

# Society sets out next steps for professional body

Pharmacists will be consulted on the Royal Pharmaceutical Society's work on a new professional body for pharmacy, according to a briefing document for members, issued by the Society this week.

Published in response to the Clarke Inquiry's recommendations on the future body, it sets out its plans for developing the organisation in the lead-up to a January 2010 start-date, when the General Pharmaceutical Council will also begin its work.

Society President Hemant Patel urged pharmacists to take an interest in the transition process: "This is the time where pharmacists can think about their ambitions and what they want from a professional body."

Mr Patel added that the Society's Council was still in the process of considering all of the recommendations in the Clarke report. He also confirmed that a prospectus for the new body would be available for members to consider by the end of the year. This work would be undertaken by the transitional committee, he said, working with all the part-

ners wishing to be involved. "Peace appears to have broken out in pharmacy," Mr Patel told the press at a briefing in London, "and organisations are working together with the commitment to ensure that the new professional body starts on a sound footing."

He also said it was a chance "to say goodbye to the policeman role" that the Society has had on account of its regulatory activities.

Jeremy Holmes, Chief Executive and Registrar at the Society, said: "We want to make sure that this new professional body has the support of the profession before it even starts so that we can look forward and do this together, rather than worry about history and conflicting interests." He added: "I think it's very important that we have a professional body that the great majority of pharmacists feel they can be part of. It needs to combine a proposition for that great majority with recognition of the leading edge of pharmacy specialist practice. It needs to do both jobs."

Mr Holmes said that, with publication of the recent pharmacy White Paper, "pharmacy

is now waking up to the fact that the opportunities are immense, and if ever we needed a focused and relevant professional leadership body that caught the imagination of the profession now is the moment we need it".

Speaking as a guest at the briefing, United Kingdom Clinical Pharmacy Association chairman Catherine Duggan said that many pharmacists pay "over and above to be part of specialist groups already", but added: "The people I feel we need to work very strongly to attract are generalists who work in community, or in any sector — generalists who may not necessarily find a professional body, as it stands at the moment, too attractive."

Richard Cattell, Guild of Healthcare Pharmacists president, told *The Journal* that, with only 18 months remaining to deliver a fully functional professional leadership body, he would not want the consultation process with members to introduce delays. He also suggested that the transitional committee would need external expertise on financial matters and becoming more member-facing.

## First pharmacists with special interests accredited in anticoagulation

Two pharmacists in Bradford have become the first to qualify as pharmacists with special interests (PhwSIs) in England, it was announced this week.

Community pharmacist Linda Hirst and locum pharmacist Marta Hildebrandt together run a weekly anticoagulation monitoring clinic at Wilsden Surgery.

Patients who would usually have been monitored in a hospital clinic are now seen by the pharmacists instead in their local surgery nearer to home.

Ms Hirst said: "We are both pleased to have become accredited. It is a step forward, bringing care closer to home and increasing patient convenience."

Rachel Urban, Bradford and Airedale Teaching Primary Care Trust community pharmacy development and clinical governance pharmacist, said the PhwSIs framework

gives PCTs a route to develop their pharmacy workforce. The PCT now plans to develop other PhwSIs in substance misuse, sexual health and diabetes, she said.

Beth Taylor, national development lead, pharmacists with special interests, NHS Primary Care Contracting, said: "This is excellent news for pharmacy and comes at an exciting time for the profession. As more specialist care moves to primary care settings, many other PCTs in England are also considering how PhwSIs could contribute to the new patient pathways that are being developed."



Linda Hirst (left) and Marta Hildebrandt discuss the anticoagulation service

The announcement was welcomed by England's chief pharmaceutical officer Keith Ridge, who said he looked forward to seeing many more PhwSIs.

## Clinical assessment service to extend function to poorly performing NHS pharmacists

The National Clinical Assessment Service, which currently provides advice and support for the NHS for dealing with poorly performing doctors and dentists, is to extend its function to include pharmacists in England from April 2009.

The NCAS aims to "bridge the governance gap" that can occur when an issue is not resolved by local management interventions, but may not be serious enough to warrant referral to the profession's regulator. Referrals for poor performance are usually received from the employer, although some practitioners choose to self-refer.

In addition to clinical capability, the NCAS assesses the health and behaviour of the professional in question, as well as his or her working conditions. Plans for improving performance specify recommendations, which may be targeted at the employer or the professional. The NCAS has no regulatory power, so it can only make recommendations.

