



P17011/01/2019-PvPI
Indian Pharmacopoeia Commission
National Coordination Centre-Pharmacovigilance Programme of India
(Ministry of Health & Family Welfare, Govt. of India)

Sector-23, Rajnagar,
Ghaziabad-201002, U.P
Dated: September 19, 2019

Subject: Pharmacovigilance Programme of India (PvPI) outcome communicated to National Regulatory Authority (NRA), Central Drugs Standard Control Organisation (CDSCO) for taking appropriate regulatory action.

The following India specific drugs safety signals/Prescribing Information Leaflet (PIL) changes are communicated to the NRA, CDSCO for taking appropriate regulatory action.

S.No	Suspected drugs	Adverse drug reactions	PvPI outcome	Action taken by CDSCO
4th Signal Review Panel (SRP) Recommendation (SRP held on December 8-9, 2014)				
1	Carbamazepine	Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)	For Drug Safety Label Change – Patient may be screened for HLA-B*1502 prior to initiating the Carbamazepine treatment	CDSCO requested all State/UT Drugs Controllers to instruct all the manufacturers licensed for the said product should be asked for inclusion of the same in prescribing information and same should be available on the official website of all the manufacturers manufacturing Carbamazepine in the country.
5th SRP Recommendations (SRP held on May9, 2015)				
2	Piperacillin and Tazobactam	Hypokalaemia, Bronchospasm	To include in PIL	CDSCO requested all State/UT Drugs Controllers to instruct all the manufacturers of the said FDC product to include Hypokalaemia and Bronchospasm in their package inserts as well as any other promotional literature.
3	Mannitol	Hypokalaemia	To include in PIL	Under consideration of CDSCO
4	Rota-Virus Vaccine	Intussusception	To include in PIL	Under consideration of CDSCO
6th SRP Recommendations (SRP held on October 6, 2015)				
5	Rabies Vaccine	Erythema Multiforme	To include in PIL	All the manufacturers and importers of Rabies Vaccine are directed to ensure that Erythema Multiforme is inserted in the drug safety label of the Rabies Vaccine.
6	Ranitidine	Cardiac Arrest	To include in PIL	Under consideration of CDSCO
7	Pulmonary Surfactant	Pulmonary Haemorrhage	To include in PIL	Under consideration of CDSCO
7th SRP Recommendations (SRP held on March 01, 2016)				
8	Ceftriaxone	Stevens Johnson syndrome	To include in PIL	Under consideration of CDSCO
9	Lamotrigine	Stevens Johnson syndrome (SJS)	To include in PIL	Under consideration of CDSCO

		and Toxic Epidermal Necrolysis (TEN)		
10	Betamethasone	Photosensitivity Reaction	To include in PIL	Under consideration of CDSCO
11	Azithromycin	Acute Generalised Exanthematosus Pustulosis (AGEP)	To include in PIL	Under consideration of CDSCO
12	Cloxacillin	Acute Generalised Exanthematosus Pustulosis (AGEP)	To include in PIL	Under consideration of CDSCO
8th SRP Recommendations (SRP held on July 8, 2016)				
13	Cefixime	Acute Generalised Exanthematosus Pustulosis (AGEP)	Signal	The 53 rd Subject Expert Committee-Antimicrobial & Antiviral on 16.01.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the concerned manufacturers to incorporate AGEP as one of the adverse effects of Cefixime in the package inserts of its formulations.
14	Sodium Valproate	Gum Hyperplasia	To include in PIL	The 43 rd Subject Expert Committee - Neurology & Psychiatry on 09.01.2019 at CDSCO, HQ recommended that the manufacturers of Sodium Valproate formulations should include following statement in the package inserts of the drug: "Long term use of the drug may be associated with gum hyperplasia".
15	Itraconazole	Photosensitivity reaction	To include in PIL	Under consideration of CDSCO
16	Ibuprofen	Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)	To include in PIL	Under consideration of CDSCO
17	Amoxicillin/Clavulanate Potassium	Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)	To include in PIL	Under consideration of CDSCO
18	Ciprofloxacin	Stevens Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)	To include in PIL	Under consideration of CDSCO
9th SRP Recommendations (SRP held on November 29, 2016)				
19	BCG vaccine	Lymphadenopathy	To include in PIL	Under consideration of CDSCO
20	Docetaxel	Candidiasis	To include in PIL	Under consideration of CDSCO
21	Itraconazole	Acute Generalised Exanthematosus	Signal	Under consideration of CDSCO

