News and updates from palliativedrugs.com

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Received 14 January 2015
Accepted 20 January 2015

To cite: Wilcock A, Charlesworth S. *BMJ Supportive & Palliative Care* 2015;**5**:7–9.

The website http://www.palliativedrugs.com has provided essential independent information about drugs used in palliative and hospice care for over a decade. It contains the online *Palliative Care Formulary* (PCF) and provides free access to a *Bulletin board* to stimulate questions and share experiences, a *Document library* containing 475 items of useful information and a *Syringe Driver Survey Database* containing details of over 2350 different drug combinations. Territory-specific book versions (the UK *Palliative Care Formulary* fifth edition, *Hospice and Palliative Care Formulary USA* second edition and *Palliative Care Formulary* Canadian edition), a PDF version of the PCF and subscription to the continually updated online PCF can also be purchased via the website. This feature provides a selection of items that have featured in the *News* and *Latest additions* sections in recent months; *for additional information, please register for free on the website*.

SAFETY UPDATES

Dexamethasone 4 mg/mL injection changes in the UK

Dexamethasone 4 mg/mL injection (Organon) has been acquired by Aspen pharmaceuticals. They have reformulated the product and it now contains 3.8 mg/mL dexamethasone *base*, available as a 1 mL *vial*, which requires storage in a fridge. Other dexamethasone injectable formulations in the UK are 3.3 mg/mL dexamethasone *base* (Hameln and Hospira), which do not require refrigeration. There are also differences in presentation and preservative/solvent content.

These changes have implications for prescribing, administration and storage, and increase the risk of confusion and error. The UK Medicines and Healthcare products Regulatory Agency (MHRA) has highlighted the issues and UK Medicines Information (UKMi) has produced a safety assessment report summarising the changes, the differences between the products and the potential next steps. A palliativedrugs.com summary sheet, clarifying the use of dexamethasone formulations in adults in palliative care, can be downloaded from our website. The online PCF systemic corticosteroids monograph has been updated to reflect this guidance.

Diclofenac dose reduced in Canada

Health Canada has reduced the maximum daily dose of diclofenac tablets and suppositories to 100 mg/day following a safety review that indicated that the cardiovascular risks of high-dose diclofenac were comparable to cyclo-oxygenase 2 inhibitors. Further, diclofenac is not recommended in patients with cerebrovascular disease or with known (or risk factors for) cardiovascular disease.

Buscopan and baclofen confusion

UKMi has highlighted the risk of confusion between Buscopan (Boehringer Ingelheim) 10 mg tablets (hyoscine butylbromide) and baclofen 10 mg tablets, following numerous reported medication errors. The majority of errors occurred while dispensing although some have occurred while prescribing or administering. Recommendations by UKMi on managing this risk have been made in a product safety assessment report.

Zolpidem updated Summary of Product Characteristics

Strengthened warnings regarding the risk of drowsiness and reduced driving ability, use in the elderly and in liver impairment have been added to the zolpidem Summary of Product Characteristics (SPC). This follows a European review and an MHRA Drug Safety Update highlighting these risks. The changes include advising patients:

- Not to readminister the dose during the same night;

- Not to drive, operate machinery or work at heights until at least 8 h after taking zolpidem, or if they are still drowsy;
- Not to take zolpidem with alcohol, illicit drugs or other central nervous system suppressants.

In addition, a maximum of 5 mg at night is recommended for people with liver impairment and the elderly.

Naloxone—Patient Safety Alert

NHS England has produced a Patient Safety Alert warning of the risks of distress and death from inappropriate doses of naloxone in patients on long-term opioid treatment (NHS/PSA/W/2014/016R). The alert highlights that the initial adult dose for the management of opioid-induced respiratory depression or sedation in those receiving palliative care and in chronic opioid use is 100–200 μg (1.5–3 μg/kg) by intravenous injection. This is *significantly lower* than the initial adult dose of 400 μg intravenously recommended for acute opioid overdose. This information is already reflected in the PCF Opioid antagonist monograph, which also details the use of even lower initial doses (20 μg intravenously) in these circumstances, as recommended by the American Pain Society.

Gabapentin and pregabalin potential for misuse

Public Health England and NHS England have published advice for prescribers on the risk of misuse of gabapentin and pregabalin.

