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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/ER-004 **Dated**: 10-03-2015

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**

ERRATA – 004 for IP 2014

As you are aware that the 7th edition of Indian Pharmacopoeia has become official from 1st April, 2014. Based on scientific inputs, some monographs, appendices needed corrections, accordingly an Errata – 004 is issued containing minor corrections. This is for notice and immediate compliance.

Yours faithfully,

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

Encl:
ERRATA – 004 for IP 2014

CC to: Publication Division to put up on IPC website.

ERRATA- 004 TO IP-2014

2.4.26 Solubility

Page 176
Change **from**: Atosibane Acetate
Change **to**: Atosiban Acetate

Page 180
Insert before **Chorionic Gonadotropin**
Chlorthalidone. Soluble in *methanol;* slightly soluble in *ethanol (95 per cent);* practically insoluble in *water,* in *ether,* and in *chloroform.*

3.1 Infrared Reference Spectra

Page 362
Change **from**: Atosibane Acetate
Change **to**: Atosiban Acetate

Acesulphame Potassium. Page 984, 3798

Related substances. Change **to**:

Related substances. Determine by liquid chromatography (2.4.14).

Test solution. Dissolve 0.1 g of the substance under examination in *water* and dilute to 10.0 ml with *water*.

Reference solution (a). A 0.004 per cent w/v solution of *acesulphame potassium impurity B RS (5-chloro-6-methyl-1,2,3-oxathiazin-4(3H)-one 2,2-dioxide RS)* in *water*. Dilute 1.0 ml of this solution to 200.0 ml with *water*.

Reference solution (b). Dilute 1.0 ml of the test solution to 100.0 ml with *water*. Further dilute 1.0 ml of this solution to 10.0 ml with *water*.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm),
- mobile phase: a mixture of 40 volumes of *acetonitrile*, 60 volumes of 0.33 per cent w/v solution of *tetrabutylammonium hydrogen sulphate*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 234 nm,
- injection volume: 20 µl.

The relative retention time with reference to acesulphame for acesulphame impurity B is about 1.6.

Inject reference solution (b). 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 for the principal peak.

Inject reference solutions (a), (b) and the test solution. Run the chromatogram 3 times the retention time of the principal peak. In the chromatogram obtained with the test solution, the area of any peak corresponding to acesulphame impurity B is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (20 ppm). 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) (0.1 per cent). The sum of areas of all the secondary peaks is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 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 (b) except for the peak due to acesulphame impurity B (0.05 per cent).

Acetazolamide Tablets. Page 986

Identification A. Line 2.
Change **from**: add 2 ml of *1 M sodium hydroxide*
to: add 10 ml of *1 M sodium hydroxide*

Alprazolam. Page 1015

Loss on drying.
Change **to**: Not more than 0.5 per cent, determined on 1.0 g by drying in an oven at 105^0.

Ambroxol Hydrochloride. Page 1025, 3802

Related substances. Chromatographic system, mobile phase, line 3
Change **from**: *ammonium phosphate*
to: *ammonium phosphate, dibasic*

Assay. Chromatographic system, mobile phase, lines 2 and 3
Change **from**: *ammonium dihydrogen phosphate*
to: *ammonium phosphate, dibasic*

Amitriptyline Hydrochloride. Page 1044

Assay. Chromatographic system, mobile phase, line 3
Change **from**: adjusted to pH with
to: adjusted to pH 7.7 with

Atorvastatin Tablets. Page 1100

Uniformity of content. *Test solution.*
Change to: Disperse one tablet in 3 ml of *water*, add 25 ml of *methanol* and mix with the aid of ultrasound, make up to 50 ml with the *solvent mixture*, filter. Dilute sufficient amount of the the filtrate with solvent mixture to produce a solution containing 0.008 per cent w/v of atorvastatin.

Atosibane Acetate. Page 1102

Change Title **to:** **Atosiban Acetate**
Para 1, line 1.
Change **from**: Atosibane Acetate
to: Atosiban Acetate
Category.
Change **to**: Oxytocin antagonist.

