

High Court rejects claims NICE acted irrationally and unfairly

Claims of unfairness and irrationality in the development of national guidance on Alzheimer's disease have been rejected by the High Court.

The pharmaceutical company Eisai, supported by the Alzheimer's Society and Shire Pharmaceuticals, challenged a National Institute for Health and Clinical Excellence appeal panel decision and subsequent guidance issued by NICE in November 2006 (*PJ*, 13 January, p42). The guidance recommended that patients with moderate Alzheimer's disease, but not those with mild disease, should receive donepezil, galantamine or rivastigmine.

Of the six grounds for the claims (see Panel), five relating to procedural unfairness and irrationality were rejected by the court. Eisai, which holds the UK marketing authorisation for donepezil, said it would appeal against the High Court's decision on these claims. "The guidance NICE has issued is morally reprehensible," the company said. "NICE has got it wrong and it has got it wrong under a shroud of secrecy."

However, the court accepted the claim that NICE's rigid adherence to mini mental state examination scores as an exclusive test of defining disease severity was discriminatory against those with problems with English and learning disabilities. Mrs Justice Dobbs said that NICE had failed to give proper consideration to its duties to promote equal opportunities and eliminate discrimination. The court has asked NICE to amend the guidance to comply with its duties under anti-discrimination legislation.

Commenting on the ruling, NICE chief executive Andrew Dillon said: "Our guidance stands and the drugs continue to be recommended only for people with moderate Alzheimer's disease, but the court has asked us to clarify our guidance when it is used for certain groups." He said it had always been NICE's intention for people with learning disabilities or whose first language is not English to have equal access to treatment.



Eisai's legal challenge is the first time NICE guidance has been tested in court

This is the first time a NICE recommendation has faced a legal challenge. At a media briefing following the High Court's judgment, Sir Michael Rawlins, chairman of NICE, said it was "gratifying" to know that NICE's procedures met the standards of the High Court. He added: "When NICE was first set up my friends told me that we would be legally challenged within the first 12 months and we've gone eight and a half years before a judicial review. But it may well happen again. Patient organisations, professional organisations, pharmaceutical companies, devices manufacturers are all entitled to challenge us; they have a legal right to do so."

□ **National dementia strategy** Plans for the first national dementia strategy have been unveiled by the Department of Health. Ministers will publish the strategy next summer following a 12-month work programme that aims to increase awareness of dementia in society, ensure early and accurate diagnosis and improve services so that people with dementia receive high quality treatment and support.

Eisai's claims and the High Court decisions

Eisai said that NICE had been procedurally unfair when it refused to disclose a fully executable version of the economic model used in NICE's assessment. Mrs Justice Dobbs said NICE had not acted unfairly. Eisai had, she said, "more than sufficient information to make intelligent response and to give proper advice" and had made comments to NICE that "could not have been made without a good understanding of how the model worked".

Eisai claimed that NICE's decision was irrational on four grounds: it assumed that patients would derive no additional benefit after six months of treatment with an acetylcholine inhibitor; it relied on the findings of one study (the AD2000 study); it failed to capture benefits to carers; and it failed to capture reductions in costs of care. In terms of NICE's assumption on benefits after six months, Mrs Justice Dobbs said that NICE had argued cogently and logically in reaching its conclusions and that the conclusions were not perverse. The court ruled that there was not unqualified acceptance of the AD2000 study — "its drawbacks were acknowledged; and in the overall scheme, the study was given reduced weight," it said. And NICE's approach to the issue of carer benefits was, the court said, "within the range of acceptable approaches" and its decision on this was not irrational.

Eisai claimed that NICE had acted unreasonably, and created a discriminatory effect in its guidance, by its rigid adherence to mini mental state examination scores as an exclusive test of defining severity of Alzheimer's disease. It was on this ground only that the High Court decided that the Eisai claim succeeded.

10,000 protest online over fee increase

More than 10,000 people have supported an online petition against the proposed 50 per cent increase in Royal Pharmaceutical Society retention fees.

Launched on 31 July, the petition gained the support of 10,092 people, including pharmacists, pharmacy technicians and some members of the public before it closed on 14 August. Some so-called signatories were anonymous and it was possible for false entries to be made.

