Australian Government
Department of Health
Therapeutic Goods Administration

Medicines Safety Update

Volume 7, Number 2, April 2016

In this issue

Updating medicine ingredient names to align with international usage

Health professionals are advised that the TGA is updating a number of medicine ingredient names to align with names used internationally.

Over the years, some medicine ingredient names in Australia have become out of date.

By using old ingredient names, the names of medicine ingredients in Australia were becoming more 'unique'.

TGA is updating some medicine ingredient names used in Australia to align with names used internationally.

There will be a four year transition period for these changes, from April 2016 to April 2020.

What type of changes?

Some changes are minor, for example changing a 'y' to an 'i', and will not affect how the ingredient name is pronounced.

Some changes are more significant. For these products, medicine labels will need to use both the old and new ingredient name for an additional three years after the end of the transition period (until 2023). This will help consumers and health professionals become familiar with the new name.

The full list of medicine ingredient names that will be changing is available at: www.tga.gov.au/updating-medicine-ingredient-names-list-affected-ingredients

Adrenaline and noradrenaline

Adrenaline and noradrenaline will remain as approved names in Australia.

There is no plan to use epinephrine and norepinephrine as the new ingredient names.

Instead, labels of medicines containing adrenaline or noradrenaline will include the international name (epinephrine and norepinephrine, respectively) in brackets after the ingredient name.

For example, medicines containing adrenaline hydrochloride will be labelled as 'adrenaline (epinephrine) hydrochloride'.

By including this information on labels indefinitely, the TGA hopes to reduce confusion for health professionals and consumers.

Information for health professionals

From April 2016, new ingredient names will start to appear on medicine labels, in product information and consumer medicine information leaflets and within medication software systems.

Depending on turnover, medicine labels using the old ingredient names will still be available on shelves as stock is run down.

Please take particular care when prescribing and/or dispensing medicines to ensure that the right product is selected.

Some of the new ingredient names may be unfamiliar to patients.

Health professionals are asked to reassure patients that only the name of the ingredient has been changed and there is no change to the medicine's formulation, quality, safety or efficacy.

Medicines Safety Update is the medicines safety bulletin of the Therapeutic Goods Administration (TGA)

TGA Health Safety Regulation

Xgeva and osteonecrosis of the jaw

Xgeva (denosumab) is now contradicted in patients with unhealed lesions from dental or oral surgery due to increased risk of osteonecrosis of the jaw.

Denosumab is a fully human monoclonal antibody to the receptor activator of nuclear factor-kB ligand (RANKL) that blocks its binding to receptor activator of nuclear factor-kB (RANK), inhibiting the development and activity of osteoclasts, decreasing bone resorption, and increasing bone density.

It is available in Australia as two brands, Prolia and Xgeva, which have different indications.

Xgeva (120 mg) is given once every four weeks for the prevention of skeletal-related events in adults with bone metastases from solid tumours.

Prolia (60 mg) is given once every six months for the treatment of osteoporosis in postmenopausal women, and for the treatment of men with osteopaenia who are receiving androgen deprivation therapy for non-metastatic prostate cancer.

Osteonecrosis of the jaw (ONJ) is a known adverse event associated with denosumab. The Product Information (PI) documents for Xgeva and Prolia include information about ONJ in their respective Precautions and Adverse Effects sections. Xgeva is higher dose and administered more frequently than Prolia, which further increases the risk of ONJ.

A TGA review of this issue followed Xgeva's contraindication in patients with unhealed lesions from dental or oral surgery in the United Kingdom.

Based on this review, the TGA worked with the sponsor of Xgeva to add the same contradiction to the Australian PI.

Information for health professionals

Xgeva should not be prescribed to patients with unhealed lesions from dental or oral surgery.

Advise patients who are taking either Xgeva or Prolia that good oral hygiene practices should be maintained during treatment.

If required, preventive dentistry is recommended prior to Xgeva or Prolia treatment, especially in patients with risk factors for ONJ. If invasive dental procedures during treatment cannot be avoided, consider the individual circumstances of the patient to determine an appropriate management plan.

If ONJ occurs during treatment with either medicine, a temporary interruption of therapy should be considered based on individual risk-benefit assessment until the condition resolves.