Identification. Line 2.
Change **from**: *atosibane acetate RS*
to: *atosiban acetate RS*

Related substance. *Reference solution.*
Line 1.
Change **from**: *atosibane acetate*

to: *atosiban acetate RS*

Ciprofloxacin. Page 1399

Identification B. Line 2.
Change **from**: *silica gel G*
to: *silica gel GF254*

Ciprofloxacin Injection. Page 1400

Identification. Line 2.
Change **from**: *silica gel G*
to: *silica gel GF254*

Ciprofloxacin Hydrochloride. Page 1401

Identification B. Line 2.
Change **from**: *silica gel G*
to: *silica gel GF254*

Ciprofloxacin Tablets. Page 1403

Identification B. Line 2.
Change **from**: *silica gel G*
to: *silica gel GF254*

Clemastine Tablets. Page 1415

Identification A. Line 1.
Change **from**: peak
to: spot

Clotrimazole Cream. Page 1443

2-Chlorotritanol. After chromatographic system, para 1, line 2
Change **from**: 6000 theoretical plates.
to: 1800 theoretical plates .

Clotrimazole Pessaries. Page 1444

Related substances. After chromatographic system, para 1, line 3
Change **from**: 6000 theoretical plates.
to: 1800 theoretical plates.

Assay. After chromatographic system, para 1, line 3
Change **from**: 6000 theoretical plates.
to: 1800 theoretical plates.

Dalteparin Sodium Injection. Page 1505

Anti-factor Xa activity. *Reference solution*. Lines 1 and 2
Change **from**: *dalteparin sodium solution for bioassays RS*

to: low molecular mass heparins

Anti-factor IIa activity. *Reference solution*. Lines 1 and 2

Change **from**: *dalteparin sodium solution for bioassays RS*

to: low molecular mass heparins

Dexamethasone Injection. Page 1526

Identification.

Change **to**: In the assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak due to dexamethasone sodium phosphate in the chromatogram obtained with the reference solution (a).

Free dexamethasone. *Reference solution (b)*. line 2

Change **from**: *dexamethasone phosphate RS*

to: *dexamethasone sodium phosphate RS*

Assay. *Reference solution (a)*. line 2

Change **from**: *dexamethasone phosphate RS*

to: *dexamethasone sodium phosphate RS*

Reference solution (b). line 2

Change **from**: *dexamethasone phosphate RS*

to: *dexamethasone sodium phosphate RS*

Dobutamine Hydrochloride. Page 1604

Related substances. After chromatographic system, para2, line 6.

Change **from**: not more than 0.2 times the area

to: not more than the area

Para 2, line 8

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

to: reference solution (b) (0.5 per cent)

Flavoxate Tablets. Page 1764

Related substances. Insert after *Reference solution (c)*.

Reference solution (d). A 0.03 per cent w/v solution of *3- methylflavone-8-carboxylic acid RS* in *chloroform*.

Last para, lines 1 and 2

Change **from**: Apply 50 µl of test solution (a), 10 µl of reference solution (a) and 25 µl of reference solution (b).

to: Apply 10 µl of reference solution (a), (c), (d), test solution (b), 25 µl of reference solution (b) and 50 µl of test solution (a).

Flucytosine. Page 1770

Heavy metals (2.3.13). Line 2.

Change **from**: Method D (20 ppm)

to: Method B (20 ppm).

Fludrocortisone Acetate. Page 1777

Identification C. *Reference solution (a)*

Change **from**: *Fludrocortisone RS.*

to**:** *Fludrocortisone acetate RS*

Fludrocortisone Tablets. Page 1778

Identification . *Reference solution (a)*
Change **from**: *Fludrocortisone RS.*
to**:** *Fludrocortisone acetate RS*

Fluoxetine Capsules. Page 1792

Related substance. After chromatographic system. para 2, line 8,
Change **from**: 0.05 time
to: 0.1 times

Fluoxetine Tablets. Page 1795

Related substance. After chromatographic system. para 2, line 8,
Change **from**: 0.05 time
to: 0.1 times

Flupentixol Decanoate. Page 1796

Dose.
Change **to**: Intramuscular injection, 20 to 40 mg.

Related substance. After chromatographic system. Para 3, lat line.
Change **from**: reference solution (d)
to: reference solution (c)

Assay. Para 2, line 1.
Change **from**: 0.0294 g
to: 0.02944 g

Flutamide Capsule. Page 1809

Dissolution. Para 1, last line.
Change **to**: Calculate the content of $C_{11}H_{11}F_3N_2O_3$ in the medium form a known concentration of *flutamide RS* prepared by initially dissolving in *methanol* and further diluting with the dissolution medium.