However, having said last week that it would not take the petition into account in its consultation on the planned increase, the Society has now agreed to include it. Ann Lewis, the Society's Secretary and Registrar said this week: "The Society has asked that, to ensure that the petition is taken into account by the Council, it should be submitted to the fees consultation e-mail address, or to the Secretary and Registrar's Office by 3 October. This will ensure that the petition is analysed as part of the consultation process and that the analysis will reflect the complete picture."

Suffolk pharmacist Mark Cheeseman, who instigated the petition, said that the electronic petition could be printed out and submitted to the Society. Mr Cheeseman said that he hoped the petition and the consultation would be used to highlight pharmacists' concerns about the planned increase. Commenting on the level of support elicited by the petition, he said: "I was staggered by the number. I thought I'd be lucky to get 100 signatures."

□ **Guild view** The Guild of Healthcare Pharmacists is to submit a response to the Society's fees consultation exercise on behalf of its 4,000 members. This week the guild said that it expected any organisation facing financial difficulties to review and make significant financial and organisational changes to make itself viable. This review should include the cost of running the Society's Council. The guild added that many NHS organisations had gone through such exercises in 2006–07, but that there was little evidence of such a review within the Society.

Leadership inquiry chairman

Nigel Clarke has been appointed independent chairman of the Royal Pharmaceutical Society's inquiry on a future professional leadership body (*PJ*, 16 June, p693). Mr Clarke is currently chairman of the General Osteopathic Council. The inquiry will start from late August and will include two stages of consultation, review of relevant documents, roadshows and formal evidence sessions. Mr Clarke will report to the Council with a proposed way forward before the annual general meeting in May 2008.

Society p189

Services for long-term conditions are improving, but need to be more joined up, says Audit Scotland

Services for people with long-term conditions in Scotland are improving but more needs to be done to create a joined-up system of care. This is the conclusion of a report published this week by Audit Scotland.

Barbara Hurst, director of public reporting, Audit Scotland, explained: "Care for people with chronic illnesses is improving but there is more that the Scottish Executive, the NHS and [local] councils can do. There have been many improvements in various clinical areas in different parts of Scotland. However these are often local projects, driven by local need or enthusiasm rather than by a national strategy."

Audit Scotland found general enthusiasm among NHS staff for shifting services from hospitals into the community, as set out in "Delivering for health" (*PJ*, 5 November 2005, p564). But it says that NHS boards and community health partnerships are finding it difficult to plan services for long-term conditions for two reasons. First, there is a lack of evidence on the activity, cost and effectiveness of services. And second, there is a need for a national strategic framework for long-term conditions, something that "Delivering



Asthma services are better developed than those for some other conditions

for health" had stated the Scottish Executive Health Department would develop by 2006.

On pharmacy, Audit Scotland highlights the new chronic medication service as something that will extend community pharmacists' role to meet the needs of people with long-term conditions. However, a lack of information is identified as a problem. "The lack of progress in providing access to comprehen-

sive patient information is seen as a major barrier to developing joined-up services for long-term conditions," the report says.

Further good news for community pharmacists comes in a survey, conducted as part of the report, on inter-professional working. GPs rated their working relationships with community pharmacists highly: 55 per cent of GPs reported "very good" relationships with pharmacists and another 40 per cent "quite good". This compared with significantly lower figures for social work, CHPs and local charities. Secondary care scored a similar overall "good" figure to community pharmacy but a lower proportion in the "very good" category.

Audit Scotland's other findings include the fact that people with more than one long-term condition are not receiving joined-up care, and that services for people with asthma and diabetes are better developed than services for other long-term conditions because of the focus of the new general medical services contract.

The report — "Managing long-term conditions" — was due to be published by Audit Scotland on 16 August.

New pre-visit questionnaires for contractors

Revision of the Community Pharmacy Assurance Framework for England has led to the introduction of a questionnaire that should be completed by pharmacy contractors before they are visited by primary care trust inspection teams.

NHS Primary Care Contracting says that experience has shown that pre-visit questionnaires allow inspection teams to concentrate on priority areas and reduce the time spent in pharmacies. It adds that aligning the questionnaire with inspection visits and the contract workbook produced by the Pharmaceutical Services Negotiating Committee minimises duplication and helps to ensure that all the requirements of the pharmacy contract are met.

