HEALTH HAWKE'S BAY
Te Oranga o Te Matau-a-Māui

Best Practice Message

November 2024

Adverse Reaction Reporting

Practice changing moments

- Suspected adverse reaction reports are an important contribution to the safety monitoring of medicines and vaccines in Aotearoa.
- It is estimated that only 5% of adverse reactions are reported.
- There may be inequities in adverse reaction reporting for Māori patients.
- See appendix for **10 significant learnings from the CARM database.**

Background

The ninth annual *Medicines Safety Week* is 4 to 10 November 2024. The goal of the campaign is to encourage patients and health care professional to report suspected adverse reactions of medicines or vaccines. Medsafe defines adverse reactions as: A harmful effect suspected to be caused by a medicine or vaccine. They are also known as adverse drug reactions (ADRs), side effects or undesirable effects.

All medicines and vaccines undergo clinical trials to assess safety and efficacy. Due to the controlled environment of clinical trials and subsequent limitations, they often do not reflect real life. For this reason, post marketing suspected adverse reaction reporting is an essential part of pharmacovigilance. Medsafe collects and processes reports at the Centre for Adverse Reactions Monitoring (CARM) and uses these reports to quickly detect and respond to possible safety signals of medicines and vaccines in Aotearoa. The Medsafe-CARM pharmacovigilance voluntary reporting programme is a 'no blame' system for collecting data on medicines, vaccines, natural health products and devices. See appendix one for examples of significant learnings from the CARM database.

In Aotearoa we are diligent at reporting adverse reactions to medicines, with the highest rate of reporting of in the world. However, it is estimated that still only 5% of all reactions are reported.[1]

Focus on equity

In 2018 16.5% of the Aotearoa population were Māori, in the 2023 census the number was 17.3%. Only 13% of the CARM reports received between 2018 and 2022 were for Māori patients.[2]
A recent study showed that Māori were over 40% more likely to be admitted to hospital because of complications related to adverse effect of medications than non-Māori.[3] A specific example of this is the almost 3 times higher rate of hospitalisation for Māori patients with upper GI bleeding on NSAIDs than European patients.[4]

Getting the most out of CARM reports

Including as much data as possible in reporting contributes to the integrity of the report. Ideally list **all** medicines including OTC and herbal or alternative remedies with start and stop dates. Giving ample details of the adverse reaction is crucial for causality assessment. Include details such as date of onset, list of symptoms, past medication history, details of any rechallenge and alternative diagnoses that have been explored.[1]

Useful links

- Report a suspected adverse reaction to a medicine or vaccine
- Search for suspected adverse reactions to medicines and vaccines reported in New Zealand
- Patient information on adverse reaction reporting

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Appendix one: Summary of Dr Jennifer Lee and Dr Ruth Savage Goodfellow conference 2024 presentation: 10 significant learnings from the NZ Centre for Adverse Reactions Monitoring (CARM) database

1. **Empagliflozin and Fournier's gangrene/necrotising fasciitis**

Whilst Fournier's gangrene and necrotising fasciitis of the perineum and genitalia had been identified as a potential reaction previously, there appears to be a disproportionally high number of cases reported to CARM. This is an important observation as this condition can progress rapidly, with most cases reported requiring surgical debridement. There appears to be an overrepresentation in Māori and Pacific people, even accounting for high use in this group due to the Special Authority access criteria. This observation led Medsafe and others to produce prescriber updates as well as patient information regarding genital hygiene and early warning signs for seeking medical attention.

2. **Empagliflozin and euglycemic diabetic ketoacidosis**

Diabetic ketoacidosis (DKA) is more common with empagliflozin even when blood glucose is normal or only a little elevated. The report presented by Dr Jennifer Lee and Dr Ruth Savage is a reminder consider DKA even when the presentation is unusual. In this report a woman developed leg tingling after starting empagliflozin and becoming dehydrated. Risk factors for DKA are dehydration and acute illness. It is therefore important that, as for insulin, patients need careful counselling on sick day medication management. Also be mindful of patients considering low carbohydrate (<90g daily) or keto diets.

3. **Allopurinol and DRESS**

There are several CARM case reports for allopurinol suspected drug reaction with eosinophilia and systemic symptoms. The risk of this reaction is higher if starting at a high dose, or titrating too quickly, and for patients with the HLA-B*5801 allele (predominantly in Han Chinese or Thai ancestry). The starting dose of allopurinol is dictated by the patient's renal function. See this article for allopurinol initiation and titration.

4. **ACE inhibitor and angioedema**

Angioedema is potentially life threatening. The time of onset is typically withing the first month of initiation but can be delayed by months or years. Initially symptoms can be mild and self-resolving so identifying the cause may delayed. See Dermnet for more details on risk factors and treatment.

5. **Pimafucort** (hydrocortisone, neomycin, natamycin) **and contact dermatitis**

Dermnet states that "Neomycin is prone to causing allergic contact dermatitis and was declare the contact allergen of the year in 2010 by the American Contact Dermatitis Society." Avoid using Pimafucort in underarm and groin areas.

6. **Colchicine toxicity**

There have been fatal events reported involving accidental or intentional overdose with colchicine. Patients should be educated on safe storage, returning of unused tablets to pharmacy and consider blister packing.

7. **Montelukast and neuropsychiatric symptoms**

There have been reports of suspected montelukast induced neuropsychiatric symptoms. In 2024 the montelukast datasheet was updated to include: "Post-market reports with use of montelukast include agitation, aggressive behaviour or hostility, anxiousness, depression, dream abnormalities, hallucinations, insomnia, irritability, restlessness, somnambulism, suicidal thinking and behaviour and tremor. Events have been reported mostly during montelukast treatment, but some were reported after montelukast discontinuation. In many cases symptoms resolved after stopping montelukast, however, in some cases, symptoms persisted."

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8. Thyroxine considerations

CARM presented a case example of persistently elevated TSH in a nasogastric fed inpatient. The medicine was administered with their feeds. This article outline the considerations of dosing regimes with thyroxine. Patients should be advised to take levothyroxine at a regular and routinely convenient time for them.

9. Zoledronic acid and Iron infusions

There have been several infusion related reactions reported to CARM. Medsafe has published this article on adverse reactions following zoledronic acid infusion and this article on hypophosphatemia in parenteral iron treatment.

10. Isotretinoin for females of childbearing potential

There are case reports of suspected isotretinoin associated congenital malformations. See NZF for pre-treatment screening and monitoring requirements and contraception advice. Although there are no reports found in the CARM database for suspected acitretin associated congenital anomalies, foetal exposure to acitretin always involves a risk of congenital malformation. See NZF for pre-treatment screening and monitoring requirements and contraception advice for acitretin.

References:

1. Guide to Adverse Reaction Reporting [Internet]. [cited 2024 Oct 24]. Available from: https://www.medsafe.govt.nz/profs/PUArticles/ADRreport.htm
2. Adverse reaction reporting in New Zealand – 2021 [Internet]. [cited 2024 Oct 24]. Available from: https://www.medsafe.govt.nz/safety/reports-and-promotion/ADRStatistics/2021.asp
3. Svensen G, Hikaka J, Cavadino A, Kool B. Ethnic variation in hospitalisation due to treatment injury and complications of healthcare in older adults residing in New Zealand. N Z Med J. 2023 Jul 21;136(1579):70–85.
4. Tomlin A, Woods DJ, Lambie A, Eskildsen L, Ng J, Tilyard M. Ethnic inequality in non-steroidal anti-inflammatory drug-associated harm in New Zealand: A national population-based cohort study. Pharmacoepidemiol Drug Saf. 2020 Aug;29(8):881–9.

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