Drug Safety Update

Latest advice for medicines users

The monthly newsletter from the **Medicines and Healthcare products Regulatory Agency** and its independent advisor the **Commission on Human Medicines**

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Contents

The **Medicines and Healthcare products Regulatory Agency** is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The **Commission on Human Medicines** gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

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This month we report the increased risk of tuberculosis, or reactivation of latent tuberculosis, during treatment with tumour necrosis factor alpha (TNF-alpha) inhibitors. Tuberculosis in patients receiving TNF-alpha inhibitors can be life-threatening, and deaths from tuberculosis have occurred in these patients. TNF-alpha inhibitors are therefore contraindicated in patients with active tuberculosis or other severe infections. Screen patients for active and latent tuberculosis before starting treatment with a TNF-alpha inhibitor. Monitor patients closely for infectious diseases before, during, and after treatment and provide a patient alert card —see article A1.

We have recently updated the online Yellow Card form to increase and improve reporting of suspected adverse reactions to medicines taken during pregnancy. These reports will improve our understanding of a medicine's effect during pregnancy and inform treatment decisions to maximise the benefit and minimise the risk to the woman and child—see article Y1.

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Drug safety advice

A1 Tumour necrosis factor alpha inhibitors: risk of tuberculosis—screen all patients before starting treatment and monitor them closely

There is an increased risk of tuberculosis, or reactivation of latent tuberculosis, during treatment with tumour necrosis factor alpha (TNF-alpha) inhibitors. Tuberculosis in patients receiving TNF-alpha inhibitors can be life-threatening, and deaths from tuberculosis have occurred in these patients. TNF-alpha inhibitors are therefore contraindicated in patients with active tuberculosis or other severe infections. Screen patients for active and latent tuberculosis before starting treatment with a TNF-alpha inhibitor. Monitor them closely for infectious diseases including tuberculosis before, during, and after treatment

TNF-alpha inhibitors are a class of biological medicines that block the proinflammatory cytokine TNF-alpha. The TNF-alpha inhibitors authorised in the UK are adalimumab, certolizumab, etanercept, golimumab, and infliximab. TNF-alpha inhibitors are authorised for the treatment of inflammatory and autoimmune conditions, such as rheumatoid arthritis, ankylosing spondylitits, Crohn's disease, ulcerative colitis, psoriasis, and psoriatic arthritis.

Increased risk of tuberculosis

TNF-alpha plays an important role in inflammatory processes, and is involved in autoimmune diseases, and immune responses to infection. TNF-alpha inhibition increases susceptibility to infectious diseases, including tuberculosis, and increases the risk of reactivation of latent tuberculosis. An increased risk of tuberculosis in patients treated with TNF-alpha inhibitors has been confirmed in large observational studies. Reports of tuberculosis, including fatalities, in patients treated with TNF-alpha inhibitors continue to be received via the Yellow Card Scheme. In many cases extrapulmonary tuberculosis, presenting as either local or disseminated disease has been reported. In one recent case, a patient receiving a TNF-alpha inhibitor died from tuberculosis that had not been diagnosed.

Patient alert card

Companies are required to produce a patient alert card for TNF-alpha inhibitors which healthcare professionals should give to patients (see example below). The alert card warns patients of the risk of infectious diseases, particularly tuberculosis. The card describes possible signs and symptoms of tuberculosis, and advises patients to inform their doctor if they have signs of an infection.

Advice for healthcare professionals:

- TNF-alpha inhibitors are contraindicated in patients with active tuberculosis or other severe infections.

Pretreatment screening

- Assess all patients for active and latent tuberculosis before starting treatment with a TNF-alpha inhibitor and record the results on the patient's alert card. This assessment should include:
    - a detailed medical history of possible previous contact with tuberculosis and any history of immunosuppressive therapy;
    - tuberculin skin test;
    - chest radiograph

- Be aware of the risk of false-negative tuberculin skin-test results, especially in patients who are severely ill or immunocompromised.

Diagnosis of tuberculosis

Active infection

- If active tuberculosis is diagnosed, do not start treatment with a TNF-alpha inhibitor.

Latent infection

- If latent tuberculosis is diagnosed, start treatment for this infection before treatment with a TNF-alpha inhibitor
- If latent tuberculosis is suspected, consider antituberculous therapy before starting treatment with a TNF-alpha inhibitor
- In these situations, consult a physician with expertise in tuberculosis treatment, and carefully consider the balance of benefits and risk for TNF-alpha inhibitor treatment.

Monitoring

- Closely monitor patients for infectious diseases, including tuberculosis, before, during, and after treatment with a TNF-alpha inhibitor.

Advice to give to patients

- Inform all patients that they should seek medical advice if symptoms of tuberculosis develop during or after treatment with a TNF-alpha inhibitor (eg, persistent cough, weight loss, low-grade fever)
- Give patients being treated with a TNF-alpha inhibitor a patient alert card, which includes information on the risk of tuberculosis and other infectious diseases.

