Medicines Safety Update

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Therapeutic Goods Administration

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Quetiapine and QT prolongation

Health professionals are advised that the Product Information for quetiapine has been updated to include additional information regarding risks of QT prolongation.

Postmarketing reports of QT prolongation associated with quetiapine treatment have occurred not only in the context of overdose, but also with concomitant illness and in patients taking other drugs known to cause electrolyte imbalances or increase the QT interval.

Quetiapine, which is marketed as Seroquel and multiple generics, is an atypical antipsychotic drug indicated for the treatment of schizophrenia and bipolar disorder.

TGA investigations found that, while the Australian Product Information (PI) had a precaution for use with cardiovascular disease, family history of QT prolongation, congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalaemia and hypomagnesaemia, it did not specifically state the need to avoid use in circumstances that may increase the occurrence of torsades de pointes and/or sudden death.

New information

The PI for quetiapine products now advises, particularly in elderly patients, to avoid concomitant treatment with antipsychotics and other drugs that are known to prolong the QT interval. These include:

- Class IA antiarrhythmics (such as disopyramide)
- Class III antiarrhythmics (such as amiodarone and sotalol)
- antipsychotics (such as ziprasidone, chlorpromazine and haloperidol)
- antibiotics (such as erythromycin)
- others (such as citalopram, pentamidine and methadone).

The updated information also advises that quetiapine should be avoided in circumstances that may increase the risk of torsades de pointes and/or sudden death, including a history of cardiac arrhythmias, hypokalaemia or hypomagnesaemia, and congenital prolongation of the QT interval.

Additionally, the PI has also been updated to include further information about the risk of:

- venous thromboembolism (VTE)
- akathisia
- neutropenia.

Adverse event reports in Australia

Over the 13 years that quetiapine has been registered in Australia, from March 2000 to August 2013, there have been a total of 807 adverse event reports made to the TGA relating to its use. Of those reports, 23 involved QT prolongation. More than half involved concomitant drugs that can increase the QT interval.

There were two reports of cardiac arrest in which QT prolongation was also noted, and another report of fatal cardiac arrest in which QT prolongation was not reported. Meanwhile there was one report of torsades de pointes, associated with hypokalaemia and hypomagnesaemia.

Information for health professionals

Health professionals are encouraged to review the latest PI for quetiapine and particularly the updated information regarding QT prolongation, VTE, akathisia and neutropenia in the precautions section.

Quetiapine treatment in combination with antipsychotics and other drugs that are known to prolong the QT interval should be avoided, particularly in elderly patients.

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

TGA Health Safety Regulation

MEDICINES SAFETY UPDATE

bioCSL Fluvax – not for children under 5 years

Despite a range of actions taken in 2013 to ensure the safe use of seasonal influenza vaccines in children, there were still 43 confirmed cases of bioCSL Fluvax being administered to children under 5 years of age last year.

Health professionals are reminded that bioCSL Fluvax is registered for use in children from the age of 5 years and should not be used in children under 5 years of age. Additionally, bioCSL Fluvax should only be used in children aged 5 to under 9 years based on careful consideration of potential benefits and risks in the individual child. This information is reinforced in the black box warning (Fig. 1) in the Product Information.

During the 2010 influenza season, an excess number of febrile reactions and febrile convulsions occurred in children under 5 years of age after immunisation with bioCSL Fluvax. As a result, the approved indication for bioCSL Fluvax was changed.

The TGA also advises health professionals to avoid using 'Fluvax' as a generic term for influenza vaccine to minimise the potential for confusion.

bioCSL Fluvax safety initiatives

While some errors are still occurring, actions taken to ensure the safe use of bioCSL Fluvax in children have been effective in significantly reducing the number of cases of incorrect administration. In 2013, there were 43 confirmed cases of children under 5 years of age being given bioCSL Fluvax out of 48 361 influenza vaccines recorded on the Australian Childhood Immunisation Register in this same age group. This compares to 115 confirmed reports in 2012.

Safety initiatives undertaken during 2013 included:

- communication activities by the Commonwealth and State and Territory health departments regarding bioCSL Fluvax and other influenza vaccines that can be used in children, as well as the need to report adverse events for all ages
- communication activities by bioCSL, including a medical communications campaign following market research into provider practices
- changes to packaging for bioCSL Fluvax, including a warning on the outer packaging, syringes and syringe wraps, and development of a vaccine refrigerator sticker (Fig. 2)
- direct follow-up by State and Territory public health units of general practitioners who were noted as having administered bioCSL Fluvax to children under 5 years of age during the year.

The TGA received no reports of adverse events involving the administration of bioCSL Fluvax to a child under 5 years of age during 2013. Similarly, no additional safety concerns were detected by two enhanced influenza adverse events surveillance projects funded by the Department of Health.

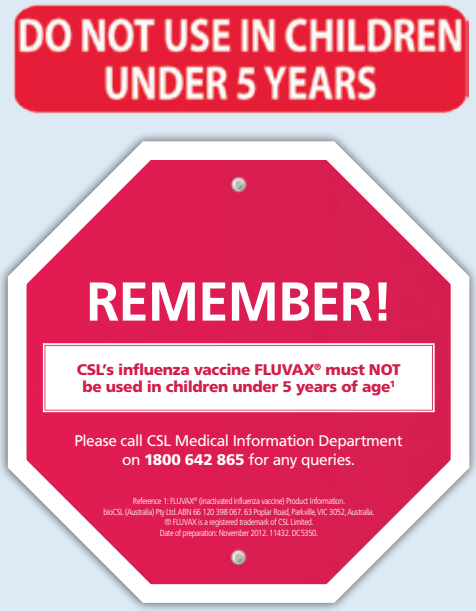
Actions for 2014

In addition to actions taken in 2013, this year bioCSL Fluvax will have warnings on both sides of the packaging and a safety message will be included in the Influenza Specialist Group communication materials. Online learning tools for immunisation providers are also being developed by bioCSL.

Figure 1
Black box warning in bioCSL Fluvax Product Information

WARNING: This season's vaccine is indicated for use only in persons aged 5 years and over. It must not be used in children under 5 years (see Contraindications). It should only be used in children aged 5 to under 9 years based on a careful consideration of potential risks and benefits in the individual (see Precautions).

Figure 2
bioCSL Fluvax packaging warning and the vaccine refrigerator sticker



How you can play a vital role in medicine regulation

The TGA draws on the expertise of highly qualified health professionals from around Australia to help it regulate medicines and other therapeutic goods.

Health professionals with a broad range of skills and experience are appointed to the TGA's various statutory advisory committees. They provide independent advice regarding medicines, vaccines, biologicals and medical devices.

One such expert advisory committee is the Advisory Committee on the Safety of Medicines (ACSOM).

This committee serves to advise and make recommendations to the TGA on:

- the safety of medicines
- the risk assessment and risk management of medicines.

The ACSOM may also provide advice to the TGA on other matters related to the detection, assessment, understanding and prevention of adverse events, and any other matters referred to it.

A major role for this committee is to provide advice on the quality and appropriateness of Risk Management Plans for high-risk medicines (such as those from a new class), which are designed to define and proactively manage risks relating to a medicine over its entire lifecycle.

The TGA regularly seeks expressions of interest from people interested in joining expert advisory committees. By serving as a member of one of these committees, you can help the TGA to effectively regulate increasingly complex therapeutic goods to protect the continuing health and safety of all Australians.

For further information visit the TGA website www.tga.gov.au.

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 and with the October issue of *Australian Prescriber*
- **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 Office of Product Review 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 Office of Product Review at ADR.Reports@tga.gov.au or 1800 044 114

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