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**INDIAN PHARMACOPOEIA COMMISSION**
**MIN. OF HEALTH & FAMILY WELFARE**
**GOVERNMENT OF INDIA**
**SECTOR -23, RAJ NAGAR, GHAZIABAD - 201002**

**No. IPC/7035/IP-2014/AL-1** **Dated**: 31-03-2014

**To,**

1. **DCG (I)/ CDSCO, Zonal Offices**
2. **All State Drug Controllers**
3. **Members of Scientific Body of the IPC**
4. **Members of Sub-committee of Scientific Body of the IPC**
5. **Government Analysts**
6. **Director of Drug Laboratories**
7. **IDMA/OPPI/BDMA/FFSAI/Small Scale Industry Associations**

## AMENDMENT LIST- 1 FOR IP 2014

As you are aware that the 7th edition of Indian Pharmacopoeia i.e. IP 2014, would be official from 1st April, 2014. Based on scientific inputs, some monographs, appendices needed upgradation, accordingly an Amendment List No. 1 is issued containing such amendments. This is for notice and immediate compliance.

Yours faithfully,

(Dr. G. N. Singh)
Secretary-cum-Scientific Director

**Encl:**
**Amendment List-1 for IP 2014**

# AMENDMENT LIST- 1 TO IP 2014

***NOTE- There are common printing errors observed in some monographs as 'µ' sign is missing before g or l and 'x' missing between the column dimensions and may be added as required.***

## Introduction. Page xix

**New Drugs Substances Monographs**. Page xxiii, column 3, line 22
Delete: "Levo Bupivacaine Hydrochloride"

Line 24
Insert before Moexipril Hydrochloride
"Mitiglinide Calcium Dihydrate"

**Changed Titles of Monographs**. Page xxvii, column 3, last para
Change **from**: Omeprazole Tablets to Omeprazole Gastro- resistant Tablets
**to**: Omeprazole Capsules to Omeprazole Gastro- resistant Capsules

### 2.4.26. Solubility

Page 184
Insert before **Erythromycin**
**Erlotinib hydrochloride**. Slightly soluble in *methanol*, practically insoluble in *acetonitrile*, *acetone*, *ethyl acetate* and *hexane*.

Page 201
**Travoprost**. Line 2
Change **from**: slightly soluble in *water*.
**to**: insoluble in *water*.

## 4.1. Buffer solutions

Page 760
Insert before **Phosphate Buffer pH 3.6**
**Phosphate Buffer pH 3.2.** To 900 ml of a solution prepared by dissolving 4 g of *sodium dihydrogen phosphate* in 1000 ml of *water* and 100 ml of a solution prepared by diluting 2.5 g of *phosphoric acid* in 1000.0 ml of *water*. Adjust the pH to 3.2 if necessary with *1M sulphuric acid* or *1M sodium hydroxide* as required.

## Acebutolol Tablets. Page 980

**Related substances**. *Reference solution (c)*
Change **to**: *Reference solution (c).* Dilute 1.0 ml of the reference solution (a) to 100.0 ml with *methanol*.

*Reference solution (d).* Delete the requirement.

Last para, line 9
Change **from**: reference solution (d)
**to**: reference solution (c)

## Albendazole. Page 1004

**Identification** B.
Change **to**: B. In the test for Related substances, the principal peak in the chromatogram obtained with test solution corresponds to that of Albendazole in the chromatogram obtained with reference solution (b).

## **Albendazole Oral Suspension**. Page 1005

**Related substances**. Insert before *Test solution*.
*Solvent mixture*. 30 volumes of *0.015 M ammonium dihydrogen orthophosphate* and 70 volumes of *methanol*.

*Test solution*. Line 4
Change **from**: mobile phase A
**to**: the solvent mixture

*Reference solution (a)*. Line 2
Change **from**: mobile phase A
**to**: the solvent mixture

*Reference solution (b)*. Lines 3 and 4
Change **from**: mobile phase A
**to**: the solvent mixture

## **Alginic Acid**. Page 1011

**Assay**. Insert after line 3
Repeat the operation without the substance under examination. The difference between the titrations represents the amount of sodium hydroxide required.

