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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 'Report an Adverse Event'.
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, 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:

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

Infliximab: Risk of Cervical Cancer

Overview

Infliximab is a tumour necrosis factor-alpha (TNFα) inhibitor with multiple indications including rheumatoid arthritis, adult and paediatric Crohn's disease, adult and paediatric ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis.

Background of Safety Issue

The Swiss regulatory authority, Swissmedic, reviewed the safety of infliximab following publication of a study showing a 2- to 3-fold increased incidence of cervical cancers in infliximab-treated women with rheumatoid arthritis compared to biologics-naïve patients or the general population, including women over 60 years of age. This population-based retrospective cohort study used data from Swedish national health registries involving about 47,000 patients with rheumatoid arthritis, and 330,000 individuals of the general population. The review concluded that a causal relationship between infliximab and cervical cancers cannot be excluded.

Swissmedic required the product information of infliximab and its biosimilars to be updated with information on this safety issue, ensuring the overall benefit-risk ratio of infliximab remains favourable when used according to the approved indications.

Local Scenario

In Malaysia, there are two (2) registered products containing infliximab, which are Remicade® and Remsima® (biosimilar product). Remicade® is approved for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, Crohn's disease, paediatric Crohn's disease, fistulising Crohn's disease and ulcerative colitis. The approved indications of Remsima® are limited to rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and psoriasis.

Following this review, the local package inserts have been updated with safety information regarding the risk of cervical cancer and advice on regular screening.

Adverse Drug Reaction Reports

NPRA has received a total of 55 reports with 116 adverse events following the use of infliximab since the product was first registered in year 2004. The most commonly reported adverse events were tuberculosis (10 reports, 8.6%), shortness of breath (9, 7.6%), itching (6, 5.2%), rash (6, 5.2%) and urticaria (6, 5.2%). To date, no ADRs on malignancies or malignant cervical neoplasms related to infliximab-use have been reported to NPRA.

Advice for Healthcare Professionals

- Periodic screening for cervical cancer should be carried out in women treated with infliximab, including those over 60 years of age.
- The risk of cervical cancer may apply to approved indications other than rheumatoid arthritis, therefore cervical cancer screening should be performed for all women treated with infliximab, regardless of indication.
- Please report any ADRs related to infliximab-use to the NPRA.

Implanon NXT® (etonogestrel implant): Reports of Implants Found in the Vasculature and Lung

Overview

Implanon NXT® is a radiopaque etonogestrel implant indicated for contraception. This implant contains barium sulfate in the core matrix which increases the possibilities for localisation by allowing it to be X-ray visible.

Background

The NPRA initiated a safety review of Implanon NXT® following post-marketing reports of etonogestrel implants (non-radiopaque and radiopaque) found in the vasculature and the chest wall, as identified from the product registration holder's global safety database.

Of the total 18 reports identified, 17 reported location of the implant in the vasculature (including 9 found in the pulmonary artery or lung), whereby one (1) reported an implant located in the chest wall. For the radiopaque etonogestrel implant, the reporting rate is approximately 1.3 per million implants sold. Some cases reported associated adverse events including dyspnoea, haematoma or excessive bruising at the insertion site. Potential risk factors identified for this issue were deep insertion, insertion in an inappropriate site, or insertion in thin arms.

Evidence from the literature shows that implants found in the vasculature can become endothelised into the pulmonary artery. If they are located early enough, it is possible to remove them by an endovascular procedure.

While the existing product package insert already discusses the possible risks and complications regarding insertion, localisation, removal, and migration of the implant, it was decided that updates were required to clarify the instructions for insertion, and provide further advice on the removal.

Local Scenario

Implanon NXT® was first registered in Malaysia in 2010, replacing the previous non-radiopaque implant, Implanon®. A single implant is inserted subdermally and can be removed at any time but not later than three years after the date of insertion.

A Direct Healthcare Professional Communication (DHPC) was approved by the NPRA in November 2016 for distribution by the holder. The package insert of Implanon NXT® has been updated with information on this safety issue.

Adverse Drug Reaction Reports

Since the year 2000, the NPRA has received **13 adverse drug reaction (ADR) reports** related to this product, with **19 adverse events**. Among the most frequently reported adverse events were metrorrhagia, medicine ineffective, pregnancy, and decreased blood pressure. There were no local reports related to implant migration or intravascular insertion.

Advice for Healthcare Professionals

- Prior to inserting or removing Implanon NXT®, all healthcare professionals should receive instructions and training on the correct procedure. Please contact the holder for further details and training materials (Tel. no.: 03-7499 1800; Fax no.: 03-7499 1697).
- Please avoid insertion over the sulcus (groove) between the biceps and triceps, and the neurovascular bundle that lies there deeper in the subcutaneous tissue.
- **Counselling**: Women should be shown how to locate the implant immediately following insertion, and advised to check the position of the implant frequently for the first few months.
- Any implant that cannot be palpated should be localised and removed as soon as medically appropriate.
- Chest imaging should be performed when implants cannot be located in the arm by palpation or imaging.
- Surgical or endovascular procedures may be required for the removal of any implant found within the vasculature or chest.
- All ADRs suspected to be related to Implanon NXT® should be reported to the NPRA.