Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Medicines Safety Update

Volume 3, Number 1, February 2012

In this issue

Pneumovax 23 – updated revaccination recommendations

In April 2011 the Therapeutic Goods Administration (TGA) advised health professionals not to administer a second or subsequent dose of Pneumovax 23 vaccine pending the outcome of a review of an apparent increased rate of injection site reactions following administration of the second dose. This review has now been completed and the TGA is advising health professionals not to routinely revaccinate immunocompetent individuals. Revaccination of patients at high risk of serious pneumococcal disease should be in accordance with the Product Information (PI).

Pneumovax 23 is used to prevent life-threatening infections by pneumococcal bacteria. The TGA review noted that the adverse events observed were consistent with the known high rates of local reactions which occur more commonly after a repeat dose of Pneumovax 23. The review concluded that the adverse events were not due to a problem with the vaccine manufacturing or handling. The outcomes from the review are available on the TGA website.[1]

Updated TGA advice about revaccination

The TGA is advising that revaccination with Pneumovax 23 should be undertaken in accordance with the approved PI.

Revaccination:

- should not be given routinely to immunocompetent individuals; and
- should be considered for patients at a high risk of serious pneumococcal disease, provided that at least five years have passed since the previous dose of Pneumovax 23.

This advice differs from that in the current Australian Immunisation Handbook,[2] which recommends routine revaccination five years after the first dose. The Australian Technical Advisory Group on Immunisation has reviewed the place of Pneumovax 23 in the National Immunisation Program and their updated recommendations have been published at www.immunise.health.gov.au.

Adverse reactions to Pneumovax 23

Pneumovax 23 is known to be associated with a high rate of local injection site reactions, which can result in extensive swelling and pain that can limit the use of the patient's arm. Cellulitis-like reactions and abscesses can also occur, however these are rare.

Further information about possible adverse reactions is available in the Pneumovax 23 PI.[3]

Advice is specific to Pneumovax 23

This advice does not apply to Prevenar, Prevenar 13 and Synflorix pneumococcal conjugate vaccines.

REFERENCES

1. Pneumovax 23 - updated revaccination recommendations. TGA; 2011 Dec. www.tga.gov.au/safety/alerts-medicine-pneumovax-111223.htm [cited 2012 Jan 9]
2. NHMRC. The Australian Immunisation Handbook. 9th ed. Canberra: Australian Government; 2008.
3. Pneumovax 23 Product Information. Merck Sharp & Dohme (Australia) Pty Limited. 2011 Aug.

Medicines Safety Update is the drug safety bulletin of the Therapeutic Goods Administration (TGA). It is published in each issue of *Australian Prescriber*. You can also read it and sign up for free Medicines Safety Update emails on the TGA website at www.tga.gov.au/hp/msu.htm

TGA Health Safety Regulation

Caveat emptor 'buyer beware' – the risks of purchasing unregistered medicines online

The inherent dangers of purchasing unregistered products via the internet have been highlighted recently with a series of serious adverse events, including disfigurement and death, reported to the TGA.

Since 1 July 2011 the TGA has published nine safety alerts related to herbal products bought over the internet and which laboratory tests have found to contain prescription medicines. The most common herbal products reported are for slimming or weight loss and erectile dysfunction.

Herbal slimming products

Tests of herbal slimming and weight loss products purchased over the internet by the TGA Laboratories have shown varying amounts of the anorectics sibutramine and fenfluramine, and the laxative phenolphthalein. All of these products have been withdrawn from the Australian market for safety reasons, including increased risk of cardiac events and stroke (sibutramine in 2010), reports of valvular heart disease and pulmonary hypertension (fenfluramine in 1997) and concerns regarding carcinogenicity (phenolphthalein).

In addition, TGA laboratory testing has identified propranolol, nifedipine and ephedrine in some of these products.

Herbal erectile products

There have also been several safety alerts since 1 July 2011 related to herbal products for improving sexual function, which on testing have been found to contain sildenafil (also known as Viagra). The TGA has also identified or received reports of additional prescription medicines, such as glibenclamide, being included in these herbal products bought overseas and advertised on the internet. When taken at high doses, glibenclamide-containing products have resulted in severe hypoglycaemia and death.

Injectable cosmetic agents

Injectable cosmetic products such as dermal fillers and botulinum toxin-like products are being increasingly marketed on the internet as 'do it yourself' cosmetic kits.

The TGA is aware of consumers who have purchased these 'do it yourself' cosmetic kits and experienced severe reactions, such as anaphylactic reactions and facial scarring. Some consumers experiencing these adverse events have required ongoing medical care. Use of these agents can lead to facial swelling, infection, scarring and severe abscess formation that can, in some instances, require surgical intervention. Reports of these reactions have also appeared in the mainstream media.[1]

Information for health professionals

Herbal products available on international websites are not regulated by the TGA and therefore may not meet the same standards of safety and quality as products that are listed on the Australian Register of Therapeutic Goods, and approved by the TGA for sale in Australia.

The TGA advises consumers that they should exercise extreme caution about purchasing medicines from overseas internet sites, as products purchased in this way may contain undisclosed and potentially harmful ingredients.