Further information:

Patient alert card example (Cimzia, certolizomab pegol) http://www.mhra.gov.uk/home/groups/dsu/documents/publication/con404197.pdf

BNF section 10.1.3 Drugs that suppress the rheumatic disease process: cytokine modulators http://www.medicinescomplete.com/mc/bnf/current/PHP6607-cytokine-modulators.htm?q=tumour%20necrosis&t=search&ss=text&p=2

Product information for TNF-alpha inhibitors is available on the MHRA website http://www.mhra.gov.uk/Safetyinformation/Medicinesinformation/SPCandPILs/

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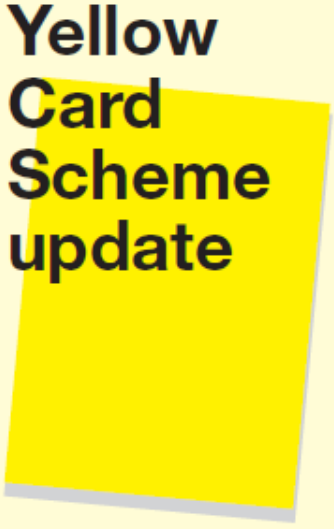

Y1 Reporting suspected adverse reactions experienced by the woman or child associated with medicines taken during pregnancy: update to Yellow Card form

It is sometimes necessary for women to take medicines while pregnant. Some women may take medicines before they know they are pregnant. However, there is commonly little information available on a medicine's effect on human pregnancy before the medicine is licensed. Therefore it is important to collect reports of suspected adverse reactions experienced by the woman or child associated with medicines taken during pregnancy. This information improves our understanding of a medicine's effect during pregnancy and informs treatment decisions to maximise the benefit and minimise the risk to the woman and child.

Update to online Yellow Card form

We have updated the online Yellow Card form to increase and improve reporting of suspected adverse reactions to medicines taken during pregnancy. When you enter data on a female 16 years or older, you will now be asked:

- If the woman is pregnant
- The dates of her last menstrual period if she is pregnant
- Expected date of delivery if she is pregnant

We also encourage you to provide the following in the "additional information" field of the Yellow Card:

- Information on previous pregnancies
- Dates and findings of ultrasonography
- If and when the woman started or stopped taking any other medicines and supplements during pregnancy (including folic acid)

If the suspected reaction is in the child, this helps us to identify when the fetus was exposed to the medicine and track the pregnancy outcome. We will request more detailed information if necessary (eg, details of any delivery complications, birth defects, or developmental concerns).

Please describe further details of congenital abnormalities following exposure to a medicine during pregnancy in the "additional information" field of the Yellow Card form.

Update to paper Yellow Card form

Download Yellow Card forms from here:http://yellowcard.mhra.gov.uk/_assets/files/HCP-Yellow-Card-07-2013-vFinal.pdf

We are updating the paper Yellow Card forms. These are available at the back of the British National Formulary (BNF), in the Monthly Index of Medical Specialities (MIMS) or by electronic download from the MHRA website. We will publish a supporting guide on the MHRA and Yellow Card websites to help you report suspected adverse reactions experienced by the woman, fetus, or child following medicine use during pregnancy. In the meantime, please include any pregnancy-related information in the "additional information" section of the paper Yellow Card form.

Please continue to report to the Yellow Card Scheme

Thank you for continuing to send us your suspected adverse reaction reports. Every Yellow Card received is a valuable contribution to monitoring of the safety of medicines in the UK. In 2013, the majority of Yellow Card reports from healthcare professionals (72%) and members of the public (84%) were submitted electronically. Electronic Yellow Cards accounted for nearly 75% of all Yellow Cards received.

Please continue to report any suspected adverse reactions to us through the Yellow Card Scheme website: www.mhra.gov.uk/yellowcard (if you choose to register, you can also keep track of any Yellow Cards that you send). Alternatively, prepaid paper Yellow Cards are available as summarised above. When reporting please provide as much information as possible, including information about pregnancy and postnatal outcomes, medical history, any concomitant medication, onset time of reaction, and treatment dates.

Article citation: Drug Safety Update volume 7 issue 9, April 2014: Y1.

Stop press

S1 Dispensing and medication errors: please ensure appropriate checking procedures are in place to help minimise risk

Pharmacists and dispensers should take care to ensure that checking procedures are in place to reduce the risk of drug-name confusions and drug strength and quantity confusions. For controlled drugs these procedures should include recording the strength of the product and the quantity dispensed. Guidance is available from the Royal Pharmaceutical Society's Medicines Ethics and Practice.

Royal Pharmaceutical Society's Medicines Ethics and Practice http://www.rpharms.com/support/mep.asp

Morphine sulfate preparations: new packaging to help ensure correct strength is dispensed

The packaging of some morphine sulfate products is being updated to better highlight the strength of the medicine on the pack. Examples of the new packaging for the medicines involved are illustrated below. The new packs will begin to appear in the marketplace from April onwards.

This measure is in response to a recent fatal dispensing error, in which 60 milligram capsules of morphine sulfate were supplied instead of 10 milligram capsules. The error was due to confusion between the declaration of the capsule strength and the declaration of the quantity of capsules in the pack. Please be aware when dispensing morphine sulfate preparations.

Drug-name confusion: vigilance required

Drug Safety Update article April 2013: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON266137

Drugs names that look alike or sound alike (or both) can also lead to medication errors (see Drug Safety Update article April 2013). More recently, we have become aware of a case of confusion between bumetanide (a diuretic) and buspirone (a treatment for anxiety disorders), resulting a person receiving the wrong medicine which contributed to that person's death.

Please report medication errors through the National Reporting and Learning System (NRLS) or, if the NRLS is not available and harm occurred, on a Yellow Card (www.mhra.gov.uk/yellowcard).

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Medicines and Healthcare Products Regulatory Agency