SAFETY ALERT

DRAP SAFTEY ALERT NO. 54

Safety Alert of Risk of severe cutaneous adverse reactions with Cefotaxime

Date: 27th of March, 2025.

Target Audience.

- Provincial Health Departments/Provincial PV Centres/Healthcare Commissions;
- Manufacturers and importers of Cefotaxime; and
- Healthcare Professionals.

Background.

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicine Agency (EMA) in its January 2024 meeting recommended updating the product information (Warnings and Precautions and Adverse Drug Reaction sections) for cefotaxime, to include the risk of drug reaction with eosinophilia and systemic symptoms (DRESS) and to strengthen advice on severe cutaneous adverse reactions (SCARs) including DRESS.

The updated product information's undesirable effect of Cefotaxime should list Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) as an ADR with frequency "Not known".Whereas, the warnings and precautions section for cefotaxime should state the following:

- SCARs, including acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and DRESS, which can be life-threatening or fatal, have been reported post-marketing in association with cefotaxime/ethambutol treatment.
- At the time of prescription, patients should be advised of the signs and symptoms of skin reactions.
- If signs and symptoms suggestive of these reactions appear, cefotaxime/ethambutol should be withdrawn immediately.
- If the patient has developed AGEP, SJS, TEN or DRESS with the use of cefotaxime/ethambutol, treatment with cefotaxime/ethambutol must not be restarted and should be permanently discontinued.

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- In children, the presentation of a rash can be mistaken for the underlying infection or an alternative infectious process, and physicians should consider the possibility of a reaction to cefotaxime in children who develop symptoms of rash and fever during therapy with cefotaxime.

Action in Pakistan.

The case was discussed in the 5th meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC) of the DRAP held on 2nd of Janauary, 2025 which decided as per Rule 10 (1) (h) (iv) of Pharmacovigilance Rules, 2022, that registration holders should include information related to severe cutaneous adverse reactions (SCARs) in the warning and precaution section of the prescribing information/label of cefotaxime and also list the Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) as an ADR with frequency "Not known" in the prescribing information.

Therapeutic Good.

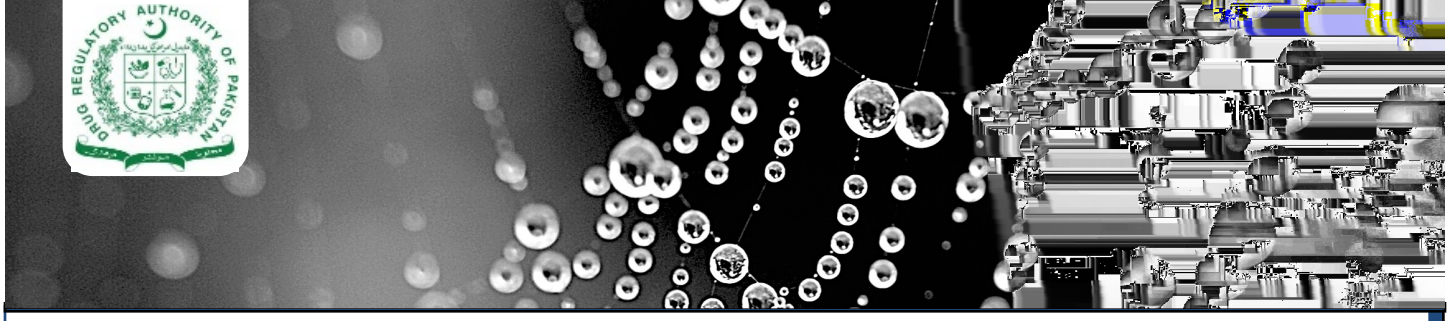
Name: Cefotaxime is an injectable third-generation cephalosporin antibiotic used to treat a variety of bacterial infections.

Advice for Healthcare Professionals.

Severe Cutaneous Adverse Reactions (SCARs), including AGEP, SJS, TEN, and DRESS, have been reported post-marketing with cefotaxime that can be life-threatening. Patients should be informed of skin reaction symptoms at the time of prescription, and treatment must be discontinued immediately if symptoms appear. If SCARs occur, cefotaxime must not be restarted. In children, rashes may be mistaken for infections, so clinicians should consider SCARs if rash and fever develop during treatment.

Advice for patients.

Patients are informed that serious skin reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP) have been reported in association with cefotaxime treatment. Stop using cefotaxime and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions. Furthermore, must discuss with your doctor if you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking cefotaxime or other cephalosporins.



Guidelines for reporting Adverse Drug Reactions (ADRs).

Both healthcare professionals and patients are requested to report any adverse drug reaction with Cefotaxime to the National Pharmacovigilance Centre (NPC), Drug Regulatory Authority of Pakistan (DRAP) through the Med Vigilance E-Reporting System (E-forms) available on the DRAP website. Similarly, ADRs can also be reported through the VigiMobile App, which can be downloaded by scanning the barcode available on the DRAP website.

References.

- Minutes of the 5th meeting of the Pharmacovigilance Risk Assessment Expert Committee (PRAEC), DRAP.
- EMA-PRAC recommendations on signals adopted at the 8-11 January 2024 PRAC meeting.