxetine Hydrochloride contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{17}H_{21}NO$,HCl calculated on the anhydrous basis.

Benzoic Acid. Page 1346

Identification. Change **to**:

Identification

A. Melting point (2.4.21). 121° to 124°.

B. A 5.0 per cent w/v solution in *ethanol (95 per cent)*, gives reaction (a) of benzoates (2.3.1).

Buprenorphine and Naloxone Sublingual Tablets. Page 4622

Para 1, line 3

Change **from** : 94.0 per cent

to : 90.0 per cent

Line 4

Change **from** : 106.0 per cent

to : 110.0 per cent

Assay

Test solution. Change **to**:

Test solution. Disperse a suitable numbers of intact tablets (not less than 13 tablets) in 35 ml of the solvent mixture with the aid of ultrasound for 15 minutes with occasional swirling and shake for 15 minutes, dilute with the solvent mixture to obtain a solution containing 0.052 per cent w/v of Buprenorphine.

Reference solution. Change **to**:

Reference solution. A solution containing 0.057 per cent w/v of *buprenorphine hydrochloride IPRS* and 0.013 per cent w/v of *naloxone hydrochloride IPRS* in the solvent mixture.

Calcium Folinate Injection.Page 1456

Related substances. Last para, line 9 and 10

Change **from** : The sum of areas of all the secondary peaks

to : The sum of areas of all the secondary peaks, other than folinate impurity A

Cyclosporine Eye Drops. Page 4630

Para 1

Change **to**: Cyclosporine Eye Drops is a sterile solution of Cyclosporine in a suitable vehicle.

Assay. Change **to**:

Assay. Determine by liquid chromatography (2.4.14).

Test solution. Dilute a suitable volume of the eye drops containing 20 mg of Cyclosporine to 100.0 ml with *methanol.*

Reference solution. A 0.02 per cent w/v solution of *cyclosporine IPRS* in *methanol.*

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with dimethylsilane bonded to porous silica (5 µm),
- column temperature: 70°,
- mobile phase: a mixture of 55 volumes of *acetonitrile*, 40 volumes of *water*, 5 volumes of *methanol* and 0.05 volume of *orthophosphoric acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 700 theoretical plates, the tailing factor is not more than 1.5 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 $C_{62}H_{111}N_{11}O_{12}$ in the eye drops.

Dolutegravir, Lamivudine and Tenofovir Disoproxil Fumarate Tablets.

Page 4641

Dissolution. Last para

Change **to**: Calculate the content of $C_8H_{11}N_3O_3S$ in test solution (a) and $C_{19}H_{30}N_5O_{10}P$,$C_4H_4O_4$ and $C_{20}H_{19}F_2N_3O_5$ in test solution (b) in the medium.

Ferrous Ascorbate. Page 465

Assay

Ascorbic acid, line 5

Change **from** : wine-red

to : persistent blue

Glycerin. Page 4658

Impurity A and related substances. Change **to**:

Ethylene glycol, diethylene glycol and related substances. Determine by gas chromatography (2.4.13).

Test solution. Mix 5.88 g of Glycerin in *methanol* and dilute to 100.0 ml with *methanol.*

Reference solution (a). A solution containing 0.1 per cent w/v, each of, *ethylene glycol IPRS* and *diethylene glycol IPRS* in *methanol*. To 5.0 ml of the solution, add accurately weighed quantity of 5.88 g of Glycerin and dilute to 100.0 ml with *methanol*.

*Reference solution (b).*A solution containing 0.05 per cent w/v, each of, *glycerin*, *ethylene glycol IPRS* and *diethylene glycol IPRS* in *methanol*.

Chromatographic system
- a fused silica column 30 m × 0.32 mm, packed with 14 per cent cyanopropylphenyl and 86 per centdimethyl-polysiloxane (1µm) (Such as DB-1701),
- temperature:
  column. 100° to 220° @ 7.5° per minute, maintained at 220°,
  inlet port. 220° and detector 250°,
- split ratio: 1:20,
- flame ionization detector,
- flow rate: 38 cm per second using nitrogen as thecarrier gas,
- injection volume: 1µl.