## **Amlodipine Besylate**. Page 1046

**Related substances**. A, *Reference solution (b)*.
Change **to**: *Reference solution (b)*. Dilute 0.5 ml of reference solution (a) to 5.0 ml with *methanol*.

## **Aspirin.** Page 1091

**Salicylic acid**. Delete the requirement.

## **Aspirin and Caffeine Tablets**. Page 1093

Change **from**: Aspirin and Caffeine Tablets contain not less than 330 mg and not more than 370 mg of aspirin, $C_9H_8O_4$, and not less than 27.5 mg and not more than 32.5 mg of caffeine, $C_8H_{10}N_4O_2$.
**to**: Aspirin and Caffeine Tablets contain not less than 92.5 per cent and not more than 107.5 per cent of the stated amount of aspirin, $C_9H_8O_4$ and caffeine, $C_8H_{10}N_4O_2$.

## **Atomoxetine Hydrochloride**. Page 1098

**Dose**. Line 5
Change **from**: 40 mg per kg
**to**: 40 mg

Line 6
Change **from**: 80 mg per kg
**to**: 80 mg

## **Bambuterol Hydrochloride**. Page 1134

**Related substances**. Last para, line 8
Change **from**: 0.1 times
**to**: 0.25 times

## **Betaxolol Hydrochloride**. Page 1183

**Identification.** B
Insert at the end.
The test is not valid unless the chromatogram obtained with reference solution (b) shows two clearly separated spots.

## **Betaxolol Eye Drops**. Page 1184

Para 2, line 3
Change **from**: $C_{18}H_{29}O_{3.}$
**to**: $C_{18}H_{29}NO_{3.}$

**Assay**. Last line
Change **from**: $C_{18}H_{29}O_{3.}$
**to**: $C_{18}H_{29}NO_{3.}$

## **Bisacodyl Gastro-resistant Tablets**. Page 1195

**Uniformity of content**. *Test solution*. Line 2
Change **from**: 100.0 ml
**to**: 50.0 ml

## **Bortezomib**. Page 1200

Para 2, last line
Change **from**: anhydrous basis.
**to**: dried basis.

**Water**. Change **to**:
**Loss on drying** (2.4.19). Not more than 5.0 per cent, determined on 0.5 g by drying over *phosphorus pentoxide* at room temperature, under vacuum at a pressure of 1.5kPa to 2.5kPa for 3 hours.

## **Bromocriptine Capsules**. Page 1205

**Identification**. B. Line 2
Change **from**: test solution (b)
**to**: test solution

Line 3
Change **from**: reference solution (d)
**to**: reference solution (e)

**Related substances**. *Reference solution (e)*. Line 1
Change **from**: 0.023 per cent
**to**: 0.23 per cent

## **Bromocriptine Tablets**. Page 1207

**Identification**. C. Line 2
Change **from**: test solution (b)
**to**: test solution

Line 3
Change **from**: reference solution (d)
**to**: reference solution (e)

**Related substances**. *Reference solution (e)*. Line 1
Change **from**: 0.055per cent
**to**: 0.55 per cent

## **Budesonide**. Page 1209

**Dose**. Line 2
Change **from**: 200 to 400 mg twice daily
**to**: 200 to 400 µg twice daily

## **Calamine**. Page 1238

**Sulphates.** Line 1
Change **from**: Dissolve 0.25 g
**to**: Dissolve 0.025 g

**Assay**.
Insert after line 7.
Repeat the operation without the substance under examination. The difference between the titrations represents the amount of sodium hydroxide required.

## **Calcipotriol Ointment**. Page 1242

**Assay**. *Test solution*.
Change **to**: *Test solution*. Disperse a quantity of ointment containing 75 µg of Calcipotriol with 5 ml of *tetrahydrofuran*. Add 35 ml of the solvent mixture and sonicate for 45 minutes with intermittent shaking and dilute to 50 ml with the solvent mixture, centrifuge and filter.

## **Carboplatin**. Page 1276

**Chlorides.** Line 2
Change **from**: The filtrate complies with the limit test of chlorides (100 ppm).
**to**: The filtrate complies with the limit test of chlorides (100 ppm).Prepare the standard using 8.0 ml of chloride standard solution (5 ppm).

