

Clinical developments in 2005

As a practising pharmacist, part of your responsibility will be to keep up to date with your knowledge. Harriet Adcock looks back at the medicines launched during 2005 and considers some of the more significant clinical developments of the past year

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Throughout 2005, discussions began and led to the welcome announcement that pharmacists would be able to prescribe from an unrestricted formulary, albeit with the exception of Controlled Drugs (*PJ*, 19 November 2005, p621). When independent prescribing becomes a reality it will allow pharmacists to develop their clinical skills in a way many might have thought impossible just a few years ago.

The new community pharmacy contract in England and Wales was another significant milestone of 2005. The contract was formally introduced on 1 April and pharmacists working under it had until October to get to grips with the essential services. In scale alone, these services, along with medicines use reviews offered as an advanced service, will have a huge impact on patient care. September saw the first specification details for enhanced services (*PJ*, 10 September 2005, p299), giving forward-looking pharmacists (with help from willing primary care organisations) the chance to progress further the clinical care of their patients.

With all these huge developments for pharmacy as a profession it was perhaps a blessing in disguise that 2005 was not filled with major new drug launches.

Despite the pharmaceutical industry continuing to catapult new products onto the world market and trumpeting their arrival as significant advances for patients, many of the products launched in 2005 are "me too" drugs and are not likely to have a significant impact on health.

Cardiovascular system

Patients with cardiovascular disease were not offered many new pharmacological treatment options in 2005, a trend that continued from the previous year.

Still on the horizon is ximelagatran (Exanta), a direct-thrombin inhibitor

poised to be the first oral anticoagulant since the development of warfarin more than 50 years ago. Its manufacturer, AstraZeneca, filed a licence application for the drug with European regulators in July 2002. It had some luck, gaining marketing approval in France in December 2003 and launching in Germany in June 2004. However, in September 2004, the US Food and Drug Administration requested more data to support the approval of the drug, a move which appears to have delayed its launch elsewhere in the world and in the UK.

Merck Sharp & Dohme and Schering-Plough collaborated to launch Inegy, a product containing ezetimibe and simvastatin. The combination of a selective inhibitor of dietary and biliary cholesterol absorption (ezetimibe) with an HMG-CoA inhibitor (simvastatin) is intended to offer patients an effective treatment for reducing low-density lipoprotein cholesterol in a product that reduces pill burden and aids compliance.

Respiratory system

In general, patients with respiratory disease did not see any major alterations to their drug therapy in 2005. Asthma guidelines remained essentially unchanged. However, two new medicines were launched that offer potential benefits for patients with asthma.

Ciclesonide (Alvesco) is a once-daily corticosteroid used for prophylaxis in asthma. It was launched by Altana Pharma in January 2005.

The new asthma therapy omalizumab (Xolair) was launched by Novartis in October. It is a humanised monoclonal antibody that selectively binds to human immunoglobulin E. The drug blocks the binding of free serum IgE to mast cells and basophils and so inhibits the release of various inflammatory mediators. Omalizumab is a subcutaneous treatment used as add-on therapy to improve asthma control. It should only be considered for patients with IgE-mediated asthma (ie, those with serum IgE levels of

between 30 and 700IU/ml before treatment is initiated).

Guidance on the use of omalizumab in asthma is due to be published by the National Institute for Health and Clinical Excellence (NICE) in February 2008.

Central nervous system

In 2005 new therapies emerged for Parkinson's disease, epilepsy, depression and nausea and vomiting.

Rasagiline (Azilect) is a new selective and irreversible monoamine oxidase-B inhibitor used for the treatment of idiopathic Parkinson's disease. It can be used as monotherapy in early-stage disease or as an adjunct to levodopa in patients with end-of-dose fluctuations. Unlike many drugs used in Parkinson's disease, Lundbeck's rasagiline does not require dose titration.

A new anti-epileptic agent zonisamide (Zonegran) was launched in June by Eisai. It is a benzisoxazole derivative with a sulphonamide group and is chemically unrelated to other anti-epileptic agents. Its mechanism of action is not fully understood, but it appears to act on voltage-sensitive sodium and calcium channels, disrupting synchronised neuronal firing. Zonisamide is licensed as adjunctive therapy in the treatment of adults with partial seizures, with or without secondary generalisation.