The elution order is ethylene glycol, diethylene glycol and glycerin.

Inject reference solution (a) and (b). Run the chromatogram 3 times the retention time of the glycerin peak.The test is not valid unless the resolution between the peaks due to ethylene glycol and diethylene glycol is not less than 40 and between the peaks due to diethylene glycol and glycerin is not less than 10 in the chromatogram obtained with reference solution (b) and the relative standard deviation for replicate injections is not more than 10 per cent in the chromatogram obtained with reference solution (a).

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to ethylene glycol and diethylene glycol, each of, is not more than the area of the corresponding peaks in the chromatogram obtained with reference solution (a) (0.1 per cent) and the area of any other secondary peak is not more than 0.1 per cent, calculated by area normalisation.

The sum of all the impurities is not more than 1.0 per cent.

Imipenem and Cilastatin Injection. Page 2280

Assay

Insert before **Test solution**

Buffer solution pH 6.8. Dissolve 0.14 g of *monobasic potassium phosphate* in 900 ml of *water*, adjusted to pH 6.8 with *0.5M sodium hydroxide* or *0.5 M orthophosphoric acid* and dilute to 1000 ml with *water* and filter.

Isopropyl Alcohol. Page 4663

Relative density.

Change **to**: 0.785 to 0.789 determined at 20°.

Benzene and related substances. After chromatographic system, para 3, line 4

Change **from**: due to 2- butanol (0. 3 per cent).

to : due to 2- butanol in the chromatogram obtained with reference solution (a) (0.3 per cent).

Assay. Change **to**:

Assay. Determine by gas chromatography (2.4.13), as described under Benzene and related substances.

Inject reference solution (a). The test is not valid unless the resolution between the peaks due to 1-propanol and 2-butanol is not less than 10.

Inject test solution (a). Calculate the content of C_3H_8O by area normalization.

Isopropyl Rubbing Alcohol. Page 4665

Assay. Chromatographic system, line 3

Change **from** : 1.8 µm

to : 1.4 µm

Lamivudine and Zidovudine Tablets.

Page 4668

Related substances.

Chromatographic system, line 1

Change **from** : 3.0 mm

to : 4.6 mm

Line 9

Change **from** : 0.5 ml per minute

to : 1 ml per minute

Luliconazole. Page 4673

Para 2, Insert at the end

calculated on the dried basis.

Luliconazole Lotion. Page 4675

Related substances.

B. *For Luliconazole Z form* and other related substances. After chromatographic system, para 2, line 3

Change **from** : 3.0.

to : 2.0.

Menotropin. Page 2524

Insert synonym

Menotrophin

Insert after **Tests**

NOTE — Menotropin is prepared by suitable collection and extraction procedures followed by purification steps. The method of preparation includes steps that have been shown to remove and / or inactivate extraneous agents including viral agents as determined by a suitable risk based approach as approved by the regulatory authority. The drug substance is negative for HIV, HCV and HBV using validated NAT (Nucleic Acid Test) based assays.

Menotropin for Injection. Page 2526

Insert synonym

Menotrophin for Injection

Insert after **Tests**

NOTE — Tests for Hepatitis B Surface antigen, HCV antibodies and HIV antibodies may be omitted if the menotropin for injection is prepared from menotropin complied as per monograph in current edition of IP. If any excipient of human origin isused, the injection must be free from HIV, HCV and HBV, confirmed by using validated NAT (Nucleic Acid Test) based assays.

Mitomycin Injection. Page 2623

Assay. *Test solution*

Change **to**: *Test solution*. Add an accurately measured volume of *N,N-dimethylacetamide* to 1 container of mitomycin for injection to obtain a solution containing 0.05 per cent w/v of Mitomycin.

Quiniodochlor. Page 3070

Related substances. *Test solution*, line 4 and 5

Change **from** : *5-chloro-7-iodo-8-hydroxyquinoline*

to : *5-7-diiodo-8-hydroxyquinoline*

Rabeprazole Gastro-resistant and Itopride Prolonged-release Capsules.