## **Chlorambucil**. Page 1346

**Dose**. Line 1
Change **from**: 100 to 200 mg per kg of body weight
**to**: 100 to 200 µg per kg of body weight

## **Chlordiazepoxide Tablets**. Page 1358

**Related substances**. *Reference solution (c).*
Change **to**: *Reference solution (c).* A 0.01 per cent w/v solution of *2-amino-5-chlorobenzophenone*.

## **Chlorpheniramine Injection**. Page 1376

**Bacterial endotoxins**. line 2
Change **from**: chlorpheniramine
**to**: chlorpheniramine maleate

## **Chlorpromazine Injection**. Page 1378

**Identification**. A, para 2, line 4**,**
Change **from**: chlorpromazine hydrochloride
**to**: chlorpromazine

**Bacterial endotoxins**. line 2
Change **from**: chlorpromazine
**to**: chlorpromazine hydrochloride

## **Chlorpromazine Tablets**. Page 1378

**Identification**. A, para 2, line 4**,**
Change **from**: chlorpromazine hydrochloride
**to**: chlorpromazine

## **Cholecalciferol Injection**. Page 1384

Lines 2 and 3

Change **from**: Cholecalciferol Injection is a sterile solution containing 0.75 per cent w/v of Cholecalciferol in Ethyl Oleate

**to**: Cholecalciferol Injection is a sterile solution of Cholecalciferol in Ethyl Oleate.

Lines 4 and 5

Change **from**: Cholecalciferol Injection contains not less than 0.67 per cent and not more than 0.83 per cent of cholecalciferol, $C_{27}H_{44}O$

**to**: Cholecalciferol Injection contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of cholecalciferol, $C_{27}H_{44}O$.

**Description**.

Change **to**: A clear, colourless to pale yellow liquid.

## **Clarithromycin**. Page 1411

**Related substances.** Last line

**Change from**: reference solution (b) (0.1 per cent).

**to**: reference solution (b) (0.2 per cent).

## **Clarithromycin Tablets**. Page 1413

**Dissolution**. *Test solution*

Change **to**: *Test solution.*Dilute the filtrate, if necessary with the dissolution medium.

## **Clindamycin Capsules**. Page 1418

**Identification**. B, line 3

Change **from**: reference solution (a)

**to**: the reference solution

## **Clotrimazole Cream**. Page 1443

**2-Chlorotritanol**. *Test solution***,** line 7

Change **from**: extraction with further quantities

**to**: extractions with two further quantities

**Assay**. Change **to**:

**Assay**. Determine by liquid chromatography (2.4.14).

*Test solution*. Extract a quantity of the cream containing 25 mg of Clotrimazole by warming with 25 ml of *methanol* in a water-bath at 50° for 5 minutes, shaking occasionally. Remove from the water-bath, shake the mixture vigorously while cooling to room temperature, cool in ice for 15 minutes, centrifuge for 5 minutes and decant the supernatant liquid. Repeat the extraction with 20 ml, of *methanol*. Dilute the combined methanol extracts to 50.0 ml with methanol.

*Reference solution (a).* A 0.05 per cent w/v solution of *clotrimazole RS* in *methanol*

*Reference solution (b).* A solution containing 0.01 per cent w/v solution each of *clotrimazole RS* and *2-chlorotritanol RS* in *methanol*

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 75 volumes of *acetonitrile* and 25 volumes of a buffer solution prepared by dissolving 4.35 g of *dibasic potassium phosphate* in 1000 ml of *water*,
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 25 µl.

The relative retention time with reference to clotrimazole for 2-chlorotritanol is about 1.2.

Inject reference solution (b). The test is not valid unless the resolution between clotrimazole and 2-chlorotritanol peaks is not less than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject reference solution (a) and the test solution.

Calculate the content of $C_{22}H_{17}ClN_2$ in the cream.

## **Cloxacillin Injection.** Page 1447

**Assay.** *Test solution,* line 3
Change **from**: 55 mg
**to**: 50 mg

## **Clozapine**. Page 1448

**Identification.** A.
Delete: A.
B. Delete the requirement.

## **Alfacyclodextrin.** Page 1477

**Identification**. D
Change **to**: Specific Optical Rotation (see Tests)

## **Betacyclodextrin**. Page 1479

**Identification**. D
Change **to**: Specific Optical Rotation (see Tests)

Insert before **pH**.
**Specific optical rotation** (2.4.22). +160.0° to +164.0°, determined in a 1.0 per cent w/v solution at 20°.