The revised framework now maps the Department of Health's standards for better health against each of the requirements of the

pharmacy contract. In addition, the clinical effectiveness programme elements of clinical governance — an essential service of the pharmacy contract — have been expanded. In this regard, NHS PCC wants to hear about approaches taken to demonstrating clinical effectiveness by both contractors and PCTs.

The revised framework also includes a template that can be used by PCTs to monitor pharmacies that open under the control-of-entry test exemptions for 100-hour and internet pharmacies. NHS PCC says that internet pharmacies may pose PCTs with a unique monitoring challenge. It adds that it would like to hear from PCTs that have developed models for good practice in this area.

Even after this revision, the monitoring framework is not set in stone and comments and suggestions that can be used to refine further it year-on-year have been invited.

English contractors must send pricing authority original CD prescriptions

Pharmacy contractors in England will be required to send original private prescription forms for Controlled Drugs (form FP10PCD), and not photocopies, to the NHS pricing office from 1 September. The same applies to the equivalent prescriptions originating from Scotland (PPCD[1]) and Wales (WP10PCD), but dispensed by pharmacies in England. Pharmaceutical Services Negotiating Committee information pharmacist Kam Amrith said the change in legal requirements would reduce contractors' workload and lead to cost savings. But the PSNC remains concerned that private CD prescriptions have to be sent to pricing offices separately from the monthly returns of NHS forms and accompanied by a form that is only available on the internet. "We believe that this continues to place an unnecessary administrative burden on pharmacy contractors and advocate integration of the submission process for NHS and private CD prescriptions," she said.

Contractors in Wales will continue to keep the originals of private prescriptions for CDs and send photocopies to Health Solutions Wales. Contractors in Scotland already have to send original of PPCD(1) forms to their NHS pricing office.

Retention fee 2008

PJ Online has a page on the proposed retention fees for 2008. It has a table of the revised fee structure with links to the Society's consultation and supporting documents. There are also news items, leading articles, letters plus Society articles and Official Notices.

www.pjonline.com/retentionfee

Access to *PJ Online* is free to all

Awards and grants

The Awards page has been revised, so that only current nominations being sought are listed.

www.pjonline.com/awards

Linking to *PJ Online*

The links section has a page to assist people wanting to link to *PJ Online*. It lists URL shortcuts to popular sections.

www.pjonline.com/links

NHS boards to outline pharmaceutical care services

NHS boards in Scotland are to produce draft pharmaceutical care service (PCS) plans this autumn that will set out how pharmacy services should be delivered. Details of the plans are explained in an NHS circular published this week.

The aim of PCS plans is for NHS boards to define what pharmacy services are currently provided in their area, to identify future service needs and any gaps in service provision. They will also include NHS boards' recommendations on how to meet these gaps.

PCS planning was first described in the Smoking, Health and Social Care (Scotland) Act 2005 (*PJ*, 1/8 January 2005, p5). Legislation is still to be introduced, but this week's circular states that it will put a new requirement on NHS boards to secure or provide the pharmaceutical care services necessary to meet their populations' needs. NHS boards have to prepare for the introduction of formal PCS planning by producing a draft PCS plan. This work will contribute to the development of the final

PCS planning tool that will be used across Scotland.

Bill Scott, chief pharmaceutical officer for the Scottish Executive, said: "This PCS planning tool is a significant step to ensuring that pharmacy is considered as a core element of the planning process within NHS boards for the benefit of patient care."

"The aim is to ensure that there is a standard and consistent approach to the planning of pharmaceutical services across Scotland."

Alex MacKinnon, head of corporate affairs, Community Pharmacy Scotland, commented: "We are supportive of the principle of NHS boards being able to plan pharmaceutical care services and contracts being based on need."

He added that CPS would be involved in further work with the Scottish Executive to finalise the PCS planning tool.

The next step is for NHS boards to develop a first draft PCS plan and submit it to the Scottish Executive by the end of November. Following a review of these sub-

missions, NHS boards will have to produce a final draft PCS plan by March next year. The circular recommends that boards should ensure local pharmacy groups are involved in the process.

Originally it had been intended for NHS boards to hold lists of the registered pharmacists who could provide pharmaceutical care services in that area. "However, this policy is currently subject to review in light of action being taken as a consequence of the review of non-medical regulation," the circular states.