Page 4695

Dissolution. Change **to**:

Dissolution (2.5.2).

For Rabeprazole Sodium —

NOTE — Prepare the solutions immediately before use, protect the solutions from light.

A. Apparatus No. 2 (Paddle),
Medium. 750 ml of *0.1 M hydrochloric acid*,
Speed and time. 50 rpm and 2 hours.

Determine by liquid chromatography (2.4.14).

Solvent mixture. Equal volumes of mobile phase A and B.

Test solution. Withdraw the medium completely without any loss of residue. Transfer the residue into 50-ml volumetric flask, disperse in 25 ml of mobile phase B, with the aid of ultrasound with intermittent shaking for 10 minutes, at a temperature not exceeding 20°. Add 15 ml of mobile phase A, further ultrasound for 25 minutes with intermittent shaking, at a temperature not exceeding 20°, allow to be at room temperature and dilute to volume with mobile phase A, filter. Dilute 5.0 ml of the solution to 100.0 ml with the solvent mixture.

Reference solution. A 0.002 per cent w/v solution of *rabeprazole sodium IPRS* in the solvent mixture.

Chromatographic system

- a stainless steel column 15 cm × 4.6 mm, packed with octylsilane bonded to porous silica (5 µm) (Such as Hypersil BDS C8),
- sample temperature: 10º,
- mobile phase: A. a buffer solution prepared by dissolving 3.4 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 7.3 with *triethylamine*,
  B. equal volumes of *acetonitrile* and *methanol*,
- a gradient programme using the conditions given below,
- flow rate: 1 ml per minute,
- spectrophotometer set at 284 nm,
- injection volume: 20 µl.

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	62	38
11	62	38
12	40	60
15	40	60
16	62	38
20	62	38

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 $C_{18}H_{20}N_3O_3SNa$ released in the acid medium by subtracting the content of $C_{18}H_{20}N_3O_3SNa$ in the test solution from the total content of rabeprazole sodium $C_{18}H_{20}N_3O_3SNa$ determined in the Assay.

Complies with the acceptance criteria given under acid stage.

B. Apparatus No. 2 (Paddle),

Medium. 1000 ml of a buffer solution pH 8.0 prepared by dissolving 1.56 g of *anhydrous disodium hydrogen phosphate* in 900 ml of *water*, adjusted to pH 8.0 with *dilute orthophosphoric acid* and dilute to 1000 ml with *water*. Add 5 g of *sodium lauryl sulphate* and mix,

Speed and time. 100 rpm and 30 minutes.

Determine by liquid chromatography (2.4.14).

Transfer another 6 capsules and run the apparatus for 2 hours in *0.1 M hydrochloric acid*. Decant the medium without losing the residue, add the buffer solution pH 8.0 and run the apparatus for 30 minutes. Withdraw a suitable volume of the medium and filter.

Testsolution. To 5.0 ml of the filtrate, add immediately 2.0 ml of *0.2M sodium hydroxide* and dilute to 10.0 ml with the dissolution media.

Reference solution. Dissolve 50 mg of *rabeprazole sodium IPRS* in 10 ml of *0.2 M sodium hydroxide*, with the aid of ultrasound, and dilute to 100.0 ml with the dissolution medium. To 1.0 ml of the solution, add 10 ml of *0.2 M sodium hydroxide* and diluteto 50.0 ml with the dissolution medium.

Use chromatographic system as described under test A, using following modification.

- sample temperature: 20º,

Inject the reference solution and the test solution.

Calculate the content of $C_{18}H_{20}N_3O_3S,Na$ in the medium.

Q. Not less than 70 per cent of the stated amount of $C_{18}H_{20}N_3O_3S,Na$.

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

NOTE — Prepare the solutions immediately before use, protect the solutions from light.

Solvent mixture. Equal volumes of mobile phase A and B.