## **Cyclosporine Capsules**. Page 1488

**Dissolution**.
*For capsules containing liquid*- Insert after speed and time

Place 1 capsule in each vessel, and allow the capsule to sink to the bottom of the vessel before starting rotation of the blade. Observe the Capsules, and record the time taken for each Capsule shell to rupture.

Tolerances - The requirements are met if all of the Capsules tested rupture in not more than 15 minutes. If 1 or 2 of the Capsules rupture in more than 15 but not more than 30 minutes, repeat the test on 12 additional Capsules. Not more than 2 of the total of 18 Capsules tested rupture in more than 15 but not more than 30 minutes.

## **Cytarabine Injection**. Page 1494

**Usual strengths**.
Change **to**: **Usual strengths**. 100 mg per vial; 500 mg per vial; 1 g per vial.

## **Daunorubicin Injection.** Page 1512

**Identification.** Line 3.
Change **from**: reference solution
**to**: reference solution (a).

## **Dexamethasone Sodium Phosphate Injection.** Page 1526

Insert before **Identification**
**Description**. A clear, almost colourless solution.

## **Diethanolamine.** Page 1565

**Triethanolamine.** Insert in the beginning
Not more than 1.0 per cent.

Line 7.
Change **from**: light. Weigh 20 g
**to**: light, add 20 g

Line 11.
Change **from**: Titrate with *0.5 M ethanolic sulphuric acid solution*, determine the end point potentiometrically (2.4.25)
**to**: Titrate with *0.5 M ethanolic sulphuric acid solution*.

**Assay**. Change **to**:
**Assay**. Dissolve 2.0 g in 50.0 ml of *water*. Titrate with *0.5 M hydrochloric acid* using *bromocresol green solution* as indicator. Carry out a blank titration.

1 ml of *0.5 M hydrochloric acid* is equivalent to 0.05257 g of $NH(C_2H_4OH)_2$.

## Disodium Edetate. Page 1594

**Assay**. Line 5.
Change **from**: 1 ml of *0.1 M lead nitrate* is equivalent to 0.03362 g of $C_{10}H_{14}N_2Na_2O_8$.
**to**: 1 ml of *0.1 M lead nitrate* is equivalent to 0.03722 g of $C_{10}H_{14}N_2Na_2O_8,2H_2O$.

## Disodium Edetate Injection. Page 1595

**Assay**. Lines 6 and 7.
Change **from**: 1 ml of *0.1 M lead nitrate* is equivalent to 0.03722 g of $C_{10}H_{14}N_2Na_2O_8,2H_2O$.
**to**: 1 ml of *0.1 M lead nitrate* is equivalent to 0.03362 g of $C_{10}H_{14}N_2Na_2O_8$.

## Docetaxel Trihydrate. Page 1608

**Specific optical rotation**.
Change **to: Specific optical rotation** (2.4.22). -38.5° to -41.5°, determined in 1.0 per cent w/v solution in *methanol*.

## Etoricoxib. Page 1726

**Assay**. *Reference solution*,line 1
Change **from**: 0.01 per cent
**to**: 0.005 per cent

## Flavoxate Hydrochloride. Page 1763

**Related substances**. *Reference solution (c)*. line 2
Change **from**: 0.00015 per cent
**to**: 0.003 per cent

## Flurbiprofen Eye Drops. Page 1808

Para 2, line 3
Change **from**: flurbiprofen sodium, $C_{15}H_{12}FNaO_2$
**to**: flurbiprofen sodium dehydrate, $C_{15}H_{12}FNaO_2.2H_2O$

**Assay**. Last line
Change **from**: $C_{15}H_{12}FNaO_2$
**to**: $C_{15}H_{12}FNaO_2.2H_2O$

## Fluticasone Propionate. Page 1811

**Water** (2.3.43). Lines 2 and 3
Change **from**: using as solvent a mixture of equal volumes of *chloroform* and *methanol*
**to**: using *methanol* as solvent.