Pharmaceutical care

Pharmaceutical care services are defined as "essential" services — the four core services in the new community pharmacy contract which must be provided by all pharmacies who have an NHS contract — and "additional" services which are locally negotiated but expected to be based on nationally agreed specifications.

Scottish Medicines Consortium accepts five drugs and rejects four in latest appraisals

Dopamine receptor agonist rotigotine (Neupro) is among five drugs accepted for use within NHS Scotland this week. The Scottish Medicines Consortium rejected a further four drugs.

Rotigotine transdermal patch is accepted by the SMC for the treatment of the signs and symptoms of advanced Parkinson's disease in combination with levodopa. Its use is restricted to patients for whom this route of delivery would facilitate treatment, says the SMC.

Clopidogrel tablets (Plavix) are accepted for patients with acute myocardial infarction, in combination with aspirin. Treatment is restricted to four weeks and has been shown to improve the condition of the infarct-related artery as well as clinical endpoints, says the SMC. Nebivolol tablets (Nebilet) have also been approved for elderly patients with stable mild and moderate chronic heart failure.

The SMC has accepted insulin detemir (Levemir) injected via the InnoLet device for the treatment of diabetes mellitus in patients for whom insulin detemir is an appropriate choice of insulin and who have poor visual acuity and dexterity problems. Vinorelbine capsules (Navelbine) have been accepted for the treatment of advanced breast cancer following an abbreviated submission to the SMC.

Four drugs have been rejected. The manufacturers did not present sufficiently robust economic analyses, the SMC says. These are:



Rotigotine transdermal patch has been accepted for use within NHS Scotland

bortezomib (Velcade) for the treatment of progressive multiple myeloma in patients who have received at least one prior therapy and have already undergone or are unsuitable for bone marrow transplantation; idursulfase (Elaprase) for the long-term treatment of patients with Hunter syndrome; liposomal cytarabine suspension (DepoCyte) for the treatment of lymphomatous meningitis; and pregabalin capsules (Lyrica) for the treatment of central neuropathic pain in adults.

Incentive payments to be made for ETP in Scotland

Incentive payments are being offered in Scotland to encourage pharmacists to process prescriptions electronically. The aim of the payments is to encourage the introduction of the electronic transmission of prescriptions (ETP).

Details of the new payments were announced in an NHS circular published this week. It says that the payments will be based on the number of prescription forms (not items) processed electronically.

The first 500 ETP forms a pharmacy processes electronically in any one month will attract a supplementary fee of 5p per form. Any additional ETP forms will receive 2p per form, with no upper limit.

The circular states that the payments will be made until the chronic medication service has been introduced. At that time, it will become a contract requirement for all ETP forms to be processed electronically. Payments will be on offer from September when the roll-out of ETP in community pharmacies is scheduled to begin.

Community Pharmacy Scotland says the payments are good news but it flagged up a concern that contractors will not benefit if their pharmacy computer supplier is slow at providing ETP software.

Alex MacKinnon, head of corporate affairs at CPS, said: "We welcome the payments and encourage contractors to engage in the new ETP system. Our only concern is the ability of some patient medication record system suppliers to achieve the ETP deadlines."

MHRA asks people what they think of its plans

Consultation has started on the key challenges and priorities that the Medicines and Healthcare products Regulatory Agency believes it will face over the next five years.

The consultation paper says that the agency's overall objective is to safeguard public health by deciding whether the benefits of any medicine or medical device outweigh its risks and continue to do so throughout the life of the product. This will require further strengthening of the agency's reporting systems and other sources of information.

Second on the MHRA list of priorities is information and communication; information, because most regulatory action after initial licensing leads to changes to the

information, advice or warnings associated with a product, rather than to its withdrawal, and communication, because this information needs to be communicated effectively both to health professionals and to the public.

The agency also believes that it needs to ensure that the regulatory system does not make research and development unduly slow or expensive and that it should enable, rather than hamper, the development of new treatments.

At an international level, the MHRA is keen to maintain its position as one of the leading regulators in Europe and worldwide. It notes that some national regulators in the EU are specialising in particular types of

work, but believes that it should retain expertise across all types of medicine and enhance its capacity in new areas, such as tissue engineering.

The consultation runs until 2 November and will include meetings with organisations that represent patients, the public and health care professionals, because the MHRA believes that it needs to foster more effective links with these groups. The outcome of the consultation process is expected to be published as a strategy document before April next year.