		Pustulosis (AGEP)		
22	Furosemide	Dermatitis Lichenoid	Signal	The 24 th Subject Expert Committee - Reproductive & Urology on 20.04.2017 at CDSCO, HQ agreed with the recommendation of Signal Review Panel, PvPI and update the package inserts accordingly.
23	Lithium Carbonate	Drug Reaction with Eosinophilia and Systemic symptoms Syndrome (DRESS)	Signal	The 26 th Subject Expert Committee - Neurology and Psychiatry on 17.03.2017 at CDSCO, HQ agreed with the recommendation of Signal Review Panel, PvPI to incorporate Lithium Carbonate associated DRESS in to the package inserts of suspected drug marketed in India.
24	Phenytoin	Acute Generalised Exanthematosus Pustulosis (AGEP)	To include in PIL	The 26 th Subject Expert Committee - Neurology and Psychiatry on 17.03.2017 at CDSCO, HQ agreed with the recommendation of Signal Review Panel, PvPI to incorporate Phenytoin associated AGEP in to the package inserts of suspected drug marketed in India.
10th SRP Recommendations (SRP held on May 16, 2017)				
25	Sulfasalazine	Stevens Johnson Syndrome (SJS)	To include in PIL	The 19 th Subject Expert Committee –Gastroenterology & Hepatology on 23.05.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of formulations of Sulfasalazine to include Stevens Johnson Syndrome (SJS) as an ADR in the package insert of the product.
26	Sulfasalazine	Toxic Epidermal Necrolysis (TEN)	To include in PIL	The 19 th Subject Expert Committee –Gastroenterology & Hepatology on 23.05.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of formulations of Sulfasalazine to include Toxic Epidermal Necrolysis (TEN) as an ADR in the package insert of the product.
11th SRP Recommendations (SRP held on October 5, 2017)				
27	Fluconazole	Hyperpigmentation	Signal	The 57 th Subject Expert Committee –Antimicrobial & Antiviral on 22.05.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of formulations of Fluconazole to include Hyperpigmentation as an ADR in the package insert of the product.
28	Terbinafine	Acute Generalised Exanthematosus Pustulosis (AGEP)	To include in PIL	The 57 th Subject Expert Committee –Antimicrobial & Antiviral on 22.05.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of formulations of Terbinafine to include Acute Generalised Exanthematosus Pustulosis (AGEP) as an ADR in the package insert of the product.
29	Dipeptidyl peptidase-4	Arthralgia	To include in PIL	Under consideration of CDSCO

	(DPP4) Inhibitors			
12th SRP Recommendations (SRP held on March 27, 2018)				
30	Carbamazepine	Drug Reaction with Eosinophilia and Systemic symptoms Syndrome (DRESS)	To include in PIL	The 48 th Subject Expert Committee-Neurology & Psychiatry on 12.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Carbamazepine formulation to include DRESS Syndrome as an ADR of Carbamazepine.
31	Meropenem	Hypokalaemia	To include in PIL	The 58 th Subject Expert Committee-Antimicrobial & Antiviral on 13.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Meropenem formulation to include Hypokalaemia as an ADR of Meropenem.
32	Artemether + Lumefantrine	Stevens Johnson syndrome (SJS)	To include in PIL	The 58 th Subject Expert Committee-Antimicrobial & Antiviral on 13.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Artemether + Lumefantrine formulation to include Stevens Johnson syndrome (SJS) as an ADR of Artemether + Lumefantrine.
33	Diclofenac	Nicolau Syndrome	To include in PIL	The 51 st Subject Expert Committee-Analgesic & Rheumatology on 13.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Diclofenac injection to include Nicolau Syndrome as an ADR of Diclofenac injection.
34	Lamivudine	Hearing Loss	To include in PIL	The committee deliberated the recommendation of the NCC-PvPI & recommended that further details including that of ICSRs should be obtained from NCC-PvPI for further review.
35	Amlodipine	Alopecia	To include in PIL	The 65 th Subject Expert Committee-Cardiovascular & Renal on 07.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Amlodipine formulation to include Alopecia as an ADR of Amlodipine.
36	Cefixime	Mouth Ulceration	To include in PIL	The 58 th Subject Expert Committee-Antimicrobial & Antiviral on 13.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Cefixime formulation to include Mouth Ulceration as an ADR of Cefixime.
37	Carvedilol	Hyperkalaemia	To include in PIL	The 65 th Subject Expert Committee-Cardiovascular & Renal on 07.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Carvedilol formulation to include Hyperkalemia as an ADR of Carvedilol.