Uniformity of content. Delete the test.

Gentamicin Sulphate. Page 1856

Sulphate. Line 2.
Change **from**: anhydrous basis
to: dried basis

Hydroxychloroquine Sulphate. Page 1915, 3868

Related substances. Chromatographic system, gradient programme,
Change **to**:

Time (in min.)	Mobile phase A (per cent v/v)	Mobile phase B (per cent v/v)
0	100	0
2	100	0
10	85	15
18	0	100
25	0	100

Human Insulin. Page 1963.

Para 1, lines 2 to 5.

Change **from** : It is produced either by enzymatic modification and suitable purification of insulin obtained from the pancreas of the pig or by a method based on recombinant DNA (rDNA).

to: It is produced by a method based on recombinant DNA (rDNA) technology.

Biphasic Isophane Insulin Injection. Page 1977.

Tests

pH (2.4.24).

Change **from**: 6.9 to 7.5

to: 6.9 to 7.8

Irbesartan and Hydrochlorthaizide Tablets. Page 1995, 3878

Dissolution (2.5.2). Chromatographic system. mobile phase. line 2

Change **from**: 1.36 g of *monobasic potassium phosphate,*

to: 1.36 g of *monobasic potassium phosphate* in 1000 ml of *water,*

Diluted Isosorbide Dinitrate. Page 2012.

Identification A.

Change **to**: In the assay, the principal peak in the chromatogram obtained with the test solution (b) corresponds to the peak in the chromatogram obtained with the reference solution (b)

Heavy metals. Delete the test.

Loss on drying. Delete the test.

Assay. *Reference solution (a).*

Change **from**: *isosorbide dinitrate RS*

to: *diluted isosorbide dinitrate RS*

Reference solution (d), Line 1.

Change **from**: 20 mg

to: 10 mg

Isosorbide Dinitrate Tablets. Page 2013

Identification A. *Reference solution.* Line 1

Change **to**: *diluted isosorbide dinitrate RS*

Uniformity of content. *Reference solution.*
Change **to**: A solution *diluted isosorbide dinitrate RS* equivalent to 0.005 per cent w/v of isosorbide dinitrate in the mobile phase

Dissolution. *Reference solution.* Line 1
Change **from**: *isosorbide dinitrate RS*
to: *diluted isosorbide dinitrate RS*
Assay. *Reference solution (a).* Line 2.
Change **from**: *isosorbide dinitrate RS*
to: *diluted isosorbide dinitrate RS*

Labetalol. Page 2048

Insert before **Assay.**
Other tests. Comply with the tests stated under Parenteral preparations.

Metoclopramide Tablets. Page 2212, 3899

Uniformity of content. Change **to**:

Uniformity of content. Complies with the test stated under Tablets.

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

Test solution. Disperse one tablet in 30 ml of *water*, with the aid of ultrasound for 20 minutes and dilute to 100.0 ml with *water*. Centrifuge and use the supernatant liquid.

Calculate the content of $C_{14}H_{22}ClN_3O_2$, HCl in the tablet.

Nitrazepam Tablets. Page 2343

Dissolution. Insert in the beginning

NOTE - Carry out the following procedure in subdued light.

Pemetrexed Disodium Heptahydrate. Page 2442, 3916

Enantiomeric purity. Chromatographic system, mobile phase
Change **from**: α-cyclodextrin
to: β-cyclodextrin

Related Substance. Chromatographic System,
Change **from**:

Name	Relative retention time
Pemetrexed impurity A[1]	0.82
Pemetrexed impurity B[2]	0.87
Pemetrexed impurity C[3]	0.88
Pemetrexed (Retention time: about 26 minute	1.0

[1](2*S*)-2-[[4-[2-(2-amino-1-methyl-4-oxo-4,7-dihydro-1H-pyrrolo[2,3-*d*]pyrmidin-5-yl)ethyl]benzoyl]amino]- pentanedioic acid,

[2] (2*S*, 2'*S*) – 2,2'- [[(5*R*)- 2,2'- diamino- 4,4'6-trioxo-1,4,4',6,7,7'-hexahydro-1'*H*, 5*H*-5,6'-bipyrollol[2,3-*d*]pyrimidine-5,5'-diyl]bis(ethylenebenzene-4,1diylcarbonylimin)]dipentanedioic acid,