The consultation paper is available from the MHRA website (www.mhra.gov.uk) and via *PJ Online* (www.pjonline.com/links/pj).

CPW board member provides lifestyle advice for Eisteddfod festival attendees

Richard Evans, a community pharmacist and Community Pharmacy Wales board member, provided healthy lifestyle advice to over 60 people at Eisteddfod, the annual Welsh cultural festival, held in Mold, north-east Wales, last week. Mr Evans was on the Welsh Assembly Government stand promoting pharmacists' role in advising on healthy living. A district nurse, Llio Glyn Griffiths from Dolgellau, measured visitors' blood pressure and height before passing them on to Mr Evans to be weighed and receive lifestyle advice. Any smokers en-



Richard Evans, customer Peter Evans from Llandysul, and Llio Glyn Griffiths (L to R)

countered, were referred to the All Wales Smoking Cessation Service, also on the WAG stand.

Regulatory alliance tells minister how European law will put patients at risk

Risks to patients introduced by a new European law allowing health professionals to take short-term work in other countries without being subject to the full rigour of national regulation have been reported to the Department of Health by the Alliance of UK Health Regulators on Europe (*PJ*, 23 June, p730).

A letter sent by the alliance, which includes the Royal Pharmaceutical Society, earlier this month, says that public protection issues discussed with the current minister's predecessor in May have not been addressed.

In particular, the alliance is concerned that proposed UK legislation based on the European law will allow foreign health professionals to work in the UK without the

same level of indemnity insurance that is required of UK registered staff.

Another concern is that no checks equivalent to Criminal Records Bureau enquiries can be made on the possible criminal record of European professionals seeking temporary registration.

A third concern relates to continuing professional development. The new law will not make temporary European staff subject to UK CPD requirements. Instead, it will rely on the requirements of the country of original registration of workers. This is despite the fact that some health and social care professionals, such as osteopaths and chiropractors, are not regulated at all in some European countries.

New service frameworks

Competencies and training frameworks for provision of a smoking cessation service (intermediate level), supervised consumption of prescribed medicines for substance misusers, and needle and syringe exchange have been produced by the harmonisation of accreditation group (HAG).

Set up by the North West Pharmacy Workforce Development Group (*PJ*, 3 February, p122), HAG develops frameworks that allow recognition of pharmacists' enhanced services training by neighbouring primary care trusts. The frameworks are available on the NHS Primary Care Contracting website at www.primarycarecontracting.nhs.uk.

News in brief

MeReC Bulletin on arthritis

The August *MeReC Bulletin* covers issues in rheumatoid arthritis, including the use of disease modifying drugs, biologic therapies and corticosteroid-induced osteoporosis. The August issue of *MeReC Extra* looks at the cardiovascular risks of rosiglitazone and the use of patient decision aids (www.npc.co.uk).

Pandemic influenza

An updated summary of the risk of an influenza pandemic originating from an H5N1 virus and the use of antiviral drugs, antibiotics, pre-pandemic and pandemic vaccines, has been published by the Department of Health (www.dh.gov.uk).

Waste medicines

A new National Pharmacy Association information leaflet on waste disposal explains how to comply with the law on accepting, storing, transporting and disposing of waste medicines.

First treatment launched this week for rare blood disease

Treatment for patients with a rare blood disorder — paroxysmal nocturnal haemoglobinuria (PNH) — is now available following the launch of the monoclonal antibody drug eculizumab. Until now PNH patients have received only supportive care.

Marketed by Alexion as Soliris and designated as an orphan drug, eculizumab is the first drug to be assessed under the European Medicines Agency's accelerated assessment procedure. PNH is an acquired disorder that disrupts the formation of blood corpuscles and platelets and affects about 850 patients across England and Wales.

Patients with PNH have a gene that leaves some of their red blood corpuscles abnormally susceptible to break down. Previously, patients have mainly been managed supportively, with folic acid and iron supplements, transfusions, anticoagulants and heparin. Eculizumab prevents the development of a protein that mediates corpuscle destruction in PNH.

Trials have shown that the drug reduces the need for transfusion, cuts thrombosis and increases quality of life. The manufacturers believe that 35–50 per cent of patients could benefit from treatment with eculizumab.

