

# CLINICAL DEVELOPMENTS IN 2007

**Harriet Adcock discusses some of the important clinical developments, the medicines that came to market and some of the significant drug safety issues that surfaced in 2007**

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Independent prescribing became a reality in 2007 when the first pharmacist in Britain wrote a prescription unhindered by the constraints of a clinical management plan (*PJ*, 24 February 2007, p209). Although this may have been a fairly straightforward step for the pharmacist involved — Beth Hird, a senior practice pharmacist at Nottinghamshire County Teaching Primary Care Trust, who had already been working as a supplementary prescriber — it was, nevertheless, a historic step for the profession.

Further progress for advanced clinical practitioners was seen throughout the year. A rigorous accreditation process for pharmacists with special interests was revealed in May (*PJ*, 5 May 2007, p515) and a consultant pharmacist was appointed in the field of oncology. Because of devolution, pharmacists in Scotland witnessed a different set of developments in 2007 — the electronic transfer of prescriptions started to take hold (*PJ*, 8 December 2007, p642), paving the way for the acute medication service. And the country's minor ailment service bedded down in 2007, with 15 per cent of people registering for the service by June (*PJ*, 29 September 2007, p340).

In England and Wales, provision of clinical services under the community pharmacy contract came under scrutiny. The value of medicines use reviews (MURs) was questioned by MPs (*PJ*, 23 June 2007, p727) and research from Keele University suggested that some pharmacists were unsure about

the difference between MURs and clinical medication reviews. A major evaluation of the contract, presented at the British Pharmaceutical Conference in September, revealed that 60 per cent of pharmacies were providing MURs and prescription intervention services with 87 per cent providing at least one enhanced service (*PJ*, 15 September 2007, p280). The recent introduction of a more user-friendly MUR form (*PJ*, 22/29 December 2007, p701) will, perhaps, encourage pharmacists to perform more MURs in 2008.

The year ended with a vote of confidence in pharmacy when the Government announced plans for dealing with an influenza pandemic: a consultation suggests community pharmacists will be given powers to supply medicines and provide services in a more flexible manner (*PJ*, 1 December 2007, p609). Furthermore, Lord Darzi, the health minister charged with leading a review of primary care services, indicated his support for provision of oral contraception through pharmacies without prescription (*PJ*, 15 December 2007, p669).

In terms of new medicines, 2007 delivered a handful of innovations as well as the usual trickle of me-too drugs.

## **Cardiovascular system**

A new treatment option for patients with essential hypertension — aliskiren — was launched in September by Novartis and was, arguably, the most important new product to emerge in

2007 for fighting cardiovascular disease. Sitaxentan sodium (Thelin) was also made available to specialists in March for the treatment of patients with pulmonary arterial hypertension.

Safety concerns in the field of cardiovascular medicine arose for aprotinin, which lost its licence for the prevention of major blood loss during coronary artery bypass graft surgery. (*PJ*, 8 December 2007, p641). Early findings from a clinical trial suggest that the drug increases the risk of death compared with other antifibrinolytics.

## **Diabetes**

Patients with type 2 diabetes saw a couple of therapeutic innovations hit the market in 2007. The new arrivals included two first-in-class medicines — exenatide, an incretin mimetic, and sitagliptin, a dipeptidyl peptidase type 4 inhibitor. Insulin-dependent patients, however, had their therapy options reduced when Pfizer announced that it was to stop marketing Exubera, its inhaled insulin product. The company decided further investment was unwarranted after its product failed to gain acceptance among patients and doctors.

The safety of the thiazolidinediones rosiglitazone and pioglitazone was much debated throughout 2007: a number of studies raised concerns about an increased risk of bone fracture and heart attack. A review of evidence conducted by the European Medicines Agency concluded that the drugs' benefits continue to outweigh risks for



their approved indications (*PJ*, 27 October 2007, p460). However, the regulator recommended careful evaluation of individual risk when considering rosiglitazone as therapy for diabetic patients with ischaemic heart disease.

### Arthritis

Patients with rheumatoid arthritis who have failed on antitumour necrosis factor therapy have seen their treatment options expand with the introduction of a new immunosuppressant, abatacept.

Another anti-inflammatory agent — lumiracoxib (Prexige) — had its marketing authorisation suspended by the Medicines and Healthcare products Regulatory Agency in November because of concerns about liver damage (*PJ*, 24 November 2007, p575). Further restrictions on the use of piroxicam were issued in 2007 because of the risk of gastrointestinal side effects and serious skin reactions (*PJ*, 30 June 2007, p760).

### Malignancy

A number of therapeutic advances in oncology were seen. The most notable new medicine was lenalidomide, launched in June by Celgene. Another antineoplastic agent, nelarabine (Atriance), was launched by GlaxoSmithKline in September. It is licensed for the treatment of patients with T-cell acute lymphoblastic leukaemia and T-cell lymphoblastic lymphoma.

Licence extensions for existing therapies also bolstered the arsenal of cancer drugs. Roche's erlotinib (Tarceva), used in combination with gemcitabine, gained a new indication for metastatic pancreatic cancer.

Bevacizumab (Avastin), another Roche product, widened its reach with licence extensions for first-line treatment of metastatic breast cancer and for advanced or recurrent non-squamous, non-small cell lung cancer in combination with carboplatin and paclitaxel.

The market for two more Roche products expanded with licence extensions for capecitabine (Xeloda) — for first-line treatment of advanced gastric cancer in combination with a platinum-based regimen — and trastuzumab (Herceptin), in combination with an aromatase inhibitor, for the treatment of postmenopausal patients with hormone receptor-positive metastatic breast cancer.

