

डा. राजीव सिंह रघुवंशी
सचिव-सह-वैज्ञानिक निदेशक

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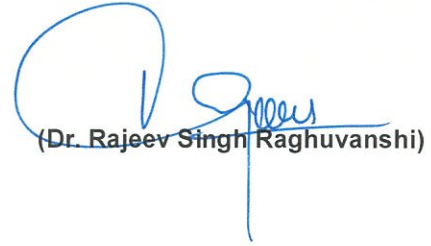
Dr. Rajeev Singh Raghuvanshi
Secretary-cum-Scientific Director

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

IPC is a member of the Pharmacopoeial Discussion Group (PDG)

INDIAN PHARMACOPOEIA
(IP)
Official Book of Drug Standards
in India

IP REFERENCE SUBSTANCES
(IPRS) AND IMPURITIES
Official Physical Standards for
Assessing the Quality of Drugs

NATIONAL FORMULARY OF INDIA
(NFI)
Reference Book to Promote Rational Use
of Generic Medicines

PHARMACOVIGILANCE PROGRAMME OF INDIA
(PvPI)
WHO Collaborating Centre for Pharmacovigilance in
Public Health Programmes and Regulatory Services

4.5. Volumetric Reagents and Solutions

Page 1145

Disodium Edetate, 0.1 M. Para 2, last lineChange **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**Alprostadi Injection.** Page 1407**Assay.** *Internal standard solution.* Line 2Change **from**: *ethylparaben***to**: *ethylparaben IPRS***Amitriptyline Hydrochloride.** Page 1443**Related substances.** *Reference solution (a).* Line 1 to 3Change **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 4Change **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 1Change **from**: 0.8 per cent**to**: 0.4 per cent*Reference solution (c).* Line 2Change **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 3Change **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 1-7Change **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 2Change **from**: *2-vinylpyridine***to**: *2-vinylpyridine IPRS (betahistine mesylate impurity A)***Betahistine Tablets.** Page 1614**Related substances.** *Reference solution (c).* Line 2Change **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:** ¹1-methylpiperazine, ²diphenylmethanol.

to: ¹N-methylpiperazine, ²diphenylmethanol; 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 C₂₄H₂₉ClO₄.

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 50° 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 2Change **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 1Change **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 3Change **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 3Change **from:** *fumaric acid***to:** *fumaric acid IPRS***Metronidazole.** Page 5220**Related substances.** *Reference solution.* Line 2 and 3Change **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 3Change **from:** *tinidazole related compound A IPRS***to:** *2-methyl-5-nitroimidazole IPRS (tinidazole related compound A)**Reference solution (b).* Line 3Change **from:** *tinidazole related compound A IPRS***to:** *2-methyl-5-nitroimidazole IPRS (tinidazole related compound A)***Assay.** *Reference solution (b).* Line 3Change **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 3Change **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 3Change **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 2Change **from:** *nortriptyline impurity A IPRS***to:** *dibenzosuberone IPRS (nortriptyline impurity A)*

Oleic Acid. Page 5243**Loss on ignition.** Line 1Change **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 3Change **from:** chromatogram obtained with the reference solution (a).**to:** chromatogram obtained with the reference solution.**Pantoprazole Sodium.** Page 5249**Related substances.** B, impurity table, line 15 and 16Change **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 3Change **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 6Change **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 4Change **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 paraChange **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: 10°,

Related substances. A. *Reference solution (c)*. Line 2Change **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 2Change **from:** *salicylic acid impurity A***to:** *4-hydroxybenzoic acid IPRS (salicylic acid impurity A)***Sertraline Hydrochloride.** Page 3574**Impurity E.** *Reference solution (a)*. Line 2Change **from:** *sertraline impurity E (mandelic acid)***to:** *mandelic acid IPRS (sertraline impurity E)**Reference solution (b)*. Line 2 and 3Change **from:** *mandelic acid (sertraline impurity E)***to:** *mandelic acid IPRS (sertraline impurity E)***Sertraline Tablets.** Page 3576**Related substances.** *Reference solution (b)*. Line 2Change **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 2Change **from:** not more than**to:** not less than**Sodium Propylparaben.** Page 3623**Related substances.** *Reference solution (a)*. Line 2 and 3Change **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 C₁₇H₂₅N₃O₂ in the medium.

The percentages of the labelled amount of vildagliptin, C₁₇H₂₅N₃O₂ 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)