Test solution. Disperse a quantity of the mixed powered content of the capsules containing 100 mg of Rabeprazole Sodium in 250 ml of mobile phase B, with the aid of ultrasound for 10 minutes with intermittent shaking, at a temperature not exceeding 20°. Add 100 ml of mobile phase A, further ultrasound for 20 minutes with intermittent shaking, at a temperature not exceeding 20°, allow to be at room temperature and dilute to 500.0 ml with mobile phase A, filter.

Reference solution. A solution containing 0.02 per cent w/v of *rabeprazole sodium IPRS* and 0.15 per cent w/v of *itopride hydrochloride IPRS* in the solvent mixture. Dilute 2.0 ml of the solution to 200.0 ml with the solvent mixture.

Use chromatographic system as described under Dissolution with the following modification.

– a stainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Kromasil C18),

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	75	25
60	50	50
70	50	50
72	75	25
80	75	25

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 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 at a relative retention time of about 0.21, 0.52 and 1.83 with respect to itopride peak, each of, is not more than 0.75 times the area of the itopride peak in the chromatogram obtained with the reference solution (0.75 per cent), the sum of the areas of all the secondary peaks related to itopride is not more than the area of the itopride peak in the chromatogram obtained with the reference solution (1.0 per cent). The area of any other secondary peak is not more than the area of the rabeprazole peak in the chromatogram obtained with the reference solution (1.0 per cent) and the sum of the areas of all the secondary peaks, excluding itopride impurities is not more than twice the area of the rabeprazole peak in the chromatogram obtained with the reference solution (2.0 per cent).

Assay. Change **to**:

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

Test solution. Mix the contents of 20 capsules. Disperse a quantity of the mixed powdered contents equivalent to 100 mg of Rabeprazole Sodium in 125 ml of mobile phase B, with the aid of ultrasound with intermittent shaking for 10 minutes, at a temperature not exceeding 20°. Add 100 ml of mobile phase A, further ultrasound with intermittent shaking for 25 minutes,at a temperature not exceeding 20°. Allow to be at room temperature and dilute to 250.0 ml with mobile phase A, filter. Dilute 5.0 ml of the solution to 100.0 ml with the solvent mixture.

Reference solution. A solution containing 0.04 per cent w/v of *rabeprazole sodium IPRS* and 0.3 per cent w/v of *itopride hydrochloride IPRS* in the solvent mixture. Dilute 5.0 ml of the solution to 100.0 ml with the solvent mixture.

Inject the reference solution and the test solution.

Calculate the content of $C_{18}H_{20}N_3O_3SNa$ and $C_{20}H_{26}N_2O_4HCl$ in the capsules.

Remdesivir Injection. Page 4702

Related substances. *Test solution*

Change **to**: *Test solution.* Reconstitute 5 vials with 20 ml each, with the solvent mixture and pool the contents in 200-ml volumetric flask, dilute to volume with the solvent mixture. Dilute a suitable volume with the solvent mixture to obtain a solution containing 0.1 per cent w/v of Remdesivir.

Assay. *Test solution*

Change **to**: *Test solution.* Reconstitute 5 vials with 20 ml each, with the solvent mixture and pool the contents in 200-ml volumetric flask, dilute to volume with the solvent mixture. Dilute 2.0 ml of the solution to 50.0 ml with the solvent mixture.

Streptokinase Injection. Page 3263

Insert after **Tests**

NOTE — Tests for Streptodornase and Streptolysin may be omitted if the Streptokinase injection is prepared from Streptokinase complied as per monograph in current edition of IP.

Tenofovir Alafenamide Fumarate.Page 4716

Fumaric acid and tenofovir impurity. After chromatographic system, RRT table

Change **from**:

Name	Relative retention time
Tenofovir alafenamide	1.0
Fumaric acid[1]	3.5
Tenofovir impurity[2]	7.5

[1](2*E*)-but-2-enedioic acid,

[2]({[1-(6-amino-9*H*-purin-9-yl)propan-2-yl]oxy}methyl) phosphonic acid.

to:

Name	Relative retention time
Fumaric acid[1]	0.2
Tenofovir impurity[2]	0.43
Tenofovir alafenamide (Retention time: about 17 minutes)	1.0

[1](2E)-but-2-enedioic acid,

[2]({[1-(6-amino-9*H*-purin-9-yl)propan-2-yl]oxy}methyl) phosphonic acid.

