Humalog - an accident waiting to happen

There have been an increasing number of significant events from both primary and secondary care concerning the prescribing and dispensing of Humalog insulin preparations.

There are now three Humalog insulin preparations:

- Humalog – a rapid acting insulin (containing 100% insulin lispro)
- Humalog Mix 25 – a mixture of rapid and intermediate acting insulin (containing 25% insulin lispro and 75% insulin lispro protamine)
- Humalog Mix 50 – a mixture of rapid and intermediate acting insulin (containing 50% insulin lispro and 50% insulin lispro protamine)

Errors have been reported where:

- The wrong product has been selected from a drop down menu in electronic prescribing or dispensing systems
- A patient has described the insulin they are on as Humalog 25, twice daily, and been prescribed Humalog (rapid acting alone, not the mix) 25 units, twice daily, when they were actually on Humalog Mix 25.

Prevention of incidents:

- Inform the patient about the risk of incidents so they are fully informed about which Humalog insulin preparation they are on and the importance of describing it accurately. This can also be written on a patient medicine card.
- Always prescribe insulin using the full brand name
- Check with the patient about which sort of insulin preparation they are on, e.g. not only the brand name but also rapid, intermediate or long acting – this acts as an extra check.

Safer prescribing of tramadol

From 1 June, 2010 tramadol will be available fully subsidised on the Pharmaceutical Schedule.

Tramadol has been used widely in hospitals for several years, but experience of its use in primary care is limited. A Prescriber Update article from Medsafe is planned to be circulated, and prescribers are advised to consult the Medicines Safety Datasheet for detailed information.

The following are some important prescribing tips for the safe and appropriate use of tramadol:

- Tramadol is not a first line analgesic. It is classed as a weak opioid on the analgesic ladder and is neither more effective, nor better tolerated, than other weak opioids such as codeine.
- For people coming off dextropropoxyphene, a straight switch to tramadol is not recommended. The patient's analgesic requirements should be initially assessed with regular paracetamol, and then codeine added if necessary.
- Drug dependence, withdrawal reactions and misuse have all been reported with tramadol, although they are generally less problematic than with other opioids.
- Tramadol acts at opioid receptors and shares some of the typical adverse effects of opioid analgesics, including nausea, constipation and

respiratory depression. However, it has additional pharmacological actions which result in a different spectrum of adverse effects and drug interactions.

- Tramadol has serotonergic effects similar to SSRIs, such as fluoxetine and paroxetine. Serotonin toxicity (and syndrome) has been reported after use of tramadol with other serotonergic agents such as antidepressants and St John's wort.
- Changes in the INR have been reported in people taking warfarin. Monitor INR in these patients if tramadol is added or stopped.
- The seizure threshold is reduced by tramadol and the effect appears to be dose related. Extreme caution is required in people with epilepsy (only consider if epilepsy is well controlled), a history of seizures or those already taking medicines that reduce seizure threshold, such as antipsychotics and antidepressants.
- Tramadol should not be used in people:
    - With acute alcohol intoxication or taking hypnotics, analgesics, opioids or psychotropic medicinal products
    - Who are receiving monoamine oxidase inhibitors (MAOIs) or have taken them in the past 14 days
    - With epilepsy that is not adequately controlled by treatment
    - With severe renal impairment (creatinine clearance <10 mL/min)

Recommended reading

1. Waitemata DHB. Tramadol- safe prescribing; consider the risks. Safer Rx. Available from: **www.saferx.co.nz/full/tramadol.pdf**
2. Medsafe datasheet. Available from: **www.medsafe.govt.nz/profs/Datasheet/a/arrowtramadolcap.pdf**

NEWS UPDATE: On 26 May, 2010 the US Federal Drug Agency issued an alert, notifying prescribers of increased safety concerns with tramadol. The FDA strengthened warnings of the risk of suicide for patients prescribed tramadol, who are prone to addiction or currently taking tranquilisers or antidepressants. This follows reports of tramadol-related deaths that have occurred in patients with a previous history of emotional disturbance, suicidal ideation or substance misuse (including prescription medicines).

For further information visit:
www.fda.gov/Safety/MedWatch/default.htm

New evidence shows less benefit of gabapentin for neuropathic pain

The effectiveness of gabapentin for neuropathic pain, including data from previously unpublished trials, has been re-evaluated. Recent litigation procedures in the United States have revealed that the promotion of Neurontin (gabapentin), for the treatment of pain conditions, was assisted by selective publication and citation of studies with favourable outcomes.

Countries which have licensed gabapentin for neuropathic pain (including New Zealand) would not have had access to these hidden trials and would have based recommendations only on the available published data.

Previous data indicated that gabapentin has a moderate analgesic effect in about 25 % of patients with neuropathic pain (NNT* of 4).[1] Inclusion of the hidden data indicates that gabapentin has a minor role in pain control and that

the NNT is about 6–8, that is, only about 15% of patients will derive some benefit. Furthermore, newly available information shows that adverse effects can occur such as dizziness (NNH† of 8), confusion or ataxia (NNH of 10) and oedema (NNH of 11). Finally, there is very little evidence that the degree of analgesia is dose related, whereas toxicity is dose dependent.

Conclusions and recommendations (adapted from Therapeutics Initiative, 2010[2])

- Evidence from all clinical trials suggests that gabapentin has a minor role in pain control
- Gabapentin reduces neuropathic pain by less than 1 point on a 0 – 10 scale and may benefit about 15% of patients
- Adverse effects occur in about the same number of people, although these can be relatively mild.
- A test of benefit versus harm can be made after one to two days at a low dose (100 – 900 mg daily)
- Benefit is unlikely to increase with higher doses or longer treatment
- Gabapentin should be used with caution in people at risk of cognitive disturbance, falls or when oedema may aggravate an underlying condition
- Regularly assess patients taking gabapentin. Assessment of benefits or adverse effects can be made by stopping for one to two days.

As with other antiepileptics, gabapentin can increase suicidal thoughts and behaviour. Patients should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviour, or any unusual changes in mood or behaviour.[3]

* Number need to treat

† Number needed to harm

References

1. Wiffen PJ, McQuay HJ, Rees J, Moore RA. Gabapentin for acute and chronic pain. Cochrane Database Syst Rev 2005;3: CD005452.
2. Therapeutics Initiative. Gabapentin for pain: New evidence from hidden data. Therapeutics Letter 75. University of British Columbia. Available from: www.ti.ubc.ca/letter75 (Accessed May, 2010).
3. Medsafe. Gabapentin Data Sheet. Available from: www.medsafe.govt.nz/profs/Datasheet/a/ArrowGabapentincap.htm (Accessed May 2010).