## Fluvoxamine Tablets. Page 1820

**Related substances**. Change **to**:

**Related substances**. Determine by liquid chromatography (2.4.14).

*Test solution*. Disperse a quantity of powdered tablets containing 0.25 g of Fluvoxamine Maleate with 125 ml of the mobile phase for 10 minutes and dilute to 250.0 ml with the mobile phase. Centrifuge and use the supernatant liquid.

*Reference solution (a)*. Dilute 1.0 ml of the test solution to 100.0 ml with the mobile phase.

*Reference solution (b)*. Add 1.0 ml of *1 M hydrochloric acid* to 10.0 ml of the test solution and heat on a water-bath for 10 minutes.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with endcapped octylsilane bonded to porous silica (5 µm),
- column temeperature: 35°,
- mobile phase: a mixture of 40 volumes of a solution containing 1.25 per cent w/v of *diammonium hydrogen orthophosphate* and 0.275 per cent w/v of *sodium heptanesulphonate monohydrate* and 60 volumes of *methanol*, adjusting the pH to 3.5 with *orthophosphoric acid*,
- flow rate: 2 ml per minute,
- spectrophotometer set at 254 nm,
- injection volume: 20 µl.

Inject reference solution (b). The relative retention time with reference to fluvoxamine maleate (retention time: about 7 to 9 minutes) for addition product is about 0.65.

Inject reference solution (a). The test is not valid unless the column efficiency is not less than 2000 theoretical plates and the tailing factor is not more than 2.0.

Inject reference solution (a) and the test solution. In the chromatogram obtained with the test solution, the area of any peak due to 'addition product' is not more than 3 times the area of the principal peak in the chromatogram obtained with reference solution (a) (3.0 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 reference solution (a) (0.5 per cent). Ignore the peak due to maleic acid which elutes immediately after the solvent front and any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

## Gemcitabine Hydrochloride. Page 1849

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

Change **from**: 10.0 ml

**to**: 1.0 ml

## Gemcitabine Injection. Page 1850

**Related substances**. After chromatographic system, para 2

Change **to**: Inject reference solution (a) and test solution (a). In the chromatogram obtained with test solution (a), the area of any peak due to gemcitabine impurity B is not more than the area of the peak due to gemcitabine in the chromatogram obtained with reference solution (a) (0.1 per cent), the area of any other secondary peak is not more than twice the area of the peak due to gemcitabine in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of the areas of all secondary peaks is not more than three times the area of the peak due to gemcitabine in the chromatogram obtained with reference solution (a) (0.3 per cent). Ignore any peak with an area less than 0.2 times the area of the peak due to gemcitabine in the chromatogram obtained with reference solution (a) (0.02 per cent).

## Glimepiride Tablets. Page 1865

**Related substances**. After chromatographic system, para 1, line 4

Insert after replicate injections

"of glimepiride"

**Uniformity of content**. *Test solution*. Change **to**:

*Test solution*. Disperse one tablet in the solvent mixture and dilute with the solvent mixture to obtain a solution containing 0.01 per cent w/v of glimepiride.

**Assay**. *Test solution*. Change **to**:

*Test solution*. Weigh and powder 20 tablets. Disperse a quantity of powder containing 10 mg glimepiride in the solvent mixture and dilute with the solvent mixture to obtain a solution containing 0.01 per cent w/v of glimepiride.

After chromatographic system, para 1, line 4

Insert after replicate injections

"of glimepiride"

## Guaiphenesin. Page 1878

**Identification**. B. Lines 3 and 4

Change **from**: reference solution (b)

**to**: reference solution (a)

## **Hydralazine Hydrochloride**. Page 1897

Para 1, line 1
Change **from**: Hydralazine Hydrobromide
**to**: Hydralazine Hydrochloride

## **Hydrochlorothiazide**. Page 1900

**Assay**. Lines 1 and 2
Change **from**: *anhydrous pyridine*
**to**: *dimethyl sulphoxide*

## **Hydroxocobalamin Injection.** Page 1914

**Related substances.**
*Reference solution (b).*
Change **from**: Dilute 1 ml of reference solution (a) to 100 ml with the mobile phase
**to**: Dilute 1.0 ml of reference solution (a) to 50.0 ml with the mobile phase.