Duloxetine (Cymbalta), a joint development by Eli Lilly and Boehringer Ingelheim, is used for the treatment of major depressive episodes. The combined serotonin and noradrenaline reuptake inhibitor is also indicated for treatment of diabetic peripheral neuropathic pain. Its arrival on the UK market followed the launch of duloxetine as Yentreve in 2004, licensed for treatment of stress urinary incontinence. The dose for depression is 60mg *od*, compared with up to 40mg *bd* for incontinence.

Cancer patients suffering the effects of emetogenic chemotherapy now have the option of treatment with palonosetron (Aloxi), a 5HT₃ receptor antagonist launched by Cambridge Laboratories.

Palonosetron is indicated for the

prevention of acute nausea and vomiting associated with highly emetogenic cancer chemotherapy or with moderately emetogenic cancer chemotherapy.

On the horizon, other drug treatments that act on the central nervous system include rimonabant, an oral selective cannabinoid CB₁ receptor antagonist being developed by sanofi-aventis. It is the first of a new class of medicines and its likely indications include weight loss, smoking cessation and reducing cardiovascular risk factors.

Another cannabinoid marketed as Sativex from GW Pharmaceuticals, has been developed to relieve spasticity in patients with multiple sclerosis. It has not been licensed for use in the UK but it was recently made available for the condition under the terms of a special Home Office licence (*PJ*, 19 November 2005, p622).

Malignancy

Established cancer therapies, such as Letrozole (Femara) and capecitabine (Xeloda) continued to amass new indications in 2005. Letrozole was approved for use as initial adjuvant therapy in women with early hormone-responsive breast cancer and capecitabine acquired a licence extension as adjuvant therapy in colorectal cancer.

But perhaps the two most interesting additions to cancer therapies in 2005 were bevacizumab (Avastin) and erlotinib (Tarceva), both emerging from Roche.

Used for first-line treatment of patients with metastatic carcinoma of the colon or rectum, bevacizumab is a recombinant humanised monoclonal IgG1 antibody. It is the first of a new class of anti-neoplastic drugs that inhibit the formation of blood vessels by blocking the activity of vascular endothelial growth factor.

Bevacizumab is used in combination with 5-fluorouracil and folinic acid, or 5-fluorouracil, folinic acid and irinotecan.

Erlotinib, a tyrosine kinase inhibitor, was launched in September. It is used for the treatment of patients with locally advanced or metastatic non-small cell lung cancer. Erlotinib is reserved for

patients whose disease has failed to respond to at least one prior chemotherapy regimen.

NICE guidance on the use of bevacizumab for use in colorectal cancer is expected in November 2006. Guidance on erlotinib in lung cancer is set to follow in September 2007.

Nutrition and blood

Drugs used to treat hyperparathyroidism and the symptoms of thrombocythaemia were launched in 2005.

Cinacalcet (Mimpara from Amgen) is a new anti-parathyroid agent. It is used for treatment of hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy and for the treatment of hypercalcaemia in parathyroid carcinoma. Cinacalcet directly reduces parathyroid hormone levels by increasing the sensitivity of the calcium-sensing receptor to extracellular calcium. This, in turn, leads to a decrease in serum calcium concentrations.

Launched by Abbott, paricalcitol (Zemlar) is another agent used to combat hyperparathyroidism. It is an injectable synthetic vitamin D analogue used to prevent and treat secondary hyperparathyroidism associated with chronic renal failure.

Patients with essential thrombocythaemia who have an elevated platelet count and who do not respond adequately to their current therapy now have the option of treatment with anagrelide hydrochloride (Xagrid), which was launched at the beginning of 2005 by Shire Pharmaceuticals.

Musculoskeletal system

Fall out from the withdrawal of rofecoxib (Vioxx) in 2004 continued throughout 2005. Regulators reviewed safety data for the other selective cyclooxygenase-2 inhibitors (*PJ*, 2 July 2005, p5) as well as the non-selective inhibitors (*PJ*, 22 October 2005, p503).

Sales of valdecoxib (Bextra) were suspended in April 2005 following

concerns about serious skin reactions (*PJ*, 16 April 2005, p441). Suspension was followed by complete withdrawal of the drug after European regulators failed to be convinced by its risk-benefit profile. Warnings for other COX-2 inhibitors were strengthened and patients' therapies reviewed.