Erlotinib — change in indication

A study has found no demonstrable benefit of first-line maintenance treatment versus second-line treatment with erlotinib for patients whose tumours do not harbour an epidermal growth factor receptor-activating mutation. Consequently, the indication for this medicine has been updated.

Erlotinib, marketed in Australia as Tarceva, is an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor. It is used for the treatment of certain types of non-small cell lung cancer (NSCLC) and can also be used in combination with gemcitabine for the treatment of pancreatic cancer.

The IUNO study was a randomised, double-blind, placebo-controlled phase III study of first-line maintenance erlotinib versus erlotinib at the time of disease progression in patients with advanced NSCLC whose tumours do not harbour an EGFR-activating mutation, who had not progressed following four cycles of platinum-based chemotherapy. The study found that overall survival was not superior in patients randomised to receive maintenance erlotinib followed by chemotherapy upon progression, compared to patients randomised to receive maintenance placebo followed by erlotinib upon progression (hazard ratio=1.02, 95% CI, 0.85-1.22, p=0.82).

As a result of this finding, the indication for maintenance treatment in patients with locally advanced or metastatic NSCLC who have not progressed on first-line chemotherapy has been restricted to those patients with EGFR mutations only.

First-line maintenance treatment of patients whose tumours harbour an EGFR-activating mutation is not affected by these new data.

Ibrutinib and risk of hepatotoxicity

Health professionals are advised that the Product Information for ibrutinib has be updated with new safety information relating to the risk of hepatotoxicity.

Ibrutinib, which is marketed in Australia as Imbruvica, is a selective and covalent inhibitor of Bruton's tyrosine kinase. It is used for the treatment of certain types of blood cancers, including mantle cell lymphoma and chronic lymphocytic leukaemia (including small lymphocytic lymphoma).

There have been isolated case reports of severe hepatotoxicity in the post-marketing setting for patients being treated with ibrutinib. A new sub-section titled 'Hepatotoxicity' has been added to the Precaution section of the Product Information (PI).

The PI now includes the following information:

- isolated cases of severe liver toxicity have been reported in the post-marketing setting
- the time to onset was variable (five days to three months after commencing ibrutinib) and monitoring of liver function is recommended
- these events were very rare (< 1/10,000) and in most cases were resolved after dose modification
- ibrutinib treatment should be interrupted if ≥ Grade 3 liver function abnormalities develop (dose modification guidelines can be found in the Dosage and Administration section of the PI).

Information for health professionals

Monitoring of liver function is recommended and if ≥ Grade 3 elevations in liver function tests are observed, with or without a rise in bilirubin, therapy should be withheld.

Once the symptoms of hepatotoxicity decrease to Grade 1 or baseline, ibrutinib can be reinitiated at the starting dose. If toxicity recurs, the dose should be reduced by one capsule (140 mg). A second 140 mg dose reduction may also be considered if necessary.

If toxicities persist or recur after two dose reductions, ibrutinib should be discontinued.

What to report? You don't need to be certain, just suspicious!

The TGA encourages the reporting of all **suspected** adverse reactions to medicines, including vaccines, over-the-counter medicines, and herbal, traditional or alternative remedies. We particularly request reports of:

- all suspected reactions to new medicines
- all suspected medicines interactions
- suspected reactions causing death, admission to hospital or prolongation of hospitalisation, increased investigations or treatment, or birth defects.

Reports may be submitted:

- **using the 'blue card'** available from the TGA website
- **online** at www.tga.gov.au
- **by fax** to 02 6232 8392
- **by email** to ADR.Reports@tga.gov.au

For more information about reporting, visit www.tga.gov.au or contact the TGA's Pharmacovigilance and Special Access Branch on 1800 044 114.

For the latest safety information from the TGA, subscribe to the TGA Safety Information email list via the TGA website

For correspondence or further information about Medicines Safety Update, contact the TGA's Pharmacovigilance and Special Access Branch at ADR.Reports@tga.gov.au or 1800 044 114

Medicines Safety Update is written by staff from the Pharmacovigilance and Special Access Branch

Acting Editor:
Dr Bronwen Harvey

Deputy Editor:
Mr Michael Pittman

Acting TGA Principal Medical Adviser:
Dr Tony Gill

Contributors include:
Ms My Di Luu
Mr Zain Hussain