Other licence extensions included hepatocellular carcinoma for sorafenib (Nexavar; Bayer) and advanced renal cell carcinoma for sunitinib (Sutent; Pfizer).

A second human papillomavirus vaccine, GSK's Cervarix, appeared on the market some 11 months after the launch of Gardasil (Sanofi Pasteur/MSD) in 2006. A national vaccination programme for 12- to 13-year-old girls will start in 2008 (*PJ*, 3 November 2007, p490).

### Infections

An interesting clinical development in the area of infectious disease was seen when Pfizer introduced the first CCR5 antagonist for the treatment of HIV (maraviroc) in the autumn. Another protease inhibitor reached the market in March when Janssen-Cilag launched darunavir.

Treatment options for hepatitis B expanded when Novartis launched telbivudine, a thymidine nucleoside analogue, in June.

In the field of HIV, the recall of Roche's Viracept (nelfinavir) in June, because of contamination with a genotoxic substance, meant that patients, including those taking the drug as part of HIV post exposure prophylaxis, had to switch to alternative therapies. Following a temporary suspension of its marketing authorisation, steps were made to reintroduce Viracept to the EU market in September.

On a more positive note, the option to reduce the pill burden of some HIV patients came in December when Gilead launched Atripla, a fixed-combination tablet containing efavirenz, emtricitabine and tenofovir disoproxil.

### Eye conditions

Treatment options for neovascular (wet) age-related macular degeneration (AMD) — a condition that results in loss of central vision — continued to grow in 2007. February saw the launch of

ranibizumab, which, like its 2006 predecessor pegaptanib sodium (Macugen), inhibits vascular endothelial growth factor.

Another monoclonal antibody, bevacizumab, currently licensed for treatment of certain types of cancer but not for AMD, is reported to provide visual outcomes similar to ranibizumab, but costs less.

### Other therapeutic areas

Among the remaining medicines launched during 2007 there was a handful of firsts. Idursulfase (Shire Pharmaceuticals) is the first enzyme replacement treatment for people suffering from Hunter syndrome. Marketed as Elaprase, it is a purified form of iduronate-2-sulfatase lysosomal enzyme, and is produced by recombinant DNA technology in a human cell line.

Patients with another rare condition — paroxysmal nocturnal haemoglobinuria (PNH) — can now be offered treatment following the launch of Alexion's monoclonal antibody drug eculizumab. Until now PNH patients have received only supportive care.

Eculizumab prevents the development of a protein that mediates corpuscle destruction in PNH. Designated as an orphan drug, eculizumab (Soliris) is the first drug to be assessed under the European Medicines Agency's accelerated assessment procedure.

Mircera (methoxy polyethylene glycol-epoetin beta) was launched in September by Roche. The injection is licensed for the treatment of anaemia associated with chronic kidney disease. The drug is the first in a new class of erythropoiesis stimulating agents known as continuous erythropoietin

receptor activators. Compared with erythropoietin, Mircera has a slower association to and faster dissociation from the receptor, an increased activity *in vivo*, as well as an increased half-life. Other new medicines launched in 2007 are listed in Panel 1 (p28).

Safety concerns and new guidance  
In addition to the safety concerns outlined above, UK and European regulators issued advice about allergic reactions to strontium ranelate (*PJ*, 24 November 2007, p579) and the risks associated with erythropoietins and overcorrection of haemoglobin concentrations in patients with chronic renal disease (*PJ*, 8 December 2007, p637). They also recommended stronger warnings about the risk of depression in overweight patients treated with rimonabant (Acomplia) and in smokers trying to quit with the help of varenicline (Champix) (*PJ*, 22/29 December 2007, p706).

### POM-to-P switches

2007 did not bring any major POM-to-P switches. However, a number of proposals were made and pharmacists can expect to see the following medicines on pharmacy shelves before 2008 is out:

- Tranexamic acid for heavy menstrual bleeding
- Naproxen for dysmenorrhoea
- Azithromycin for asymptomatic chlamydia infection
- Diclofenac for short-term relief of headache, dental pain, period pain, rheumatic and muscular pain, backache and the symptoms of colds and influenza ■

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### Panel 1:

#### Other new medicines launched in 2007

-An allergen extract (Grazax) developed by ALK-Abelló. The sublingual tablet is licensed for grass pollen-induced rhinitis and conjunctivitis.

-A chewable tablet containing lanthanum carbonate (Fosrenol) launched by Shire. Lanthanum is a non-calcium phosphate binding agent used to control hyperphosphataemia in chronic renal failure patients on dialysis.

-Paliperidone (Invega), a once daily, prolonged-release atypical antipsychotic from Janssen-Cilag. It is an active metabolite of risperidone and is not extensively metabolised in the liver.

-Mecasermin (Increlex; Ipsen), a recombinant human insulin-like growth factor-1 for the long-term treatment of growth failure in children and adolescents with severe primary insulin-like growth factor 1 deficiency.

-A novel anticonvulsant — rufinamide (Inovelon) — launched by Eisai. The drug is for patients with Lennox-Gastaut syndrome, a severe and difficult-to-treat form of epilepsy that begins in childhood.

-Colestevlam hydrochloride (Cholestagel; Genzyme). The drug, the first of its kind to be available in the UK in tablet form, impedes the reabsorption of bile acids in the intestine. It is used to reduce low density lipoprotein-cholesterol levels in patients with primary hypercholesterolaemia.

-An antifungal agent anidulafungin (Ecalta) launched by Pfizer. This echinocandin antimycotic is used for the treatment of invasive candidiasis in adults who are not neutropenic.