Notice-board p177

New guidelines on point-of-care testing

Updated recommendations on point-of-care testing have been published by the British Committee for Standards in Haematology.

The guidelines are designed to be used in a variety of settings, and they recognise that “there is clearly scope for pharmacists to both develop and deliver point-of-care testing services”. At the same time, the BCSH says that all those undertaking point-of-care testing, including community pharmacies, should seek the advice and involvement of an accredited clinical laboratory, so that optimum quality and cost effectiveness can be achieved.

The guidelines, which replace the committee's 1995 recommendations, also recommend that equipment used for point-of-care testing should have received successful independent evaluations from official bodies such as the NHS Purchasing and Supply Agency, generate results that can be compared with



Guidelines recognise scope for pharmacy testing services

those from the local laboratory, and be properly maintained and calibrated.

In addition, records should be kept of patient identity, results, date and time of testing, reagent lot and operator identity. The BCSH also recommends that all NHS trusts establish point-of-care testing committees. These committees should take responsibility for all point-of-care testing and ensure that it is appropriate and can be accredited, it says.

Advertisement

Interferon beneficial for patients with suspected MS

Patients given interferon after a neurological episode suggestive of multiple sclerosis (MS) are less likely to develop clinically definite MS than those given placebo, a three-year follow-up study has shown (*Lancet* 2007;370:389).

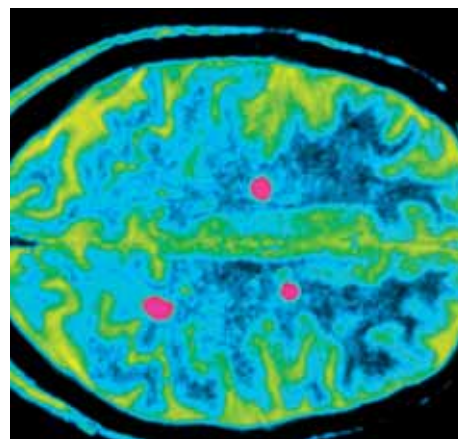
Researchers initially randomised patients with a first event suggestive of MS and at least two "clinically silent lesions" to receive either interferon beta-1b or placebo every other day for two years, after which patients were offered open-label interferon treatment. Three years after the initial randomisation, patients given early interferon were compared with those who started treatment after two years or after MS diagnosis.

The researchers found that 34 per cent of patients in the early treatment group developed clinically definite MS compared with 48 per cent in the delayed group (absolute risk reduction 14 per cent; $P=0.0011$). Patients given interferon early were also at a reduced risk of confirmed "expanded disability status

scale" (EDSS) progression than those in the delayed treatment group (absolute risk reduction 8 per cent; $P=0.022$). The researchers calculated that 12 patients would need to be treated early to avoid a single confirmed EDSS progression.

Nevertheless, in an accompanying editorial (ibid, p363), Sean Pittock, of the Mayo Clinic College of Medicine, Rochester, Minnesota, says that controversy still exists about who and when to treat. He highlights a lack of significant benefit of early treatment over delaying it for patients with limited clinical signs or symptoms (over half of participants) or limited disease dissemination by radiographic measurement (over a quarter of subjects).

Dr Pittock says: "[The authors] present the first evidence that interferon beta-1b treatment has a beneficial effect on accumulation of confirmed disability in patients with a first event suggestive of multiple sclerosis. The results should, however, be interpreted with care because the magnitude of benefit, al-



Scott Camazine/Science Photo Library

MS less likely to develop at three years if patients are treated early with interferon

though statistically significant, is clinically small." He suggests that the results should not be misconstrued as evidence for a treat-all approach.

News in brief

Leukaemia guidelines published

European guidelines on antimicrobial therapy in patients with acute leukaemia have been published as a supplement to the *European Journal of Cancer* (2007;5:1–60). The guidelines cover prophylaxis and treatment of bacterial and fungal infections in patients with acute leukaemia and recipients of haematological stem cell transplantation.

Veralipride withdrawal

The European Medicines Agency (EMA) has recommended the withdrawal of medicines containing veralipride following a safety review that indicates its side effects outweigh its limited efficacy. The drug, a treatment for hot flushes associated with the menopause, is available in Belgium, France, Italy, Luxembourg and Portugal. The EMA says that treatment should not be stopped abruptly but should be reduced gradually.