Health professionals are in a unique position to discuss the use of health products with their patients and are encouraged to discuss the potential problems associated with the use of medicines and medical devices purchased over the internet.

Health professionals are also encouraged to ask their patients about any products they may be using to manage or prevent a condition, and the source of the product, when managing health related problems.

More information about purchasing via the internet, personal importation of medical goods and counterfeit products can be found at www.tga.gov.au/consumers/information-online-overseas.htm.

Information about the products discussed in this article can be found at www.tga.gov.au/safety/alerts-current.htm, which is updated regularly with new TGA safety information, including product recalls and alerts. Subscribe to these free alerts by visiting www.tga.gov.au/newsroom/subscribe-tga-safety info.htm.

Health professionals are encouraged to report any problems associated with a medicine or medical device to the TGA via the 'Report a Problem' link on the TGA website.

REFERENCE

1. Collier, K. Shocking photos: DIY facelifts leaving patients disfigured. Melbourne: Herald Sun; 2011 May 17.

MEDICINES SAFETY UPDATE

Citalopram and QT prolongation – important changes to the dosing recommendations

A study of citalopram's effect on cardiac conduction, which showed dose-dependent QT prolongation with the medicine, has led to the recommended maximum daily dose of citalopram being reduced to 40 mg, along with other important changes to dosing recommendations for citalopram.

Citalopram is a selective serotonin reuptake inhibitor indicated for the treatment of major depression. There are a number of citalopram-containing products with different trade names registered in Australia.

A recent study has found dose-dependent QT prolongation with the use of citalopram as follows:

- with 20 mg citalopram, after 9 days, the maximum mean time-matched change in QTcF from baseline was 7.5 milliseconds (90% confidence interval 5.9–9.1 milliseconds)
- with 60 mg citalopram, the maximum mean time-matched change was 16.7 milliseconds (90% confidence interval 15–18.4 milliseconds).

There have also been rare reports of torsades de pointes with citalopram.

Given the above study results, the following changes to dose recommendations have been made.

- The recommended maximum daily dose of citalopram is now 40 mg.
- In people over 65 years of age, those with hepatic dysfunction, those taking medicines such as cimetidine or omeprazole which are known to inhibit the metabolism of citalopram, or those known to metabolise poorly via CYP2C19, the recommended maximum daily dose is now 20 mg.
- The recommended starting dose in the elderly is now 10 mg daily.

In addition, citalopram is now contraindicated in patients with congenital long QT syndrome.

Citalopram should be used with caution in patients at higher risk of developing prolongation of the QT interval, including those with:

- congestive heart failure
- bradyarrhythmias
- a predisposition to hypokalaemia or hypomagnesaemia
- concomitant medicines that prolong the QT interval.

There are also new monitoring recommendations for patients on citalopram:

- hypokalaemia and hypomagnesaemia should be corrected prior to initiation of treatment and potassium and magnesium levels should be periodically monitored
- more frequent ECG monitoring should be considered for patients at higher risk of QT prolongation.

Prescribers are reminded that suddenly stopping citalopram may cause withdrawal symptoms.

If citalopram is discontinued or the dose reduced, the patient should be monitored closely for the re-emergence or worsening of any symptoms of depression.

For full prescribing information, prescribers should refer to the Product Information, available from the TGA website.[1]

A similar study of escitalopram found much more limited dose-dependent QT prolongation. No changes to dosing recommendations for escitalopram have been made.

Clinicians are encouraged to report cases of QT prolongation with citalopram or other medicines, especially if extreme or associated with ventricular arrhythmias to the TGA.

REFERENCE

1. Cipramil Product Information. Lundbeck Australia Pty Ltd. 2011 Nov.

MEDICINES SAFETY UPDATE

Atomoxetine (Strattera) – risk of increased blood pressure and/or heart rate

The TGA is advising health professionals of important safety information regarding the risk of clinically significant increases in blood pressure and/or heart rate with the use of atomoxetine (Strattera).

This risk was identified from an analysis of combined data from clinical trials sponsored by atomoxetine's sponsor, Eli Lilly.

Health professionals are advised that atomoxetine is contraindicated in patients with symptomatic cardiovascular diseases, moderate to severe hypertension or severe cardiovascular disorders whose condition would be expected to deteriorate if they experienced clinically important increases in blood pressure or heart rate.

Atomoxetine should be used with caution in patients whose underlying medical conditions could be worsened by increases in blood pressure or heart rate, such as patients with hypertension, tachycardia or cardiovascular or cerebrovascular disease.

Atomoxetine should be used with caution in patients with, or with a family history of, congenital or acquired QT prolongation.

Patients should be screened for pre-existing or underlying cardiovascular or cerebrovascular conditions before initiation of treatment with atomoxetine and monitored during the course of treatment.

Heart rate and blood pressure should be measured in all patients before treatment with atomoxetine is started, after the dose is increased, and periodically during treatment to detect possible clinically important increases, particularly during the first few months of therapy.

The updated Product Information is available on the TGA website.

Health professionals are encouraged to report adverse reactions associated with atomoxetine to the TGA.

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, 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 April 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.

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