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Safety Notice: 011/09

7 May 2009

Allopurinol and Azathioprine

A Serious and Known Drug Interaction.

Distributed to:

- Chief Executives
- Directors of Clinical Governance
- Directors of Clinical Operations

Action required by:

- Directors of Clinical Governance

We recommend you also inform:

- Drug and Therapeutic Committees
- Area Directors of Nursing
- Area Directors of Pharmacy
- Pharmacists
- Nurses
- Medical staff

Expert Reference Group

Content reviewed by:

- NSW TAG SAFER Medicines Group
- NSW Medication Safety Strategy Committee

Quality and Safety Branch

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Background

A recent NSW incident resulting in the death of a patient highlights the seriousness of the drug interaction between allopurinol and azathioprine.

In this case, the patient was on existing azathioprine treatment when admitted to hospital and allopurinol was added by a consulting medical team. Opportunities to identify the interaction were missed by the consulting and treating medical teams and pharmacists.

Data collected from pharmacy reporting tools across NSW indicate that this combination of medicines has been unintentionally ordered for numerous other patients but harm was prevented through pharmacist intervention. Its severity and occurrence is well documented in the literature.

Allopurinol inhibits the metabolism of azathioprine, potentially leading to accumulation of toxic azathioprine metabolites which can cause bone marrow toxicity, including anaemia, leucopenia, thrombocytopenia and pancytopenia. Use of allopurinol and azathioprine in combination is best avoided. However, if the combination is required the azathioprine dose must be reduced to 25%-33% of the normal dose. Routine haematological monitoring is also recommended.

Contributing Factors:

- The consulting medical team did not assess the patient's existing therapy when recommending treatment with allopurinol.
- The patient's medicines were not thoroughly reviewed during their admission.
- The medical teams were unaware of the interaction and associated risks.
- The supervising pharmacist was not notified of the drug interaction alert automatically generated by the pharmacy dispensing software. The pharmacy dispensing software used throughout NSW utilises the Stockley drug interaction database which lists and categorises the interactions between different drugs.

Health care practitioners should observe the following points:

- A timely and thorough review of pharmaceutical treatment should occur for all patients, during each admission.
- Doctors and pharmacists should take appropriate care when prescribing, reviewing and dispensing medications to ensure that they have considered possible drug interactions.
- Pharmacists should confirm that their departmental policy ensures that drug interaction alerts are adequately assessed and managed.
- Patients should be educated about potential problems when new drugs are prescribed.

Suggested Actions by Area Health Services

1. Ensure that this safety notice is distributed to all clinical staff involved in the prescribing, dispensing and administration of medications.
2. Ensure staff members new to areas are made aware of the risks and known drug interaction associated with allopurinol and azathioprine use.
3. Ensure staff are aware of drug interaction information available via the CIAP website.
 - The CIAP is at: <http://www.ciap.health.nsw.gov.au/> or <http://internal.health.nsw.gov.au:2001/>,
 - for Mims Drug Alert is [http://www.use.hcn.com.au/login.%60\\$1%60/home.html?1=drugalert&U1=nhtrain](http://www.use.hcn.com.au/login.%60$1%60/home.html?1=drugalert&U1=nhtrain)
 - for Micromedex Drug Interaction is http://proxy1.use.hcn.com.au/hcs/librarian/ND_T/HCS/ND_CPR/Interactions/ND_PR/Interactions/CS/9EEEAC/DUPLICATIONSHIELDSYNC/A3A1F3/ND_PG/PRIH/ND_B/HCS/ND_P/Interactions/PFPUI/dkfrWHy2TV8vik/PFActionId/hcs.Interactions.FindDrugInteractions

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Further reading:

DT Kennedy, MS Hayney and KD Lake. Azathioprine and allopurinol: the price of an avoidable drug interaction. *The Annals of Pharmacotherapy* 1996; Vol. 30, No. 9, pp. 951-954.

ADRAC Allopurinol and azathioprine. Fatal interaction. *Med J Aust* 1980; 2: 130.

ADRAC A reminder - the allopurinol azathioprine interaction. *Aust Adv Drug React Bull*, February 1985.

Boyd IW. Allopurinol-azathioprine interaction. *J Intern Med* 1991; 229: 386.

ADRAC *Australian Adverse Drug Reactions Bulletin*, Volume 19, Number 1, February 2000.

<http://www.tga.gov.au/adr/aadrb/aadr0002.htm>

Obsolete