Last para

Change **to**: Inject reference solution (c) and the test solution.

Thiamine Mononitrate. Page 4724

Related substances.

Change **from** :*Reference solution (a).* A 0.00035 per cent w/v solution of *thiamine mononitrile RS* in *water*.

to : *Reference solution (a).* Dissolve 35 mg of *thiamine mononitrile IPRS* in 15.0 ml of 5 per cent v/v solution of *glacial acetic acid* and dilute to 100.0 ml with *water*. Dilute 1.0 ml of the solution to 100.0 ml with *water*.

Last para, lines 17 to 19

Change **from** : 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).

to : Ignore the peak due to nitrate ion at relative retention time of about 0.05 and 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).

Tigecycline. Page 4730

Sterility. Delete the following requirement

Ticarcillin Monosodium Monohydrate 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.

Tigecycline Injection. Page 4732

Para 2

Change **to**: The injection is constituted by dissolving the contents of the sealed container in the requisite amount of sterile Water for Injections or other suitable solvent, immediately before use.

BLOOD AND BLOOD-RELATED PRODUCTS

Human Albumin. Page 3920

Description.

Change **to**: A clear, slightly viscous liquid, it is almost colourless to greenish yellow or amber to green, depending on protein concentration and the method of fractionation used.

Tests

Haem content.

Change **from** : Dilute the preparation under examination.....at 403 nm using water as the compensation liquid is not more than 0.15(2.4.7).

to : Dilute the preparation under examination.....at 403 nm using 0.9 per cent solution of Sodium chloride as the compensation liquid is not more than 0.15 (2.4.7).

BIOTECHNOLOGY DERIVED THERAPEUTIC PRODUCTS

Follicle Stimulating Hormone. Page 3983

Follitropin oligomers.Change **to**:

Follitropin oligomers. Determine by Size-exclusion chromatography (2.4.16) using the normalisation procedure.

Solution (a). Dissolve 118 mg of *sodium dihydrogen phosphate*, 1.65 g of *disodium hydrogen phosphate dihydrate*, and 30.0 g of *sucrose* in 40 ml of *water* and dilute to 100 ml with the same solvent.

S*olution (b).* Dissolve 1 mg of *bovine albumin* in 30 ml of solution (a).

Test solution. Dissolve the preparation under examination in solution (a) to obtain a concentration of 0.25 mg per ml.

Reference solution (a). Dissolve *follitropin IPRS* in solution (a) to obtain a concentration of 0.25 mg per ml.

Reference solution (b). Dissolve the contents of a vial of *follitropin IPRS* in 200 µl of solution (a) and mix with the same volume of solution (b). If necessary, dilute further with solution (a) to obtain a concentration of 0.25 mg per ml.

Chromatographic system
- a stainless steel column 30 cm x 7.8 mm packed with hydrophilic silica gel of a grade suitable for fractionation of globular proteins in the relative molecular mass range of 10000 to 500000 (5 µm),
- mobile phase. a buffer solution prepared by dissolving 14.2 g of *anhydrous sodium sulphate* in 1000 ml of *0.1 M phosphate buffer solution pH 6.7*,
- flow rate: 0.5 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 100 µl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to bovine albumin and follitropin is not less than 1.2.

Inject reference solution (a) and the test solution. The chromatogram obtained with the test solution should correspond to the chromatogram obtained with reference solution (a). The sum of the peaks with the retention time less than that of the principal peak is not more than 0.5 per cent of the total peaks area.

Free subunits.

Last Para, Line 6

Delete the following requirement.

(iv): the recovery is not less than 75 per cent and not more than 125 per cent.

