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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.

TO REPORT AN ADVERSE DRUG REACTION

Online

1. Visit http://npra.moh.gov.my.
2. Click on 'ADR Reporting'.
3. Click to report as a healthcare professional and print out the ADR form.
4. Scan and submit the completed form via email to fv@npra.gov.my.

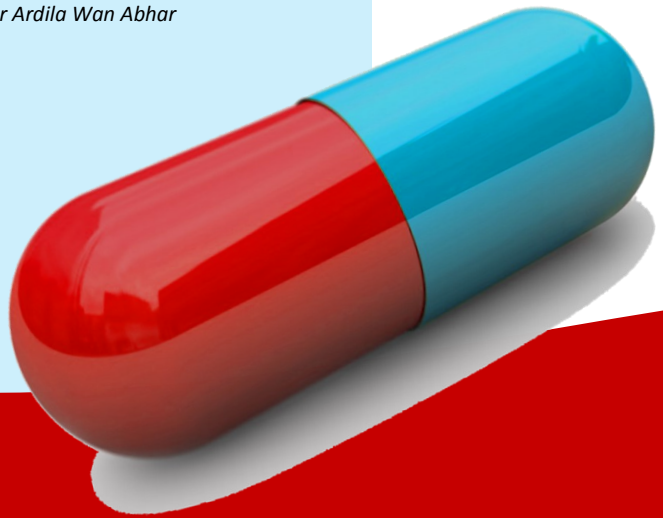
Mail

1. Print out and complete the ADR form available from our website.
2. Mail or fax to:
   The Pharmacovigilance Section,
   National Pharmaceutical Regulatory Agency (NPRA),
   Ministry of Health, Malaysia.
   Lot 36, Jalan Universiti,
   46200 Petaling Jaya, Selangor.

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

Fax
03-7956 7151

In This Issue:



A bimonthly publication by the
National Pharmaceutical Regulatory Agency (NPRA), Malaysia.

Hyoscine Butylbromide Injection: Risk of Serious Adverse Effects in Patients with Underlying Cardiac Disease

Overview

Hyoscine or scopolamine is an anti-spasmodic drug that is used to relieve spasm in the stomach, intestines or bladder. In Malaysia, hyoscine butylbromide injection is approved to reduce oral secretions before surgery, and to treat gastrointestinal or genitourinary tract spasms, as well as motility disorders of the biliary system.

Background of Safety Issue

The United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) has requested updates of the product information for all hyoscine butylbromide injections on the risk of serious adverse reactions in patients with underlying cardiac disease. This decision was triggered by eight (8) reports of patients who died after receiving hyoscine butylbromide injection. The fatal adverse reaction was reported as acute myocardial infarction or cardiac arrest in most of these cases.

Hyoscine butylbromide injection is known to cause adverse effects including tachycardia, hypotension, and anaphylaxis. However, studies have shown that these effects can be more serious in patients with underlying cardiovascular disease such as heart failure, coronary heart disease, cardiac arrhythmia or hypertension. This may be attributed to an increased number of cardiac mast cells in patients with pre-existing cardiac disease, which results in the release of high concentrations of cardiotoxic mast cell mediators during serious adverse events such as anaphylaxis. Besides that, the presence of any atherosclerotic lesions make the coronary arteries more susceptible to the effects of mast cell and basophil-derived mediators.

Local Scenario

Currently, there are five (5) injectable products containing hyoscine butylbromide registered with the Drug Control Authority (DCA). Hyoscine butylbromide was first registered in Malaysia in 1988.

Adverse Drug Reaction (ADR) Reports

From year 2002 to December 2016, the NPRA has received 147 ADR reports with 283 adverse events associated with hyoscine butylbromide (all dosage forms). The most commonly reported adverse events were minor skin reactions (rash, pruritus and urticaria).

Of the total reports received, 57 were related to hyoscine butylbromide injectable products. Besides the skin reactions mentioned above, some patients who received hyoscine injections were reported to suffer shortness of breath, blurred vision, and flushing. Adverse events involving the System Organ Class (SOC) Cardiac Disorders were palpitation, tachycardia and syncope.

NPRA has reviewed this safety issue and is looking into strengthening the precautions and warnings in local product information for hyoscine butylbromide injections. NPRA will continue to monitor this risk in relation to oral preparations.

Advice for Healthcare Professionals

- Hyoscine butylbromide injection may cause serious adverse effects including tachycardia, hypotension, and anaphylaxis.
- Exercise **caution** when using hyoscine butylbromide injection to treat patients with underlying cardiovascular disease such as heart failure, coronary heart disease, cardiac arrhythmia or hypertension.
- **Monitor** these patients closely for any adverse events, and ensure that resuscitation facilities are readily available.
- All adverse events related to hyoscine butylbromide injections should be reported to the NPRA.

Keytruda® (pembrolizumab): Risk of Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

Overview

Pembrolizumab is a monoclonal antibody that helps the immune system detect and fight cancer cells. It targets the programmed death ligand-1 (PD-1) receptor, blocks the protective mechanism on cancer cells and allows the immune system to destroy the cancer cells. Pembrolizumab is indicated for treatment of melanoma and Non-Small Cell Lung Carcinoma (NSCLC).

Background of Safety Issue

Health Canada highlighted cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) reported internationally in patients treated with Keytruda® (pembrolizumab) in clinical trials and the post-marketing setting. There were eight (8) serious cases of SJS (6 in clinical trials and 2 post-marketing) and two (2) serious cases of TEN (both post-marketing), reported in patients treated with Keytruda®. These included one fatal case each of SJS and TEN. Health Canada is working with the product manufacturer to update the pembrolizumab monograph with information on this risk.

Local Scenario

In Malaysia, currently there is one (1) registered product containing pembrolizumab.

Since the product was registered in year 2016, the NPRA has received a total of 10 ADR reports with 25 adverse events related to pembrolizumab. Among the adverse events reported were pneumonitis, shortness of breath, hypoglycaemia and hyponatraemia.

While no reports specifically of SJS or TEN have been received to date, there were three (3) reports related to unspecified skin reactions involving the use of pembrolizumab. One of the cases reported the patient suffering a skin reaction associated with mouth ulceration, oral pain and difficulty eating, the second case involved a patient who experienced a skin reaction and hypothyroidism, while the third patient suffered a severe skin reaction with fatal outcome. However, all the reports lacked information on the final diagnosis of skin reaction. All three (3) cases were given causality C3 (possibly-related to the drug).

A Direct Healthcare Professional Communication (DHPC) was approved by the NPRA in May 2017 for distribution by the holder. The package insert of Keytruda® has been updated with information on the risk of SJS and TEN.

Advice for Healthcare Professionals

- Advise patients about the **risks and benefits** of pembrolizumab before initiating treatment.
- Counsel patients on the risks of **SJS and TEN**, and advise them to seek immediate medical attention if they develop rash, fever, sore throat, or eye irritation.
- If signs and symptoms of SJS or TEN develop, withhold pembrolizumab and refer the patient for specialised care.
- Permanently discontinue pembrolizumab if SJS or TEN is confirmed.
- **Please report** all adverse events suspected to be related to the use of pembrolizumab to the NPRA.