38	Amlodipine	Gingival Hypertrophy	To include in PIL	The 65 th Subject Expert Committee-Cardiovascular & Renal on 07.06.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of the Amlodipine formulation to include Gingival Hypertrophy as an ADR of Amlodipine.
13th SRP Recommendations (SRP held on August 21, 2018)				
39	Cefotaxime	Angioedema	To include in PIL	The 53 rd Subject Expert Committee-Antimicrobial & Antiviral on 16.01.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the concerned manufacturers to incorporate Angioedema as one of the adverse effects of Cefotaxime in the package inserts of its formulations.
40	Ofloxacin	Stevens-Johnson Syndrome	To include in PIL	The 53 rd Subject Expert Committee-Antimicrobial & Antiviral on 16.01.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the concerned manufacturers to incorporate SJS/TEN as one of the adverse effects of Ofloxacin in the package inserts of its formulations.
41	Tranexamic Acid	Seizure/Convulsion	To include in PIL	The 79 th Subject Expert Committee-Oncology & Haematology on 18.01.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the concerned manufacturers to incorporate seizure/convulsion as one of the adverse effects of Tranexamic Acid in the package inserts of its formulations.
42	Quetiapine	Urinary Incontinence	To include in PIL	The 43 rd Subject Expert Committee –Neurology & Psychiatry on 09.01.2019 at CDSCO, HQ recommended that the manufacturers of Quetiapine formulations should include following statement in the package inserts of the drug: “the use of the drug may be associated with Urinary Incontinence”.
43	Sulfasalazine	DRESS Syndrome	To include in PIL	The 46 th Subject Expert Committee –Analgesic & Rheumatology on 17.01.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the concerned manufacturers to incorporate DRESS Syndrome as one of the adverse effects of Sulfasalazine in the package inserts of its formulations.
14th SRP Recommendations (SRP held on February 28, 2019)				
44	Tramadol	Hiccups	To include in PIL	The 49 th Subject Expert Committee (Analgesic & Rheumatology) meeting held on 11.04.2019 at CDSCO, HQS, New Delhi. After detailed deliberation, the SEC recommended that the details of Individual Case Safety Reports should be obtained from PvPI for further review by the Committee.

45	Phenobarbital	DRESS Syndrome	To include in PIL	The 47 th Subject Expert Committee –Neuralgia & Psychiatry on 15.05.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of formulations of Phenobarbital to include Drug Rash with Eosinophilia & Systemic Symptoms (DRESS) as an ADR in the package insert of the product.
46	Cefepime	Urticaria	To include in PIL	The 57 th Subject Expert Committee –Antimicrobial & Antiviral on 22.05.2019 at CDSCO, HQ recommended that CDSCO should request the State Drugs Controllers to direct the manufacturers of formulations of Cefepime to include Urticaria as an ADR in the package insert of the product.
47	Glibenclamide	Palpitation	To include in PIL	The 54 th Subject Expert Committee –Endocrinology & metabolism held on 23.04.2019 at CDSCO, HQ. The committee opined that palpitation is a known and reported symptom of Hypoglycemia associated with Glibenclamide which is already mentioned in package insert of Glibenclamide. It is not clear whether the palpitations as reported in 12 ICSRs are due to hypoglycaemia or otherwise. Therefore, further details in this regard should be obtained from NCC-PvPI for further consideration.
15th SRP Recommendations (SRP held on September 19, 2019)				
48	Chloroquine	TEN/SJS	To include in PIL	Under consideration of CDSCO
49	Proton Pump Inhibitors	Acute Kidney Injury	To include in PIL	Under consideration of CDSCO