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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 the ADR form available from our website.
2. Mail or fax to:
   The National ADR Monitoring Centre, Centre for Post Registration of Products and Cosmetic Control, National Pharmaceutical Regulatory Agency (NPRA), 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:

Live Attenuated Vaccines: Reminder to Avoid Use In Immunosuppressed Individuals

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

Live Attenuated Vaccines: Reminder to Avoid Use In Immunosuppressed Individuals

Vaccines: An Overview

A vaccine is a biological substance administered to individuals to elicit immunity against a specific disease[1]. The two basic types of vaccines are live attenuated and inactivated vaccines, which each have different characteristics that determine how the vaccine is used[2] (**Table 1**).

In this issue of *Reaksi*, we remind all healthcare professionals that live attenuated vaccines (LAV) should **not be given** to clinically immunosuppressed individuals, including:

- ◊ infants who have been exposed to immunosuppressive treatment from the mother in utero or via breastfeeding (e.g. TNFα antagonists or other biologics);
- ◊ immunosuppressed elderly (due to drugs e.g. transplant medication, high-dose corticosterioids; or underlying illness e.g. lymphoproliferative disorders).

The use of LAV is also generally contraindicated in those with a history of severe allergic reaction to a vaccine component or following a prior dose, and pregnant women.

Background of the Safety Issue

The National Pharmaceutical Regulatory Agency (NPRA) initiated a review into the safety of LAV following an alert by the Medicines and Healthcare Products Regulatory Agency (MHRA), United Kingdom, regarding the risk of LAV use among immunosuppressed individuals.

MHRA highlighted several adverse event reports involving immunosuppressed patients who were given a LAV, resulting in severe infection or death. These included **four (4) fatal disseminated BCG cases** in neonates after **in utero exposure to TNFα antagonists,** and several **disseminated viral infection cases post shingles vaccination** among immunosuppressed elderly[3].

Local Scenario

There are currently **13 types of live attenuated vaccines registered in Malaysia**: BCG, Oral Typhoid, Oral Polio, Measles, Rubella, Varicella, Yellow Fever, Shingles, Japanese Encephalitis, Rotavirus, Measles/Rubella, Measles/Mumps/Rubella, and Measles/Mumps/Rubella/Varicella.

Immunosuppression is a **contraindication** for all the live attenuated vaccines except rotavirus. Rotavirus vaccination is contraindicated in individuals with Severe Combined Immunodeficiency Disorder (SCID), but not for immunosuppressed infants (needs careful consideration of potential benefits & risks). Current local guidelines (Guidelines for Adult Immunisation 2nd edition & the Paediatric Protocols for Malaysian Hospitals 3rd edition) recommend **NOT** to give LAVs to immunosuppressed individuals.

Table 1: Live Attenuated Vaccines vs. Inactivated Vaccines[1,2]

Characteristics	Live Attenuated Vaccines (LAV)	Inactivated Vaccines
Method of production	• Derived from "wild" or disease-causing viruses or bacteria which are attenuated or weakened in a laboratory, usually by repeated culturing.	• Made up of whole viruses or bacteria, or fractions of either. Fractional vaccines are either protein-based (toxoid/subunit) or polysaccharide-based (pure/conjugate). • Produced by growing the bacterium or virus in culture media, then inactivating it with heat and/or chemicals (usually formalin). • For fractional vaccines, further treatment is carried out to purify only those components to be included in the vaccine.
Ability to replicate	• Replicate in the vaccinated person to produce an immune response. • The immune response is virtually identical to that produced by a natural infection.	• Not alive and thus cannot replicate.
Ability to cause disease	• Usually do not cause disease such as what may occur with the "wild" form of the organism. If disease does occur, it is usually much milder than the natural disease.	• Made from killed microorganism thus cannot cause disease.
Safety in immuno-suppressed individuals	• Live attenuated vaccines may cause severe reactions as a result of uncontrolled replication (growth) of the vaccine virus/bacteria in immunosuppressed individuals.	• Inactivated vaccines cannot cause infections in immuno-suppressed individuals. • However, inactivated vaccines may not be optimally effective in these individuals.
Duration of Immunity	• Longer	• Shorter
Multiple dose	• The first dose usually provides protection. An additional dose is given to ensure seroconversion.	• Inactivated vaccines always require multiple doses. In general, the first dose does not produce protective immunity, but only "primes" the immune system. • A protective immune response is developed after multiple subsequent doses.

Adverse Event Following Immunisation (AEFI) Reports

Since year 2000, the NPRA has received **572 AEFI reports** related to live attenuated vaccines with **972 adverse events**. Majority of the adverse events reported are mild in nature. NPRA has not received any reports involving the administration of live attenuated vaccines in immunosuppressed individuals and subsequent development of infection caused by the vaccine strain[4].

Advice to healthcare providers

- Live attenuated vaccines should not be given to people who are clinically immunosuppressed (either due to immunosuppressive drugs or underlying illness).
- Any infant who has been exposed to immunosuppressive treatment from the mother either in utero during pregnancy or via breastfeeding should have any live attenuated vaccination deferred. For in utero exposure to TNFα antagonists, live attenuated vaccination can only be given several months after the mother's last dose of TNFα antagonists (i.e.: etanercept: 4 months; adalimumab & certolizumab: 5 months; infliximab & golimumab: 6 months.
- Close contacts of immunosuppressed individuals should be fully immunised to minimise the risk of vaccine-preventable diseases in these individuals.
- Please report any adverse events following immunisation to the NPRA using the forms available on our website http://npra.moh.gov.my.

References:

1. World Health Organisation (2013). Immunization Safety Surveillance Guidelines for Immunization Programme Managers on Surveillance of Adverse Events Following Immunisation 2nd Edition.
2. Centers for Disease Control and Prevention (2015). Principles of Vaccination (http://www.cdc.gov/vaccines/pubs/pinkbook/prinvac.html)
3. Medicines and Healthcare Products Regulatory Agency (2016). Drug Safety Update: Live attenuated vaccines: avoid use in those who are clinically immunosuppressed.(https://www.gov.uk/drug-safety-update/live-attenuated-vaccines-avoid-use-in-those-who-are-clinically-immunosuppressed)
4. The Malaysian Adverse Drug Reaction database, NPRA. [Accessed: 28 September 2016].