[3](2*S*, 2'*S*) – 2,2'- [[(5*S*)- 2,2'- diamino- 4,4'6-trioxo-1,4,4',6,7,7'-hexahydro-1'*H*, 5*H*-5,6'-bipyrollol[2,3-*d*]pyrimidine-5,5'-diyl]bis(ethylenebenzene-4,1diylcarbonylimin)]dipentanedioic acid,

to:

Name	Relative retention time
Pemetrexed impurity A[1]	0.82
Pemetrexed impurity B[2]	0.87
Pemetrexed impurity C[3]	0.88
Pemetrexed impurity D[4]	0.90
Pemetrexed impurity E[5]	0.94
Pemetrexed (Retention time: about 26 minute)	1.0

[1](2*S*)-2-[[4-[2-(2-amino-1-methyl-4-oxo-4,7-dihydro-1H-pyrrolo[2,3-*d*]pyrmidin-5 yl)ethyl]benzoyl]amino]- pentanedioic acid,

[2] (2*S*, 2'*S*) – 2,2'- [[(5*R*)- 2,2'- diamino- 4,4'6-trioxo-1,4,4',6,7,7'-hexahydro-1'*H*, 5*H*-5,6'-bipyrollol[2,3-*d*]pyrimidine-5,5'-diyl]bis(ethylenebenzene-4,1diylcarbonylimin)]dipentanedioic acid,

[3](2*S*, 2'*S*) – 2,2'- [[(5*S*)- 2,2'- diamino- 4,4'6-trioxo-1,4,4',6,7,7'-hexahydro-1'*H*, 5*H*-5,6'-bipyrollol[2,3-*d*]pyrimidine-5,5'-diyl]bis(ethylenebenzene-4,1diylcarbonylimin)]dipentanedioic acid,

4(2S)-2-[[(4S)-4-[[4-[2-(2-amino-4-oxo-4,7-dihydro-1H-pyrrolo[2,3-d]pyrimidin-5- yl)ethyl]benzoyl]amino]-4-carboxybutanoyl]amino]pentanedioic acid

[5](2*R*)-2-[[4-[2-(2-amino-4-oxo-4,7-dihydro-1H-pyrrolo[2,3-*d*]pyrmidin-5 yl)ethyl]benzoyl]amino]- pentanedioic acid,

Assay. Chromatographic System. Line 10
Delete. "- a gradient programme using the condition below",

Quetiapine Tablets. Page 2608

Dissolution. Para 3, line 3,4 and 5
Change **to**: Calculate the content of $C_{21}H_{25}N_3O_2S$ in the medium.

Quinidine Sulphate. Page 2610

Dihydroquinidine sulphate. Delete this test.

Quinine Dihydrochloride. Page 2616

Dihydroquinine dihydrochloride. Delete this test.

Quiniodochlor. Page 2621

Loss on drying (2.4.19). Line 3
Change **from**: 24 hours
to: 5 hours

Ramipril and Hydrochlorthiazide. Page 2641

Labelling.
Delete the labeling.

Ritodrine Injection. Page 2675

Related substances. After chromatographic system, para 2, line 7

Add after "reference solution (a) (1.0 per cent)."

" not more than one such peak has an area greater than 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent)"

Rosuvastatin Tablets. Page 2684

Uniformity of content. *Test solution.*

Change **to**: Disperse one tablet in 50 ml of mobile phase, mix with the aid of ultrasound and dilute to 100 ml with the mobile phase, filter. Dilute further, if necessary, with the mobile phase to produce a solution containing 0 .005 per cent w/v solution of rosuvastatin.

Related substances. *Reference solution (a).*

Change **to**: Dissolve a suitable quantity of *rosuvastatin calcium RS* in the mobile phase to obtain a solution containing 0.05 per cent w/v rosuvstatin

Stearyl Alcohol. Page 2791

Assay. After chromatographic system,
Para 1, Delete the following sentence.
and the relative standard deviation for replicate injections calculated with the area ratio of stearyl alcohol to cetyl alcohol is not more than 1.5 per cent.

Sucralose. Page 2801, 3932

Assay. After chromatographic system, para 1, line 2
Change **from**: 2.0 per cent
to: 2.0.