Ray Fitzpatrick, chairman of the Royal Pharmaceutical Society's Hospital Pharmacists Group, commented: "Where there are issues of performance management, an independent opinion will be beneficial to both the employer and the individual concerned."

"However, the service will need to be applied consistently, and capability management policies in hospitals will need to be modified."

The Department of Health has agreed to fund the extension of the NCAS's remit to include pharmacists, which is expected to cost around £870,000 per year.

Heidi Wright, the Royal Pharmaceutical Society's head of practice, said the service had the potential to provide a structured and supported approach to overcoming performance concerns.

"We are pleased that NCAS will be extending its services in this way," she said.

# Users say summary care record is "too complex"

An independent evaluation of the patient summary care record (SCR) has reached mixed conclusions, according to its report published this week.

A team from University College London accepted at the end of a year-long study that having an SCR — a summary of a patient's key medical details such as medication, allergies and known adverse reactions — on a

central national electronic database was a particular advantage in emergency or unscheduled care settings. It would also be useful in cases where patients did not have English as their first language, were unconscious or confused about their medical details.

Although the researchers reported that many staff in the four SCR early adopter sites studied were enthusiastic about the initiative, a significant number of GPs had refused to participate in the project because they were concerned about the quality of the data.

Other staff complained that the system was "clunky" and "too complex", and some said they had given up using the SCR "until it works better", they found.

Patients' attitudes to their record varied according to their medical condition and were influenced by their personal trust and confidence in their primary health care team, says the report.

Most patients, especially those with a potentially stigmatising illness such as mental ill health or HIV, while supporting the idea of an SCR, were equally keen to control who had access to the information.

Gillian Braunold, clinical director of the summary care record and HealthSpace programme, said following publication of the report: "We set up the early adopter programme to ensure that problems, issues and practicalities of implementation were tested out in real-life healthcare situations in a controlled and safe environment.

"The report offers the programme the foundations on which to base the necessary planning for improvement in design and implementation before national roll out."

In response to the evaluation, President of the Royal Pharmaceutical Society Hemant Patel said: "The widespread adoption of SCRs will assist our vision to make Britain the safest place to receive medicines."

He added that pharmacists' access to records will benefit patients and enhance joint working with GPs.

"[Pharmacist access] should also . . . help the Government meet its target of reducing by 40 per cent the number of serious errors in the use of prescribed drugs as well as helping reduce the human and financial cost of prescribing errors," he said.

## NHS CfH criticised

The Government's Connecting for Health team was criticised by the researchers for focusing too much on the technology of the initiative, rather than looking at the wider picture and the benefits it could bring patients.

The report says: "A shift to a more socio-technical perspective would change the SCR programme considerably . . . it would no longer be seen as an end in itself (with 'success' measured in terms of number of records created and extent of use) but as a means to other ends (with success being defined in terms of a range of locally relevant ends)."

# Pharmacy staff do not respect drug misusers

A significant number of drug misuse service users feel that pharmacy staff do not respect them, according to findings released by the Healthcare Commission and the National Treatment Agency this week.

The findings, from the second of three annual reviews to assess the performance of 149 local drug partnerships in England, reveal that 30 per cent of local drug partnerships scored "weak" on the question of whether service users felt respected by pharmacy staff. "This was largely because partnerships have made insufficient progress in providing training for pharmacy support staff (as opposed to pharmacists) who have the most contact with service users," the report says. It adds that there had been more progress in training pharmacists.

The review also reveals that there is a national shortfall in the provision of out-of-hours needle exchange. However, the range of harm reduction information and advice



"Improving services for substance misuse" was published this week

provided by pharmacy needle exchanges was wide, with 58 per cent of partnerships scoring "excellent" on this question.

In brief

## MHRA safety update

Safety profiles of the anti-obesity drug rimonabant (Acomplia) and the incretin mimetic exenatide (Byetta) are the focus of this month's *Drug Safety Update* published by the Medicines and Healthcare products Regulatory Agency. The MHRA reminds prescribers of the psychiatric adverse reactions associated with rimonabant and the risk of acute pancreatitis with exenatide.

