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Therapeutic Goods Administration

Medicines Safety Update

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In this issue

Combined oral contraceptives and hormone replacement therapy – inflammatory bowel disease

Health professionals are advised that the TGA is working with sponsors of combined oral contraceptives and hormone replacement therapy to ensure information regarding inflammatory bowel disease is included in the Product Information documents.

The TGA has evaluated recently published research that describes a link between the use of combined oral contraceptives (COCs) and an increased risk of developing inflammatory bowel disease (IBD), including ulcerative colitis and Crohn's disease.[1,2,3]

During assessment of this information, the TGA identified corresponding data that suggested hormone replacement therapy (HRT) was also a potential risk factor for development of IBD.

The literature also suggested that these risks may be increased in women who were smokers.[4]

Related products

Progestogen-only contraceptive and HRT products and products containing tibolone as the active ingredient were not specifically considered in the data evaluated, therefore the TGA could not determine whether or not those products were associated with a potential increased risk of IBD.

One paper concluded that there was no difference in the IBD risk between oestrogen-only HRT products and oestrogen/progestogen combination HRT.[1]

TGA assessment

The TGA found that the literature had limitations. While the research did not confirm a causal relationship and the pathogenesis of IBD remained incompletely defined, the TGA concluded that health professionals should be made aware of this information.

While the Product Information (PI) documents for most COC products include a reference to the association between these drugs and IBD, this information is not consistent across all products.

Meanwhile, no PI documents for oestrogen/progestogen combination HRT products contain information about a potential association with IBD.

The TGA is negotiating with the sponsors of COCs and oestrogen/progestogen combination HRT products to ensure adequate information is provided in their PI.

REFERENCES

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2. Molodecky NA, Kaplan GG. Environmental risk factors for inflammatory bowel disease. Gastroenterol Hepatol 2010;6:339-46.
3. Cornish JA, Tan E, Simillis C, Clark SK, Teare J, Tekkis PP. The risk of oral contraceptives in the etiology of inflammatory bowel disease: a meta-analysis. Am J Gastroenterol 2008;103:2394-400.
4. Katschinski B, Fingerle D, Scherbaum B, Goebell H. Oral contraceptive use and cigarette smoking in Crohn's disease. Dig Dis Sci 1993;38:1596-600.

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

TGA Health Safety Regulation

MEDICINES SAFETY UPDATE

Metoclopramide and neurological adverse events

The Product Information for metoclopramide has been updated to include a new contraindication and changes to dosing and duration of use to reduce the risk of neurological adverse events.

Metoclopramide is a widely used antiemetic and gastroprokinetic drug. It has a number of approved indications, the most common being to control nausea and vomiting which may be associated with the following conditions:

- intolerance to essential drugs with emetic properties
- uraemia
- radiation sickness
- malignant disease
- postoperative vomiting
- labour
- infectious diseases.

There are 30 metoclopramide and metoclopramide-containing products included on the Australian Register of Therapeutic Goods. These are available as prescription and pharmacist-only medicines.

European review

The TGA has recently completed an analysis of the findings of a European Medicines Agency (EMA) review of metoclopramide.

In December 2013, the European Commission adopted the EMA's recommended changes to restrict the dose and duration of use of metoclopramide to reduce the risk of potentially serious neurological adverse events, including extrapyramidal disorders and tardive dyskinesia, as well as rare cardiac conduction disorders.[1]

Extrapyramidal disorders, including tardive dyskinesia, may continue even after cessation of metoclopramide and may not be reversible.

Adverse events

From January 1971 to 16 October 2014, the TGA received 2190 adverse event case reports associated with metoclopramide. Among these reports were 16 cases of tardive dyskinesia associated with metoclopramide use, and 86 cases of other extrapyramidal disorders. There were also nine reports of cardiac arrest and a further 63 reports of cardiac arrhythmias.

Product Information changes

The TGA has worked closely with the sponsor to update the Product Information (PI) for prescription metoclopramide products to include information about the risk of neurological adverse events.

The TGA will also be assessing labelling requirements for the over-the-counter metoclopramide products.

Information for health professionals

Health professionals are advised of the risk of neurological adverse events, including extrapyramidal disorders and tardive dyskinesia, associated with the use of metoclopramide. A risk of rare cardiac conduction disorders has also been identified.

In response to these identified risks, the following changes have been made to the PI for prescription metoclopramide:

- it is contraindicated for children aged under one year
- for young adults (aged under 20 years) and children over one year of age, it is only indicated as second-line therapy
- the total daily dosage, especially for children and young adults, should not normally exceed 0.5 mg/kg bodyweight, with a maximum of 30 mg daily
- the maximum dose for adults is 10 mg three times daily
- the maximum recommended treatment duration is now five days in all age groups.

Please report any suspected neurological adverse events and cardiac conduction disorders associated with metoclopramide to the TGA.

REFERENCE

1. European Medicines Agency. European Medicines Agency recommends changes to the use of metoclopramide. Changes aim mainly to reduce the risk of neurological side effects. 2014.

Publication changes for Medicines Safety Update

After this issue, publication of the TGA's bimonthly safety bulletin Medicines Safety Update will be changing. It will no longer be included within *Australian Prescriber*.

Medicines Safety Update will continue to be published on the TGA's website at www.tga.gov.au/publication/medicines-safety-update during the months of February, April, June, August, October and December.

Through that webpage, you can subscribe to an email list and receive a notification when each new edition becomes available.

Medicines Safety Update provides health professionals with practical information and advice on drug safety and emerging safety issues. It replaced the *Australian Adverse Drug Reactions Bulletin*, which was published from 1974 to 2009. It also provides information on adverse event reporting and how health professionals can contribute to safety monitoring in Australia.

Further important safety information for health professionals regarding all types of therapeutic goods is available on the TGA website at www.tga.gov.au/safety-information-health-professionals. This includes *Medicines Safety Update's* companion publication, *Medical Devices Safety Update*, which is published during the months of January, March, May, July, September and November.

The TGA wishes to acknowledge the ongoing collaboration and support of the publisher of *Australian Prescriber*, NPS MedicineWise, and thanks *Australian Prescriber* readers for their ongoing interest in and commitment to drug safety.

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 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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