

Your questions to the PBAC

Glucosamine

As a pharmacist doing home medicines reviews, I frequently come across patients suffering from osteoarthritis who are taking (selective or non-selective) non-steroidal anti-inflammatory drugs (NSAIDs) for relief. As these patients often also suffer from conditions such as hypertension or heart failure, my recommendations include comments about NSAIDs interfering with blood pressure control, or aggravating heart failure. Many patients are on ACE inhibitors, diuretics and the NSAID, which constitutes the 'triple whammy' that puts them at increased risk of acute renal failure. Problems arise when I wish to suggest alternatives. Regular maximum dose paracetamol is fine if it works. There is evidence that glucosamine is effective, and may slow the progression of the disease. However, many patients will not take glucosamine because of the cost, compared to their NSAID which is subsidised by the Pharmaceutical Benefits Scheme. Considering the amount spent on COX-2 inhibitors and the cost of dealing with patients hospitalised by adverse effects (gastrointestinal complications, aggravated heart failure, acute renal failure), I am surprised that glucosamine is not subsidised.

I would like to know whether a cost-effectiveness formula has been applied to glucosamine, and what the chances are of it being subsidised. Has it been considered at all? Is there no multinational drug company out there lobbying for it, so it doesn't even find its way to the Pharmaceutical Benefits Advisory Committee (PBAC). Does the PBAC only consider drugs that are presented by the drug companies, or do you ever go searching (through the clinical trials) for other (cost-effective) drugs?

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PBAC response:

The Pharmaceutical Benefits Advisory Committee (PBAC) bases its recommendations on the evidence submitted to it. An application for listing requires appropriate data and evidence supporting the submission so manufacturers are usually in the best position to provide such information. The PBAC cannot compel a manufacturer to make an application for a particular drug or condition. To date, no application meeting the criteria for listing on the Pharmaceutical Benefits Scheme (PBS) has been submitted. Consequently, the PBAC cannot recommend that glucosamine be listed on the PBS.

Medicinal mishap

Severe hyponatraemia associated with omeprazole

Prepared by Adam Morton, Physician, Mater Misericordiae Hospital, South Brisbane, and John Mackintosh, Oncologist, Mater Private Hospital, South Brisbane

Case

A 43-year-old woman presented with epigastric pain and tenderness nine days after completing her second cycle of chemotherapy for a temporoparietal lymphoma. She was prescribed omeprazole 20 mg twice a day.

Two days later, after three doses of omeprazole, the patient complained of nausea, weakness and feeling twitchy. Physical examination was unremarkable, but her serum sodium concentration had fallen from its pre-treatment value of 138 to 117 mmol/L. Her serum urate was 0.12 mmol/L, urine sodium was 35 mmol/L and urine osmolality 615 mmol/L. Plasma glucose and tests of thyroid, adrenal and renal function were normal. This is consistent with the syndrome of inappropriate antidiuretic hormone secretion.

The patient was given one litre of hypertonic saline over 24 hours and was placed on fluid restrictions. The omeprazole was ceased. Within three days her sodium concentration had returned to normal and has remained so over the ensuing eight months without fluid restrictions.

Comment

In 2003–04, omeprazole was the fourth most commonly prescribed drug on the Pharmaceutical Benefits Scheme.¹ Seven previous cases of hyponatraemia have been associated with proton pump inhibitors. With the exception of one case ascribed to lansoprazole, all these cases followed exposure to omeprazole.^{2,3,4,5,6,7,8} Consistent features were the:

- rapid onset of hyponatraemia with the majority of cases presenting within 11 days of starting treatment
- severity of hyponatraemia
- rapid recovery after cessation of the drug.

The Adverse Drug Reactions Advisory Committee has received 18 reports of hyponatraemia associated with omeprazole, including six where it, or esomeprazole, was the sole suspected drug.

Hyponatraemia has a variety of causes including renal salt wasting and inappropriate antidiuretic hormone secretion.⁹ Our patient probably had drug-induced inappropriate secretion of antidiuretic hormone.

Although we used hypertonic saline, it is important to remember not to correct the patient's sodium concentration too quickly. Rapid replacement of sodium can induce the osmotic demyelination syndrome which is potentially fatal.

Conclusion

This is a rare adverse drug reaction, but it is included in the product information of omeprazole. As our patient developed hyponatraemia after three doses, this adverse reaction needs to be considered whenever there is clinical deterioration even after brief exposure to a proton pump inhibitor.

References

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New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Committee is prepared to do this. Before new drugs are prescribed, the Committee believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Emtricitabine

Emtriva (Gilead)

200 mg capsules

Approved indication: HIV infection

Australian Medicines Handbook section 5.4.1

The current treatment of HIV infection involves giving antiviral drugs from different classes. This may require the patient to take medications several times a day.¹ Most of the regimens include nucleoside reverse transcriptase inhibitors to prevent viral replication. This class is now expanded by the addition of emtricitabine, an analogue of cytosine.

Emtricitabine is taken once a day. It is rapidly absorbed and then phosphorylated within cells to its active form. While the elimination half-life of emtricitabine is 10 hours the intracellular half-life of emtricitabine-triphosphate is 39 hours. Most of the drug is excreted in the urine so the dose requires adjustment in patients with renal impairment.

A multinational double-blind trial studied emtricitabine in 571 patients who had not previously been treated with antiretroviral drugs. These patients were randomised to take emtricitabine

or stavudine, in addition to didanosine and efavirenz. After 48 weeks 78% of the emtricitabine group and 59% of the stavudine group had fewer than 50 copies of viral RNA/mL.²

Another trial studied 440 patients who were already taking combinations of antiviral drugs including lamivudine. The patients were randomised to either continue lamivudine or to switch to emtricitabine. After 48 weeks 72% of the patients taking lamivudine and 67% of those taking emtricitabine had fewer than 50 copies of viral RNA/mL.

Common adverse effects are diarrhoea, nausea, abdominal pain and nightmares, but these may occur less frequently than with stavudine. Skin discolouration was observed in 3% of the previously untreated patients given emtricitabine.² Liver function, blood cell counts and triglyceride concentrations may be affected by emtricitabine.

Resistance can develop during treatment. In previously untreated patients, viral mutations occurred in 4% of those taking emtricitabine and 11% of those taking stavudine.² As emtricitabine is structurally similar to lamivudine, a virus which is resistant to lamivudine will probably be resistant to emtricitabine.