Travoprost. Page 2904

Assay. Chromatographic system. last line,
Change **from**: 920 100 0
to: 90 100 0

Travoprost Eye Drops. Page 2905

Related substances. *Test solution.*

Change **to**: Dilute the eye drops, if necessary with the solvent mixture, to produce a solution containing 0.004 per cent w/v of travoprost.

Related substance. Para 2, line 2. ,
Change **from**: 5-trans travoprost is 1.05
to**:** 5,6- trans travoprost is 1.1[Note—*Travaprost RS* contains a small percentage of the 5,6- trans isomer]

Related substance. Para 3, line 2.
Change **from**: 5-trans travoprost

to**:** 5,6- trans travoprost

Tropicamide Eye Drops. Page 2929

Related substances. *Test solution.*

Change **to**: Extract a volume containing 50 mg of tropicamide with 10 ml of *chloroform,* filter through *sodium sulphate anhydrous* and dilute to 10.0 ml with *chloroform.*

Para 1, line 1.

Change **from**: 20 µl

to: 40 µl

Voglibose. Page 2979

Specific optical rotation.

Add in the end. **"**at 20° ".

Zidovudine. Page 3003, 3953

Related substances. Para 1, lines 4 to 10

Change **from**: Any secondary spots observed in the chromatogram obtained with the test solution correspond to those of the principal spots in the chromatogram obtained with the reference solution. No secondary spot in the chromatogram obtained with the test solution is more intense than the principal spot in the chromatogram obtained with the reference solution (0.5 per cent).

to: Any secondary spot observed in the chromatogram obtained with the test solution corresponding to triphenylmethanol is not more intense than the corresponding spot in the chromatogram obtained with the reference solution (0.5 per cent). No other secondary spot in the chromatogram obtained with the test solution is more intense than the principal spot in the chromatogram obtained with the reference solution (0.5 per cent).

Vaccines and Immunosera for Human Use

BCG for Immunotherapy. Page 3957.

Production

General Provisions

Para 1, Lines 5 to 7,

Change **from:** Staff involved in production and testing of BCG Vaccine shall be examined periodically for tuberculosis.

to: Staff involved in production and testing of BCG for Immunotherapy shall be examined periodically for tuberculosis.

Para 2, Lines 4 and 5.

Change **from:** The vaccine is prepared from cultures which are derived from the master seed lot

to: The product is prepared from cultures which are derived from the master seed lot

SEED LOT

Bacteria and Fungi.

Change Title **to: Bacterial and Fungal contamination.**

FINAL BULK
Bacteria and Fungi.
Change Title **to: Bacterial and Fungal contamination.**

Virulent mycobacteria.
Change **to:** Examine the final bulk as prescribed under Test using 6 guinea pigs.

FINAL LOT
Tests
Change **to: Bacterial and Fungal contamination.** Carry out the test for sterility (2.2.11). The reconstituted product complies with the test for sterility, except for the presence of mycobacteria.

Temperature stability. Delete the test**.**

Labelling.
Change **to:** The label states (1) the minimum and the maximum number of viable units per vial in the reconstituted product; (2) that the product must be protected from direct sunlight at a temperature between 2 and 8º; (3) for intravescical instillation only; not intended for immunization; (4) to be used immediately after reconstitution.

Biotechnology Products

Erythropoeitin for Injection. Page 3352.
Usual strengths. Read "per vial" as "per container".

Erythropoeitin Injection. Page 3355.
Usual strengths. Read "per vial" as "per container".

Filgrastim Concentrated Solution. Page 3359
Identification
C. Determine by size-exclusion chromatography (2.4.16).
Change **to**: In the test for dimers and related substances of higher molecular mass, the retention time of the principal peak obtained with the test solution is similar to that of the principal peak obtained with the reference solution.

Filgrastim Injection. Page 3363
B. Determine by size-exclusion chromatography (2.4.16).
Change **to**: In the test for dimers and related substances of higher molecular mass, the retention time of the principal peak obtained with the test solution is similar to that of the principal peak obtained with the reference solution.

Interferon Alpha 2a Injection. Page 3369.
Tests
pH (2.4.24).
Change **to**: **pH** (2.4.24). Comply with the limits as approved by National Regulatory Authority.