



SAFETY ALERT

DRAP SAFETY ALERT NO. 56

Safety Alert of Risk of persistent corneal injury and significant visual impairment with Chlorhexidine (cutaneous use).

Date: 23rd of April, 2025.

Target Audience.

- Provincial Health Departments/Provincial PV Centres/Healthcare Commissions;
- Manufacturers and importers of Chlorhexidine;
- Healthcare Professionals; and
- Lady Health Workers (LHWs).

Background.

The Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicine Agency (EMA) in its April, 2024 meeting has recommended updating the product information for chlorhexidine for cutaneous use, indicated for skin disinfection, and relevant combination products to include the risk of persistent corneal injury and significant visual impairment. Cases of severe corneal erosion and permanent significant visual impairment due to inadvertent ocular exposure have been reported in the post-marketing phase, leading to some patients requiring corneal transplants.

The PRAC agreed that all MAHs of chlorhexidine monocomponent and fixed-combination-containing products indicated for skin disinfection and intended for cutaneous use should update the product information. The warning and precaution sections of the product information for the relevant chlorhexidine products should state:

- This product must not come into contact with the eye.
- Serious cases of persistent corneal injury, potentially requiring corneal transplant, were reported following accidental ocular exposure to chlorhexidine-containing medicinal products despite taking eye protective measures due to migration of solution beyond the intended surgical preparation area.
- Extreme care must be taken during application to ensure that this product does not migrate beyond its intended application site into the eyes. Particular care should be taken in anaesthetised patients, who are unable to immediately report ocular exposure.





- If this product comes into contact with the eyes, wash out promptly and thoroughly with water. An ophthalmologist's advice should be sought.

The PRAC also recommended updating the undesirable effect section of production information by listing Corneal erosion, epithelium defect/corneal injury, and significant permanent visual impairment as frequency “not known.”

Previously, the World Health Organization (WHO) in August 2020 issued an alert about multiple reports of administration errors causing eye injuries, such as blindness, following incorrect route of administration of chlorhexidine gluconate (CHX) to the eyes instead of to the umbilical cord in newborns.

Clean, dry cord care is recommended for newborns born in health facilities, and at home in low neonatal mortality settings. The use of chlorhexidine in these situations may be considered only to replace the application of a harmful traditional substance such as cow dung to the cord stump. The use of CHX is being implemented in many countries (South Asia and sub-Saharan Africa) as part of a package of essential newborn interventions to reduce the incidence of omphalitis. It is also listed in the WHO Essential Medicines List.

CHX causes serious harm if mistakenly applied to the eyes, resulting in severe eye injuries. Over forty (40) cases of such incorrect administration have been recorded, either as media reports or in the literature, since 2015. Injuries associated with both the liquid and gel (ointment) formulations have been reported when CHX was mistaken for eye drops or ointments. All healthcare professionals, caregivers and others involved in the distribution, use and/or administration of chlorhexidine 4% gel or solution, are advised to take all necessary measures and precautions to ensure its correct use and administration.

The following suggestions were recommended to National Neonatal and Reproductive Health Programmes and/or Regulators include the following:

- Assess what products are part of the newborn package and select the optimal primary container/dosage form for CHX or modify the design of the container to distinguish the product from other medicines typically used for newborns.
- Update the product label with appropriate information on the safe use of the product.
- Develop more detailed instructions for users (flyers, posters, pictorials etc.) that are culturally appropriate and easy to understand, to ensure correct use of the product.





- Train healthcare professionals who interact with mothers and/or provide the product to ensure a full understanding of the indications and contraindications for use and application methods.

All stakeholders were advised to remain alert to incidents of eye injury with CHX in their settings and to report these to their National Regulatory Authority (NRA). Member States are reminded that adverse events associated with the use of any medicinal product should be reported to the National Regulatory Authority.

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 January, 2025 which decided as per Rule 10 (1) (h) (iv) of Pharmacovigilance Rules, 2022 that registration holders should update the warning and precaution sections of chlorhexidine monocomponent and fixed-combination-containing products indicated for skin disinfection as well as to list Corneal erosion, epithelium defect/corneal injury, and significant permanent visual impairment as frequency “not known” in the ADR section. It was also decided that DRAP should coordinate with provincial health departments for onward coordination with hospitals to ensure that proper protective equipment are being used by persons handling chlorhexidine along with hospital labelling of “irritating agent” and include this product in the material data safety sheet.

Therapeutic Good Affected.

Name: Chlorhexidine is an antiseptic and disinfectant, which is used for skin disinfection before surgery and is applied to the umbilical cord stump during the first week of life for newborns who are born at home in settings with high neonatal mortality (neonatal mortality rate >30 per 1000).

Advice for Healthcare Professionals.

Healthcare professionals are advised that Chlorhexidine must not come into contact with the eye. Serious cases of persistent corneal injury, potentially requiring corneal transplant, were reported following accidental ocular exposure to chlorhexidine containing medicinal products despite taking eye protective measures due to migration of solution beyond the intended surgical preparation area. Extreme care must be taken during application to ensure that Chlorhexidine does not migrate beyond its intended application site into the eyes. Particular care should be taken in anaesthetised patients, who are unable to immediately report ocular exposure. If chlorhexidine solutions comes into contact with the eyes, wash out promptly and thoroughly with water. An ophthalmologist’s advice should be sought.





Advice for patients.

Talk to your doctor, pharmacist or nurse before using Chlorhexidine as it must not come into contact with the eye due to the risk of visual damage. If it comes into contact with the eyes, wash out immediately and thoroughly with water. In case of any irritation, redness or pain in the eye, or visual disturbance, ask for medical advice promptly. Serious cases of persistent corneal injury (injury to the surface of the eye) potentially requiring corneal transplant have been reported when similar products have accidentally come in contact with the eye during surgical procedures, in patients under general anaesthesia (deep painless sleep).

Guidelines for reporting Adverse Drug Reactions (ADRs).

Healthcare professionals and patients are requested to report any adverse drug reaction with Chlorhexidine and other medicines 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 April 2024 PRAC meeting.](#)
- [World health Organization report on Chlorhexidine 7.1% digluconate \(CHX\) aqueous solution or gel \(10ml\): Reports of serious eye injury due to errors in administration.](#)