Allergy service scoping survey

AAH Pharmaceuticals is surveying customers and pharmacists about a possible national allergy testing service. At least 400 customers who buy over-the-counter allergy products as well as 20 high street pharmacies will be polled to gauge the level of interest in the service and how much customers would be willing to pay for it.

Lumiracoxib withdrawn in Australia due to safety concerns

Lumiracoxib (Prexige), a COX-2 selective inhibitor used for the treatment of osteoarthritis, has been withdrawn in Australia due to liver-related side effects. Lumiracoxib is licensed in the UK and a European level review of the evidence in relation to liver reactions is currently under way. The outcome of the review is expected in September.

The Australian regulatory authority, the Therapeutic Goods Administration, has deregistered the drug following eight reports of serious liver adverse reactions, two of which were fatal and two of which required liver transplants. All reports have been received since March. Some patients' conditions have not improved since stopping lumiracoxib.

The Medicines and Healthcare products Regulatory Agency has highlighted that the majority of cases of serious liver reactions with lumiracoxib have been associated with higher doses than those licensed in the UK and EU.

"We are not aware of any fatal cases of liver toxicity in the EU," it added. The MHRA advises that if patients feel unwell or are concerned they should speak to their doctor or pharmacist.

A statement issued by Novartis, manufacturer of Prexige, said: "Novartis is collaborating with TGA; however, we continue to believe that the way in which lumiracoxib is used in the UK has a positive benefit/risk profile in the treatment of appropriate patients, especially those at risk of serious gastrointestinal side effects."

□ **Viracept** Following the recall of Viracept (nelfinavir) from the EU market in June (*PJ*, 16 June, p694) because of concerns about contamination with a genotoxic substance, the European Commission has suspended the drug's marketing authorisation. The suspension can only be lifted after assessment of new data by the European Medicines Agency.

Thiamine deficiency in diabetics may increase complications

A deficiency in plasma thiamine in patients with diabetes may increase their risk of developing microvascular complications, suggest the authors of a small case-control study published online in *Diabetologia* (4 August, www.springerlink.com).

Researchers from the University of Warwick, Coventry, assessed the thiamine status of 26 patients with type 1 diabetes and 48 patients with type 2 diabetes through analysis of plasma, erythrocytes and urine. They compared the results with those from 20 healthy volunteers.

The researchers found that plasma thiamine concentration was decreased by 76 per cent in

type 1 diabetic patients and 75 per cent in type 2 diabetic patients compared with the controls ($P<0.001$ for both comparisons). This was likely due to an increased renal clearance of 24-fold in type 1 and 16-fold in type 2 diabetic patients, say the researchers. They suggest that deficiency in thiamine may increase the fragility of vascular cells to adverse effects of hyperglycaemia and thereby increase the risk of developing microvascular complications.

"Correction of the low plasma thiamine concentration with thiamine supplements may decrease the risk of microvascular complications in diabetes," they conclude. They suggest that further research in this area is warranted.

Aliskiren and valsartan combination reduces BP

Aliskiren — developed by Novartis — has been shown to reduce blood pressure when used in combination with valsartan better than either agent used alone, according to a *Lancet* study (2007;370:221).

Researchers randomised 1,797 patients with hypertension to receive, once a day, aliskiren 150mg, valsartan 160mg, a combination of the two drugs, or placebo for four weeks, followed by a forced doubling to maximum doses for a further four weeks.

At the end of eight weeks, the combination therapy lowered patients' mean sitting diastolic blood pressure more than the individual therapies (reduction from baseline, aliskiren/valsartan 12.2mmHg, aliskiren 9.0mmHg, valsartan 9.7mmHg; $P<0.0001$ for both) and more than placebo (4.1mmHg; $P<0.0001$).

Aliskiren, a first-in-class orally active renin inhibitor, exerts its effect at the renin system's

point of activation, directly inhibiting plasma renin activity. In an accompanying editorial (ibid p195), Willem Birkenäger, of Erasmus University, Rotterdam, the Netherlands, and Jan Staessen, of the University of Leuven, Belgium, point out that dual inhibition of the renin system, using renin inhibitors combined with angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (such as valsartan), inhibits plasma renin activity, even in the presence of the reactive rise in renin that occurs with chronic inhibition.