## **Hyoscyamine Oral Solution.** Page 1934

**Usual strength**.
Change **from**: 50 mg per ml
**to**: 0.125 mg per ml

## **Hyoscyamine Tablets.** Page 1934

**Usual strength**.
Change **from**: 0.375 mg per ml
**to**: 0.125 mg per ml

## **Anhydrous Lactose**. Page 2051

**Heavy metals**.
Change **to**: **Heavy metals** (2.3.13). Dissolve 4 g in 20.0 ml of *water*. 12 ml of the solution complies with the limit test for heavy metals, Method D (5 ppm) using 10 ml of *lead standard solution (1 ppm, Pb)*.

## **Lamivudine Tablets**. Page 2056

**Related substances**. *Test solution*.
Change **to**: *Test solution*. Disperse a quantity of the powdered tablets containing 600 mg of lamivudine in 20 ml of *water*, with the aid of ultrasound. Add 20 ml of *acetonitrile*, mix with the aid of ultrasound for 10 minutes and dilute to 100.0 ml with *water* and filter.

**Assay.** *Solvent mixture.*
Change **from**: *Solvent mixture.* 50 volumes of *water* and 50 volumes of *acetonitrile*
**to**: *Solvent mixture.* 80 volumes of *water* and 20 volumes of *acetonitrile.*

## **Lansoprazole**. Page 2067

**Related substances**. Last para, line 3
Change **from**: 0.4 per cent
**to**: 0.4 times

Line 5
Change **from**: reference solution (b)
**to**: reference solution (b) (0.4 per cent)

Lines 7 and 9
Change **from**: 0.1 per cent
**to**: 0.1 times

Lines 8 and 11
Change **from**: reference solution (b)
**to**: reference solution (b) (0.1 per cent)

## Lansoprazole Gastro-resistant Capsules. Page 2069

**Assay**. After chromatographic system, para 1

Change **to**: Inject reference solutions (a) and (b). The test is not valid unless the resolution between the peaks due to lansoprazole and lansoprazole impurity A is not less than 5.0 in reference solution (a). The relative standard deviation for replicate injections is not more than 2.0 per cent in reference solution (b).

## Levofloxacin Hemihydrate. Page 2085

**Identification**. Line 3
Change **from**: levofloxacin
**to**: levofloxacin hemihydrate

**Related substances**. Change **to**:
**Related substances**. Determine by liquid chromatography (2.4.14).

*Test solution.* Dissolve 100 mg of the substance under examination in the mobile phase and dilute to 100.0 ml with the mobile phase.
*Reference solution (a).* A 0.1 per cent w/v solution of *levofloxacin hemihydrate RS* in the mobile phase.

*Reference solution (b).* Dilute 1.0 ml of reference solution (a) to 100.0 ml with the mobile phase.

*Reference solution (c).* A 0.00003 per cent w/v solution of *levofloxacin hemihydrate RS* in the mobile phase.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- column temperature: 45°,
- mobile phase: a mixture of 30 volumes of *methanol* and 70 volumes of buffer solution prepared by dissolving 8.5 g of *ammonium acetate*, 1.25 g of *cupric sulphate pentahydrate* and 1.3 g of *l-isoleucine* in *water* and diluting to 1000 ml with *water*,
- flow rate: 0.8 ml per minute,
- spectrophotometer set at 360 nm,
- injection volume: 25 µl.

| Name | Relative retention time | Correction factor |
|---|---|---|
| N-Desmethyl levofloxacin[1] | 0.47 | --- |
| Diamine derivative[2] | 0.52 | 1.11 |
| Levofloxacin N-oxide[3] | 0.63 | 0.9 |
| 9-Desfluoro levofloxacin[4] | 0.73 | --- |
| Levofloxacin | 1.0 | --- |
| D-Isomer[5] | 1.23 | --- |

[1](S)-9-fluoro-2,3-dihydro-3-methyl-10-(piperazin-1-yl)-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid,
[2](S)-9-fluoro-2,3-dihydro-3-methyl-10-[2-(methylamino)ethylamino]-7-oxo-7H -pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid,
[3](S)-4-(6-carboxy-9-fluoro-2,3-dihydro-3-methyl-7-oxo-7H-pyrido-[1,2,3-de][1,4]benzoxazine-10-yl)-1-methyl-piperazine-1-oxide,
[4](S)-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid,
[5](R)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid.