Follicle Stimulating Hormone Concentrated Solution. Page 3991

Follitropin oligomers. Change **to**:

Follitropin oligomers. Determine by Size-exclusion chromatography (2.4.16) using the normalisation procedure.

Solution (a). Dissolve 118 mg of *sodium dihydrogen phosphate*, 1.65 g of *disodium hydrogen phosphate dihydrate*, and 30.0 g of *sucrose* in 40 ml of *water* and dilute to 100 ml with the same solvent.

S*olution (b).* Dissolve 1 mg of *bovine albumin* in 30 ml of solution (a).

Test solution. Dissolve the preparation under examination in solution (a) to obtain a concentration of 0.25 mg per ml.

Reference solution (a). Dissolve *follitropin IPRS* in solution (a) to obtain a concentration of 0.25 mg per ml.

Reference solution (b). Dissolve the contents of a vial of *follitropin RS* in 200 µl of solution (a) and mix with the same volume of solution (b). If necessary, dilute further with solution (a) to obtain a concentration of 0.25 mg per ml.

Chromatographic system
- a stainless steel column 30 cm x 7.8 mm packed with hydrophilic silica gel of a grade suitable for fractionation of globular proteins in the relative molecular mass range of 10000 to 500000 (5µm),
- mobile phase. a buffer solution prepared by dissolving 14.2 g of *anhydrous sodium sulphate* in 1000 ml of *0.1 M phosphate buffer solution pH 6.7*,
- flow rate: 0.5 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 100 µl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to bovine albumin and follitropin is not less than 1.2.

Inject reference solution (a) and the test solution. The chromatogram obtained with the test solution should correspond to the chromatogram obtained with reference solution (a). The sum of the peaks with the retention time less than that of the principal peak is not more than 0.5 per cent of the total peaks area.

Free subunits.

Last Para, Line 6

Delete the following requirement.

(iv): the recovery is not less than 75 per cent and not more than 125 per cent.

Follicle Stimulating Hormone Injection.

Page 3999

Follitropin oligomers. Change **to**:

Follitropin oligomers. Determine by Size-exclusion chromatography (2.4.16) using the normalisation procedure.

Solution (a). Dissolve 118 mg of *sodium dihydrogen phosphate*, 1.65 g of *disodium hydrogen phosphate dihydrate*, and 30.0 g of *sucrose* in 40 ml of *water* and dilute to 100 ml with the same solvent.

Solution (b). Dissolve 1 mg of bovine albumin in 30 ml of solution (a).

Test solution. Use the Drug product as such.

Reference solution (a). Dissolve *follitropin IPRS* in solution (a) to obtain a concentration of 0.037 mg per ml.

Reference solution (b). Dissolve the *follitropin IPRS* in equal volume of solution (a) and solution (b). If necessary, dilute further with solution (a) to obtain a concentration of 0.037 mg per ml.

Chromatographic system

- a stainless steel column 30 cm x 7.8 mm packed with hydrophilic silica gel of a grade suitable for fractionation of globular proteins in the relative molecular mass range of 10000 to 500000 (5 µm),
- mobile phase: a buffer solution prepared by dissolving 14.2 g of *anhydrous sodium sulphate* in 1000 ml of *0.1 M phosphate buffer solution pH 6.7*,
- flow rate: 0.5 ml per minute,
- spectrophotometer set at 215 nm,
- injection volume: 100 µl.

Inject reference solution (b). The test is not valid unless the resolution between the peaks due to bovine albumin and follitropin is not less than 1.2.

Inject reference solution (a) and the test solution. The chromatogram obtained with the test solution should correspond to the chromatogram obtained with reference solution (a). The sum of the peaks with the retention time less than that of the principal peak is not more than 0.5 per cent of the total peaks area.

Recombinant Streptokinase Bulk Solution. Page 4043

Identification E.

Para 3

Change **from** :The sample should have single main band at R_f position pI 5.5 - 6.1 is observed.

to : The sample should have single main band at R_f position pI 5.0 -5.3 is observed.