However, they say: "No new class of anti-hypertensive agents should make it to routine use without hard outcome data. That necessity applies even more to dual inhibition of the renin system, which exposes patients to hyperkalaemia and renal insufficiency."

The EU's Committee for Medicinal Products for Human Use has given a "posi-



David Kneafsey/istockphoto.com

Sitting diastolic blood pressure lowered

tive opinion" to grant a marketing authorisation for aliskiren (Rasilez) for treatment of essential hypertension. This is subject to European Commission approval.

Plerixafor improves stem cell mobilisation

Plerixafor, a novel CXCR4 chemokine antagonist designed to mobilise stem cells for collection, has achieved positive outcomes in two phase III studies of non-Hodgkin's lymphoma and multiple myeloma patients.

Early data, released by Genzyme, the drug's developer, show that 59 per cent of patients with non-Hodgkin's lymphoma treated with both plerixafor and granulocyte-colony stimulating factor (G-CSF) achieved a target threshold for collection from peripheral blood of at least 5 million CD34+cells/kg (with four or fewer days of apheresis sessions) — the primary endpoint — compared with 20 per cent of patients given G-CSF plus

placebo ($P<0.0001$). This trial included 298 patients who were undergoing a haematopoietic stem cell transplant in the US and Canada.

In the study of 302 multiple myeloma patients, 72 per cent of those given plerixafor and G-CSF reached the primary endpoint of 6 million CD34+cells/kg collected in two or fewer days, compared with 34 per cent of those given G-CSF plus placebo ($P<0.0001$).

Genzyme says that plerixafor was well tolerated in both trials, with the most common side effects being mild gastrointestinal effects and injection-site redness. Genzyme expects to apply for European approval next year.

Therapeutic cancer vaccines could work with chemotherapy

Combining a therapeutic cancer vaccine with chemotherapy may bring treatment benefits, research on colorectal cancer patients suggests (*Clinical Cancer Research* 2007;13:4487).

Cytotoxic medicines have been thought to suppress immune responses and so few studies have examined the use of a cancer vaccine alongside chemotherapy. However, researchers

from Oxford BioMedica assessed immune responses in 11 patients who were receiving 5-fluorouracil, folic acid and oxaliplatin and had been vaccinated with TroVax (a modified virus encoding a tumour antigen). They detected specific responses for the tumour antigen in 10 of the patients and found a correlation between immune response and clinical benefit.

Azacitidine shows promise for myelodysplastic syndromes

Two-year survival data for patients taking azacitidine — the first of a new class of agents for myelodysplastic syndromes (where dysfunctioning bone marrow results in the production of malformed or immature blood cells) — have been released by biopharmaceutical company Pharmion.

The unpublished, phase III data from 358 patients with "higher-risk" myelodysplastic syndromes show a two-year survival rate of 50.8 per cent for patients given azacitidine

(75mg/m²/day subcutaneously for seven consecutive days every 28 days) compared with 26.2 per cent for conventional care (which included supportive care alone, with low-dose cytarabine or with standard chemotherapy; $P<0.0001$). Azacitidine-treated patients saw a median survival benefit of 9.4 months over those on conventional care (24.4 versus 15 months; $P=0.0001$), corresponding to a hazard ratio of 0.58 (95 per cent confidence interval 0.43–0.77).

R&D news in brief

Nanotechnology code of conduct

The European Commission is inviting input for the drafting of a voluntary code of conduct for research into nanosciences and nanotechnology. In its consultation document, the EC sets out the basic principles that it says should underpin such research in the future. The consultation closes on 21 September.

NX-059 shown ineffective

Experimental neuroprotective agent NXY-059 (*PJ*, 18 February 2006, p197) has failed to show efficacy (*New England Journal of Medicine* 2007;357:562). In a trial of 3,195 patients, given NXY-059 or placebo within six hours of acute ischaemic stroke, there was no difference in mortality, disability or scores of daily living between the two groups.

Animals in research

The Home Office has released the latest statistics on the use of animals in scientific procedures in Great Britain in 2006. Over 3.01 million such procedures were started last year — a 4 per cent rise on the previous year.

Improving TB immunity

Rodents vaccinated with a tuberculosis strain modified to remove a virulence-associated gene, have shown greater resistance to tuberculosis infection than those given standard vaccine (*Journal of Clinical Investigation* 2007;117:2279).