Inject reference solutions (a) and (c). The test is not valid unless the relative standard deviation for replicate injections obtained with reference solution (a) is not more than 1.0 per cent and the signal to noise ratio for the principal peak in the chromatogram obtained with reference solution (c) is not less than 10.

Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to D-isomer 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 other identified peak 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 other secondary peak is not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent) and the sum of the area of all the secondary peaks other than D-isomer is not more than 0.5 times the areas of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent). Ignore any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.05 per cent).

## Levonorgestrel and Ethinyloestradiol Tablets. Page 2091

**Identification**

*Reference solution.* Line 3.
Change **from**: *water*.
**to**: *dichloromethane.*

*Reference solution (a).* Line 2
Change **from**: *norgestrel RS*
**to**: *levonorgestrel RS*

## Medroxyprogesterone Tablets. Page 2160

**Dissolution** (2.5.2).
*Test solution*. Line 2
Change **from**: 0.0028 per cent w/v
**to**: 0.00028 per cent w/v.

*Reference solution*. Line 1
Change **from**: 0.0028 per cent w/v
**to**: 0.00028 per cent w/v.

**Impurity F**
*Reference solution.* Line 1
Change **from**: 0.5 per cent w/v
**to**: 0.01 per cent w/v.

## Menthol. Page 2173

**Related substances**. Last para, last line.
Change **from**: (0.5 per cent).
**to**: (0.05 per cent).

## Methotrexate Tablets. Page 2194

**Related substances**. Last para, line 8
Change **from**: 1.5 times
**to**: 2.5 times

Lines 9 and 10
Change **from**: reference solution (a) (0.3 per cent)
**to**: reference solution (a) (0.5 per cent)

## Methyl Salicylate Ointment. Page 2197

**Assay.** *Test solution*.
Change **to**: *Test solution (a).* A solution of ointment containing 1.0 per cent w/v of Methyl Salicylate in *petroleum spirit (boiling range 80 to 100)*.

*Test solution (b).* A solution of ointment containing 1.0 per cent w/v each of Methyl Salicylate and *benzyl alcohol* (internal standard) in *petroleum spirit (boiling range 80 to 100)*.

## Mifepristone. Page 2234

**Optical rotation**. Title
Change **to**: **Specific Optical rotation**

## **Montelukast Tablets**. Page 2248

**Related substances**. Last para

Change **to**: Inject reference solution (b) and the test solution. In the chromatogram obtained with the test solution, the area of the peak corresponding to sulphoxide impurity at relative retention time 0.63 is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (1.0 per cent), and the area of the peak corresponding to styrene impurity at about relative retention time 1.37 is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 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 (b) (0.5 per cent) and the sum of areas of all the secondary peaks is not more than 4 times the area of the peak in the chromatogram obtained with reference solution (b) (2.0 per cent).

## **Moxifloxacin Eye Drops**. Page 2255

**Assay** : Chromatographic system: Gradient programme

Change **to** :

| Time (in min) | Mobile phase A (per cent w/v) | Mobile phase B (per cent v/v) | Flow rate (ml per minute) |
|---|---|---|---|
| 0 | 69 | 31 | 0.5 |
| 30 | 69 | 31 | 0.5 |
| 31 | 60 | 40 | 0.9 |
| 36 | 60 | 40 | 0.9 |
| 37 | 69 | 31 | 0.5 |
| 42 | 69 | 31 | 0.5 |

## **Ormeloxifene Hydrochloride**. Page 2383

**Total basic substances**. Delete the requirement

## **D-Panthenol.** Page 2426

**Dose.**

Change **from**: 250 to 500 mg

**to**: 5 mg to 50 mg

## **Phenytoin Oral Suspension**. Page 2488

**Identification**. Lines 9 and 10

Change **from**: phenytoin sodium

**to**: phenytoin

**pH** (2.4.24).

Change **from**: 4.5 to 5.5 determined on 1.0 g

**to**: 4.5 to 5.5.

## **Plaster of Paris.** Page 2511

Para 1, line 2.

