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 inform you that patient reminder cards are being introduced for patients taking denosumab and intravenous bisphosphonates. These cards inform patients of the risk of osteonecrosis of the jaw and precautions to take before and during treatment. Denosumab 120 mg (cancer indication) is now contraindicated in patients with unhealed lesions from dental or oral surgery—see article 1.

Following the reformulation of Xalatan, an eye-drop formulation of latanoprost, there has been an increase in the number of reports of eye irritation. This may be due to the lower pH of the current formulation. Review treatment if patients mention excessive eye irritation with Xalatan—see article 2.

A new smartphone app for reporting side effects to the Yellow Card Scheme has now launched—see article 3 for further information. The free app enables healthcare professionals, patients, or carers to report any suspected side effects directly to us—a convenient and secure alternative to using paper Yellow Card forms or the Yellow Card website.

Finally, in June 2015, letters sent to healthcare professionals included one for the oral anticoagulant edoxaban—see article 4 for link.

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1 Denosumab (Xgeva▼, Prolia); intravenous bisphosphonates: osteonecrosis of the jaw—further measures to minimise risk

Patient reminder cards about the risk of osteonecrosis of the jaw are being introduced; denosumab 120 mg is now contraindicated in patients with unhealed lesions from dental or oral surgery.

Before prescribing denosumab or intravenous bisphosphonates:

- give patients the patient reminder card for their medicine[1]
- explain the risk of osteonecrosis of the jaw and advise patients on precautions to take—advise patients to:
  - tell their doctor if they have any problems with their mouth or teeth before starting treatment; if they wear dentures they should make sure their dentures fit properly before starting treatment
  - maintain good oral hygiene and get routine dental check-ups during treatment
  - tell their doctor and dentist that they are receiving denosumab or an intravenous bisphosphonate if they need dental treatment or dental surgery
  - tell their doctor and dentist immediately if they have any problems with their mouth or teeth during treatment (eg loose teeth, pain, swelling, non-healing sores or discharge)

- Do not prescribe denosumab 120 mg (cancer indication) to patients with unhealed lesions from dental or oral surgery

Please continue to report suspected side effects to denosumab, bisphosphonates or any other medicines on a Yellow Card www.gov.uk/yellowcard

Indication

Denosumab and bisphosphonates are used to treat osteoporosis, Paget's disease, and as part of some cancer regimens, particularly for metastatic bone cancer and multiple myeloma. Individual bisphosphonates and denosumab-containing medicines have different indications; please check the summary of product characteristics of the medicine in question.

Osteonecrosis of the jaw

Osteonecrosis of the jaw (ONJ) is a known side effect of denosumab and bisphosphonates (see Drug Safety Update articles from November 2009 and September 2014). To date, we have received 45 Yellow Card reports of ONJ in people taking denosumab (all doses) and 323 reports in people taking a bisphosphonate.[2]

In patients treated for osteoporosis (regardless of route of administration), the risk of ONJ is small compared with that in patients treated with the higher doses used for cancer-related conditions. Other drug-specific risk factors for ONJ include drug potency (higher risk for highly potent compounds such as zoledronate, pamidronate and denosumab), route of administration (higher risk for parenteral administration) and cumulative dose.

Patient reminder cards and denosumab 120 mg contraindication

The MHRA and other EU medicines regulators have reviewed measures to minimise the risk of ONJ in patients taking denosumab or bisphosphonates. The review recommended introducing patient reminder cards for denosumab and intravenous bisphosphonates to inform patients of the risk of ONJ and precautions to take before and during treatment. The review of ONJ and denosumab also recommended that denosumab 120 mg should be contraindicated in patients with unhealed lesions from dental or oral surgery.

Further information

European Medicines Agency announcement, March 2015

Content of reminder card as approved by the European Committee on Medicinal Products for Human Use

Content of Prolia (denosumab) patient card

Content of Xgeva (denosumab 120 mg) patient card

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Oral bisphosphonates: reminder of precautions to take

All bisphosphonates are associated with a risk of ONJ. Therefore before prescribing oral bisphosphonates, we remind you to tell patients to maintain good oral hygiene, attend routine dental check-ups and immediately report any oral symptoms such as dental mobility, pain, or swelling to a doctor and dentist.

1. The reminder cards are being sent by licence-holders for individual products separately and will therefore become available at different times. You can view the content of the reminder cards via the links above.
2. Yellow Card reports are reports of suspected adverse drug reactions (ADRs) submitted voluntarily by healthcare professionals and members of the public in the UK. The number of reports received should not be used to determine the incidence of an ADR. This is because neither the total number of ADRs occurring, nor the number of patients using the drug is known. ADR reporting rates are influenced by the seriousness of ADRs, their ease of recognition, and the extent of use of a particular drug, and may be stimulated by publicity about a drug.

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2 **Latanoprost (Xalatan): increased reporting of eye irritation since reformulation**

Advise patients to tell their health professional if they experience severe eye irritation.

When prescribing or dispensing the Xalatan brand of latanoprost:

- advise patients to tell their health professional if they experience severe eye irritation
- review treatment if patients mention severe eye irritation
- please continue to report suspected side effects to latanoprost or any other medicines on a Yellow Card www.gov.uk/yellowcard

Xalatan is an eye-drop formulation of latanoprost. It is licensed for the reduction of intraocular pressure in adults and children with ocular hypertension and open angle glaucoma.

In 2013 the Xalatan pH was reduced from 6.7 to 6.0 to allow for long-term storage at room temperature. Following this reformulation there has been an increase in the number of reports of eye irritation from across the EU. We received no Yellow Card reports of eye irritation in people using Xalatan in the year before the reformulation, compared with 22 reports in the year after reformulation.[1]

It is important that patients continue their treatment. Therefore advise patients to tell their health professional promptly (within a week) if they have eye irritation (eg excessive watering) severe enough to make them consider stopping treatment. Review treatment and prescribe a different formulation if necessary.

Further information

Xalatan summary of product characteristics

1. Yellow Card reports are reports of suspected adverse drug reactions (ADRs) submitted voluntarily by healthcare professionals and members of the public in the UK. The number of reports received should not be used to determine the incidence of an ADR. This is because neither the total number of ADRs occurring, nor the number of patients using the drug is known. ADR reporting rates are influenced by the seriousness of ADRs, their ease of recognition, and the extent of use of a particular drug, and may be stimulated by publicity about a drug.

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3 New Yellow Card app for reporting suspected side effects

A new smartphone app for reporting side effects to the Yellow Card Scheme has now launched.

The free app enables healthcare professionals, patients, or carers to report any suspected side effects directly to us—a convenient and secure alternative to using paper Yellow Card forms or the Yellow Card website.

On reporting, you will receive an immediate response to show that your Yellow Card report has been accepted, and it is simple to view information for any Yellow Cards already submitted (even if you don't have a side effect to report at the time).

Further information
Digital evolution for ground-breaking Yellow Card Scheme

Moreover, you can create a watchlist that enables you to receive news and alerts about particular medicines of interest, and to look up numbers of Yellow Cards received about them.

Download the app via iTunes Yellow Card for iOS devices or via PlayStore Yellow Card for Android devices.

Article citation: Drug Safety Update Volume 8 issue 12 July 2015: 3.

4 Letters sent to healthcare professionals in June 2015

Last month, letters sent included one for the oral anticoagulant edoxaban.

In each issue of Drug Safety Update we summarise drug safety letters sent to healthcare professionals that are not linked to their own Drug Safety Update article. In June 2015, letters sent included one for the oral anticoagulant edoxaban.

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