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Reaksi

DRUG SAFETY NEWS

Mission: This publication provides information and recommendations to healthcare professionals to enhance communication of drug safety updates, raise awareness of adverse drug reactions reported, and stimulate additional adverse drug reaction reporting.

This is a bimonthly publication by the Drug Safety Monitoring Centre, National Pharmaceutical Control Bureau (NPCB), Malaysia.

TO REPORT AN ADVERSE DRUG REACTION

Online

1. Visit www.bpfk.gov.my.
2. Click on ADR Reporting and Product Complaints.
3. Click to report as a healthcare professional online or via hardcopy.
4. Submit the form once completed.

Mail

1. Print out and complete the ADR form available from our website.
2. Mail or fax to:
   The Drug Safety Monitoring Centre, Centre for Post Registration of Products, National Pharmaceutical Control Bureau, Ministry of Health, PO Box 319, Jalan Sultan, 46730 Petaling Jaya, Selangor.

Telephone

03-7883 5400
(ext. 8460/ 8461/ 8463)

Fax

03-7956 7151

In This Issue:

New Alerts on Serious Skin Reactions

In Malaysia, ADR data indicates that the drugs/ classes most commonly associated with causing serious skin reactions are allopurinol, antiepileptics, antibiotics, and non-steroidal anti-inflammatory agents (NSAIDs). Early recognition and cessation of the suspected drug is vital to reduce morbidity and mortality.

Among the drug safety issues reviewed by NPCB in the past year, eight (8) involved new or additional warnings on serious skin reactions, as follow:

Clobazam, Carvedilol, Panitumumab, and Tramadol + Paracetamol (a combination product)

Direct Healthcare Professional Communications (DHPCs) were issued for these products between April-July 2014 to inform healthcare professionals about cases of Stevens-Johnson Syndrome (**SJS**) and toxic epidermal necrolysis (**TEN**) associated with the use of these drugs.

Galantamine

This drug for dementia related to Alzheimer's disease, has been associated with reports of **SJS** and acute generalised exanthematous pustulosis (**AGEP**). A DHPC was issued in December 2014 advising healthcare professionals to counsel patients on this risk.

Ustekinumab

In patients with psoriasis, **exfoliative dermatitis** has been reported following ustekinumab treatment, while patients with plaque psoriasis may develop **erythrodermic psoriasis.** As part of the monitoring of the patient's psoriasis, physicians should be alert for symptoms of these conditions. The product information leaflets for ustekimumab have been updated with this information.

Ziprasidone

Cases of **SJS** and drug reaction with eosinophilia and systemic symptoms (**DRESS**) have been reported with exposure to this antipsychotic drug. The package inserts of ziprasidone-containing products are being updated with this information.

Paracetamol (acetaminophen)

This drug has been associated with rare but serious skin reactions, including **SJS, TEN** and **AGEP**. The product information of all paracetamol preparations will be updated with a warning on this risk.

Advice for Healthcare Professionals

- Early detection: Patients on these drugs must be counselled to seek immediate medical advice at the **first signs** of a severe skin reaction, such as fever, sore throat, rash, eye irritation, or swollen lymph nodes.
- Treatment with these drugs should be **stopped immediately** if a severe skin reaction is suspected.
- Please report all suspected ADRs to the Drug Safety Monitoring Centre. The type of cutaneous ADR must be **specified** by attaching the NPCB **'Clinical Manisfestation of Cutaneous ADR' form** available on our website.

Chlorhexidine Solutions: Risk of Chemical Burns to Skin in Premature Infants

Overview

Chlorhexidine is a cationic bis-biguanide antiseptic with broad spectrum of activity against Gram +ve and Gram –ve bacteria.[1] It is widely used in disinfectants, cosmetics (as an additive to creams, toothpaste, deodorants, and antiperspirants), and pharmaceuticals (as the active substance in wound dressings or antiseptic mouthwashes, and preservative in eye drops).

Further information on the safety issue

Review into the safety of chlorhexidine was triggered by the Medicines and Healthcare Products Regulatory Authority (MHRA), United Kingdom, as severe skin reactions had been reported in premature infants who were **treated with chlorhexidine solutions prior to central venous catheterisation** (CVC).

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (EMA's PRAC) then conducted a full review with additional information from spontaneous reporting and published literature. This review identified 44 cases of **chemical burns in neonates** following use of chlorhexidine solutions, mostly prior to umbilical catheter insertions. Alcohol-based chlorhexidine solutions (0.5% and 2%) were used in 29 cases, 11 cases occurred with 2% aqueous solution, while the remaining cases did not specify the type of chlorhexidine product.

Overall, the data revealed a **higher risk** of skin toxicity in the following scenario[2]:

(i) infants born at less than 32 weeks of gestation;
(ii) chlorhexidine applied within the first 2 weeks of life;
(iii) use of chlorhexidine-impregnated dressings compared to solutions, in neonates and older children;
(iv) pooling of chlorhexidine around the umbilicus or under the infant.

However, there was limited data for neonates comparing different antiseptic agents and different types of chlorhexidine solutions, therefore no robust recommendations could be provided on the most efficacious products and their safe use.

Local Scenario

There are currently **64** products containing chlorhexidine registered with the Drug Control Authority. Chlorhexidine preparations are listed in the Ministry of Health (MOH) Drug Formulary under category C and C+ (may be initiated by paramedics/ medical officers/ specialists/ consultants) for **indications** including:

(i) as disinfectant in CVC care bundles;
(ii) hand and skin disinfection;
(iii) preoperative hand disinfection;
(iv) for wounds or burn;
(v) emergency disinfection of instruments.

Chlorhexidine is commonly used in Malaysia as an antiseptic prior to catheterisation in neonatal intensive care units (NICUs), as well as for umbilical cord care in newborns.

Adverse Drug Reaction Reports

Since year 2000, the NPCB Drug Safety Monitoring Centre has received 12 reports related to chlorhexidine with 22 adverse events. However, **none** of the reports were related to **topical use in paediatric** patients.

All the reports involved chlorhexidine used as a gargle, skin disinfectant before vaginal examination, hand rub, or body wash in patients aged 13 years and above. The adverse events reported were mainly allergy-related reactions such as rash, itching, eczema, contact dermatitis, sore throat, and facial swelling.

Advice for Healthcare Professionals[3]

- When using alcohol-based or water-based chlorhexidine solutions on premature infants, **bear in mind** the risk of severe chemical burns, while still considering any impact on antisepsis and preventing catheter-related sepsis.
- Use the **minimum amount** of chlorhexidine solution required and do not allow the solution to pool. **Remove any excess** solution, especially in skin folds, and any soaked materials, drapes, or gowns before proceeding with catheter insertion.
- **Monitor** patients frequently to detect and manage cutaneous side effects at an early stage.
- All adverse events associated with chlorhexidine-containing products should be **reported** to the NPCB Drug Safety Monitoring Centre.

References:

1. Micromedex® Healthcare Series. Chlorhexidine Gluconate: Mechanism of Action. [Accessed: 12 March 2015]
2. MHRA (2015). Direct Healthcare Professional Communication: Chlorhexidine solutions: risk of chemical burn injury to skin in premature infants. [29 Jan 2015]
3. EMA (2014). PRAC recommendations on signals: Adopted at the PRAC meeting of 8-11 September 2014 [25 September 2014_EMA/PRAC/490498/2014]