Denosumab updated information

The MHRA has sent out updated information for health professionals to minimise the risk of osteonecrosis of the jaw and hypocalcaemia for both UK formulations of denosumab (Xgeva and Prolia; Amgen). The UK SPCs have been updated in line with these recommendations.

HOT TOPICS

Cochrane reviews

The following Cochrane reviews have been published in full online:

- The use of codeine, alone and with paracetamol, for cancer pain (CD006601);
- The use of desipramine for neuropathic pain in adults (CD011003).

British guideline on the management of asthma updated

The British guidelines on the management of asthma (SIGN 141), produced jointly by the British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN), have been updated.

Drugs and driving

The new offence of driving with certain controlled drugs above specified limits in the blood, which comes into force in March 2015, is for England, Wales and Scotland only. In Northern Ireland a similar offence is under consideration. The MHRA have produced a Patient Information Leaflet.

New Scottish Palliative Care Guidelines

The new Scottish Palliative Care Guidelines have been launched. These national guidelines replace the previous pain and symptom control section of the Lothian Palliative Care Guidelines (2010).

APPM Master Formulary 2015 third edition now available

The third edition of the Association for Paediatric Palliative Medicine (APPM) Master Formulary is now available and can be downloaded from their website.

DRUG UPDATES

Naloxegol for opioid-induced constipation

The Food and Drug Administration (FDA) has approved naloxegol (Movantik; Astra Zeneca), a peripherally acting opioid antagonist, for the treatment of opioid-induced constipation in adults with chronic non-cancer pain.

FDA approves additional indication for methylnaltrexone

The FDA has approved subcutaneous methylnaltrexone injection (Relistor; Salix Pharmaceuticals) for the relief of opioid-induced constipation in adults with chronic non-cancer pain. This is in addition to the existing indication of opioid-induced constipation in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient.

FDA reschedules hydrocodone combination products

All hydrocodone combination products have been rescheduled in the USA to Schedule 2 controlled substances (formerly Schedule 3).

FDA approves additional indication for denosumab

The FDA has approved denosumab (Xgeva; Amgen) for the treatment of hypercalcaemia of malignancy refractory to bisphosphonate therapy.

In the UK, denosumab is currently only authorised for prevention of skeletal-related events in adults with bone metastases from solid cancers; and treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

Nitrofurantoin contraindications updated

The guidance for using nitrofurantoin in renal impairment has changed in the UK. Nitrofurantoin is now contraindicated in patients with an estimated glomerular filtration rate (eGFR) of <45 mL/min/1.73 m^2. However, a short course (3–7 days) may be used with caution in certain patients with an eGFR of 30–44 mL/min/1.73 m^2.

Previously, nitrofurantoin was contraindicated in patients with a creatinine clearance of <60 mL/min. The evidence for this has been reviewed by the MHRA in the context of increasing antibiotic resistance and the increasing risk of *clostridium difficile* colitis with the use of alternative broad-spectrum antibiotics. New evidence supports the revised contraindication.

Scottish Medicines Consortium accepts capsaicin patch

The Scottish Medicines Consortium has accepted capsaicin patch (Qutenza; Astellas) for restricted use within NHS Scotland for the treatment of peripheral neuropathic pain in non-diabetic adults either alone or in combination with other medicinal products for pain. It must only be used in patients who have not achieved adequate pain relief from, or have not tolerated, conventional first-line and second-line treatments.

Discontinued UK products

The following branded products have been discontinued in the UK. However, generic alternatives are available:

- Haldol brand of haloperidol injection 5 mg/mL (Janssen-Cilag);
- Rivotril brand of clonazepam 500 µg and 2 mg tablets (Roche);
- Macrodantin brand of nitrofurantoin 50 mg and 100 mg hard capsules (Amdipharm Mercury).

In addition, Novartis is discontinuing carbamazepine 100 mg and 200 mg chewable tablets (Tegretol Chewtabs). Existing stocks are expected to be depleted by May 2015.

LATEST ADDITIONS

Survey results

Results from our survey 'Domperidone—What is your experience?' (August 2014–September 2014) and our website satisfaction survey (October–November 2014) are available to download from http://www.palliativedrugs.com

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Competing interests None.

Provenance and peer review Not commissioned; internally peer reviewed.