Change **from**: Plaster of Paris is prepared by heating powdered gypsum, $CaSO_4,½H_2O$,

**to**: Plaster of Paris is prepared by heating powdered gypsum, $CaSO_4,2H_2O$,

## **Potassium Clavulanate Diluted.** Page 2525

**Light absorption.** Change **to**:

**Polymeric impurities and other impurities absorbing at 278 nm**. Disperse a quantity of the substance under examination containing 50 mg of potassium clavulanate in 10 ml of *0.1 M phosphate buffer solution pH 7.0* and dilute to 50.0 ml with the buffer solution, filter. The absorbance of the solution determined at 278 nm is not more than 0.40.

## **Procainamide Hydrochloride.** Page 2555

**Assay.** Line 2, insert after *hydrochloric acid*

", add 3 g of *potassium bromide*, cool in ice"

## Procainamide Injection. Page 2555

**Assay.** Lines 2 and 3, insert after boil for 1 minute
", add 3 g of *potassium bromide*, cool in ice"

## Procainamide Tablets. Page 2556

**Assay.** Line 4, insert after boil for 1 minute
", add 3 g of *potassium bromide*, cool in ice"

## Progesterone Injectable suspension. Page 2567

**Assay**. *Test solution*, line 4
Change **from**: 2.0 ml
**to**: 5.0 ml

## Proguanil Hydrochloride. Page 2567

**4-Chloroaniline.**
Insert after **4-Chloroaniline.**
**"**Not more than 250 ppm."

Line 10.
Change **from**: 1.25 µg
**to**: 1.25 µg per ml

## Proguanil Tablets. Page 2568

Insert after **4-Chloroaniline.**
**"**Not more than 250 ppm."

Line 14
Change **from**: 1.25 µg
**to**: 1.25 µg per ml

## Propranolol Hydrochloride. Page 2579

**Dose.**
Change **from:** Orally, 20 mg to 2 g daily, in divided doses; the initial dose should not exceed 40 mg; by slow intravenous injection, 3 to 10 mg.
**to:** Orally, 20 mg to 160 mg daily, in divided doses; the initial dose should not exceed 40 mg; by slow intravenous injection, 1 mg to 3 mg.

## Sodium Benzoate. Page 2738

**Heavy metals**.
Change **to**: **Heavy metals** (2.3.13). 2.0 g complies with the limit test for heavy metals, Method B (10 ppm).

## Sodium Formaldehyde Sulphoxylate. Page 2751

**Sodium sulphite**. Lines 7 to 11
Change **to**: Calculate the percentage of $Na_2SO_3$ from the expression $78.775(V_2 - V_1)$ (M/W),
where $V_1$ and $V_2$ are the volumes, in ml, of 0.05 M iodine consumed in this test and in the Assay respectively, M is the exact molarity of 0.05 M iodine solution and W is the weight, in g, of the substance under examination taken for the Assay.

## Sucralose. Page 2801

**Related substances**. Line 2
Change **from**: coating the plate with *silica gel*.
**to**: coating the plate with *octadecylsilanized silica gel*.

## **Trimethoprim**. Page 2922

**Related substances**. B. After chromatographic system, para 1,
Change **to**: Inject reference solution (b). The test is not valid unless the resolution between the peaks due to trimethoprim and trimethoprim impurity B is not less than 2.0.

## **Vecuronium Bromide**. Page 2962

**Related substances**. *Reference solution (b)*. Line 1
Change **from**: this solution
**to**: test solution

## **Vincristine Injection**. Page 2970

**Identification**. B. Line 3,
Delete "Reserve the residue for test D"

## **Purified Water**. Page 2988

**Acidity or alkalinity.**
Change **from:** To 10 ml, freshly boiled and cooled in a borosilicate glass flask, add 0.05 ml of *methyl red solution*; the resulting solution is not coloured. To 10 ml add 0.1 ml of *bromothymol blue solution*; the resulting solution is not coloured.
**to:** To 10 ml, freshly boiled and cooled in a borosilicate glass flask, add 0.05 ml of *methyl red solution*; the resulting solution is not red. To 10 ml add 0.1 ml of *bromothymol blue solution*; the resulting solution is not blue.

## **Zidovudine**. Page 3003

**Related substances**. B. *Reference solution (b).* Line 4,

Change **from**: a thymidine
**to**: β- thymidine

After chromatographic system, para 1, line 3
Change **from**: zidovudine-related compound B
**to**: zidovudine impurity B

Para 2, line 8
Change **from**: a-thymidine
**to**: β- thymidine