Despite all this, a new COX-2 inhibitor, lumiracoxib (Prexige), was launched by Novartis in December 2005. The drug is licensed for symptomatic relief of osteoarthritis and short-term relief of moderate to severe acute pain associated with primary dysmenorrhoea, dental surgery and orthopaedic surgery. Its product safety information came with the expected warnings about use in patients with cardiac risk factors.

Another non-steroidal anti-inflammatory drug launched in 2005 was dexibuprofen (Seractil). A prescription-only medicine, it is licensed for relief of mild to moderate pain and inflammation in osteoarthritis as well as for relief of other musculoskeletal pain, dental pain and pain associated with menstruation.

Other new medicines

Other new medicines launched in 2005 include the protease inhibitor tipranavir (Aptivus) used to treat HIV-1 infected patients. Developed by Boehringer Ingelheim, it is used in combination with low-dose ritonavir and is reserved for patients with virus resistant to multiple protease inhibitors and who have tried several treatments.

The human insulin analogue insulin glulisine (Apidra) was launched by Aventis Pharma. This rapid acting insulin is for people with type 1 or type 2 diabetes who require a basal-bolus insulin regimen.

POM-to-P switches

Alongside new product launches, the reclassification of medicines continued throughout 2005. The Medicines and Healthcare products Regulatory Agency reported in its business plan for 2005–06 that several new therapeutic classes of medicines would become available during the year. The first of these was chloramphenicol eye drops, approved as a pharmacy

medicine in June (*PJ*, 11 June 2005, p697).

In July a consultation on making trimethoprim a pharmacy medicine for the treatment of acute bacterial cystitis was announced (*PJ*, 9 July 2005, p35), and in the following month, discussions began on the reclassification of sumatriptan and zolmitriptan (*PJ*, 20 August 2005, p215). These triptans are set to become pharmacy medicines for acute relief of migraine attacks.

New guidance

NICE issued several new technology appraisals and clinical guidelines in 2005. A new system for rapid appraisals of new medicines was also announced (*PJ*, 12 November 2005, p600).

Recommendations made by NICE in the first draft of its updated guidance on medicines used to treat Alzheimer's disease evoked strong reactions from manufacturers and patient groups, which criticised the suggestion that the drugs should not be made available for use within the NHS in England and Wales. In response, NICE called on the pharmaceutical industry to supply more data on donepezil, rivastigmine, galantamine and memantine. Final guidance is expected in April 2005.

Recommendations for NHS Scotland were issued by the Scottish Medicines Consortium (SMC) and the Scottish Intercollegiate Guidelines Network (SIGN). For example, SIGN issued guidance on the management of breast cancer and epilepsy in 2005.

In addition to advice from NICE, the SMC and SIGN, the Department of Health published standards for treatment for chronic conditions within two national service frameworks. Part two of the NSF for Renal Services set out standards for the care of patients with chronic kidney disease (*PJ*, 12 February 2005, p166). The NSF for Long-term Conditions followed, focusing on neurological conditions (*PJ*, 19 March 2005, p328).

Drug availability and safety

Drug availability and safety issues frequently made the headlines in

2005. Shortages of diamorphine tested the resourcefulness of the NHS, with patients being transferred to equivalent doses of morphine (*PJ*, 12 February 2005, p169).

Another prescription pain killer — co-proxamol — came under the spotlight when the MHRA decided to withdraw it from the UK market (*PJ*, 5 February 2005, p135). Although many NHS organisations were already restricting the drug's availability, the MHRA was criticised for the way in which it announced the withdrawal, having failed to communicate with health professionals before the news was reported in the national press.

Another supply issue that came to a head in 2005 was related to the threat of an influenza pandemic and this was complicated by worries over transmission of avian influenza. The antiretroviral drug oseltamivir (Tamiflu) was heralded as the best option available to treat those affected in a flu pandemic and has been stockpiled by governments around the world. Seasonal flu vaccines were also in demand and supplies ran short when more patients than expected came forward to be vaccinated (*PJ*, 26 November 2005, p654).

The availability of trastuzumab (Herceptin) for early breast cancer was another hot topic in 2005. Several patients threatened to take their primary care organisations to court and were granted their request to be treated with the drug, despite it not having a licence for this stage of the disease.

Conclusion

So 2005 does not stand out as a year in which many innovative new medicines became available. However, changes introduced in the way pharmacy is practised look set to make a real difference to the clinical care of patients. Let us hope that new, safe and more effective medicines follow in 2006. 🙏