## Prescribing profiles

Six pharmacist prescribing case studies have been published on the Department of Health website ([www.dh.gov.uk](http://www.dh.gov.uk)) to help the NHS understand how non-medical prescribing can help to deliver services. The pharmacists featured prescribe in the areas of hypertension, sexual health, respiratory medicine, long-term conditions and older people.

## Saturday opening for NPA

The National Pharmacy Association's information service will open on Saturday mornings from this weekend. The extended opening hours are in response to an NPA survey that revealed that almost 17 per cent of respondents considered waiting times for the telephone service were too long.

# DoH sets out details for human papillomavirus vaccinations

Details of the Government's plans to introduce human papillomavirus vaccine into the national immunisation programme in England were set out in a letter sent to healthcare professionals last week.

The letter, from chief pharmaceutical officer Keith Ridge and colleagues at the Department of Health, says that the first cohort to be immunised will be girls born between 1 September 1995 and 31 August 1996

(school year 8 in 2008–09). It also says that guidance for both professionals and the public will be produced.

The details follow a study that reveals that parents are reluctant to allow their daughters to be immunised against cervical cancer because they have too little information about the human papillomavirus vaccine and are unsure about its long-term safety (*BMJ Online First*, 24 April 2008, [www.bmj.com](http://www.bmj.com)).

# Judicial review ruling could slow NICE appraisals

Drug appraisals by the National Institute for Health and Clinical Excellence, which govern prescribing guidance in England and Wales, may take longer in the future following what is being seen as a landmark Court of Appeal ruling.

The Court last week decided that NICE was wrong to refuse to publish the full health economic model that supported its decision over the availability of Alzheimer's disease drugs.

Lord Justice Richards, one of three judges sitting in the Court of Appeal, said: "Procedural fairness does require release of the fully executable version of the model."

In the judicial review ruling he said: "It is true that there is already a remarkable degree of disclosure and of transparency in the consultation process; but that cuts both ways, because it also serves to underline the nature and importance of the exercise being carried out."

"The refusal to release the fully executable version of the model stands out as the one exception to the principle of openness and transparency that NICE has acknowledged as appropriate in this context."

Failure to release the model, he said, puts pharmaceutical companies at a significant disadvantage if they want to challenge the reliability of the model.

The judges rejected the reasons given by NICE for not publishing the model as unsound and of insufficient weight to justify NICE's position.

NICE had argued that the model should only be available as a read-only document —



**Andrew Dillon: decision will increase complexity of drug appraisals**

which in practice would prevent any drug company adapting the model for its own analytical purpose — because the information is confidential and subject to intellectual property rights.

After the ruling, NICE chief executive Andrew Dillon said the decision will "increase the complexity of our drug appraisals in some cases and they may take longer as a result".

He pointed out, however, that NICE's decision about the availability of drugs to treat Alzheimer's disease — that donepezil, galantamine and rivastigmine should only be available on the NHS for people with moderate disease — remains. He said: "The judgment concerns

a small but important step in our process and method for making decisions on the best way to use new treatments in the NHS."

Responding to the judgment, Richard Baker, director general of the Association of the British Pharmaceutical Industry, which supported the appeal lodged by drug manufacturer Eisai Ltd, said: "Companies will in future be able to use the same system to judge whether, for example, treating different groups of patients with a particular medicine might result in it being more cost effective."

The judicial review was brought by Eisai Ltd, manufacturer of Aricept (donepezil). The company was appealing against an earlier High Court ruling that NICE was right not to release a working economic model that supported its decision only to recommend donepezil, galantamine and rivastigmine for people with moderate Alzheimer's disease.

Nick Burgin, managing director of Eisai Ltd, said: "As soon as we have reviewed [NICE's] cost-effectiveness calculations we will submit any new findings to NICE. We hope that this action will ultimately restore access to anti-dementia medicines for those patients at the mild stages of Alzheimer's disease."

John Young, managing director of Pfizer Ltd, which supported Eisai's appeal, said: "The failure of NICE to disclose these fundamentally important calculations has impaired the ability of stakeholders to engage fully in the appraisal process in order to provide final guidance that truly helps budget holders and clinicians make the best quality decision possible for individual patients."

## Low-strength Kaletra tablets launched for children infected with HIV

Children prescribed lopinavir/ritonavir (Kaletra) to treat HIV could find it easier to take their medicines with the launch of a low-strength Kaletra film-coated tablet (100mg/25mg).

Deepak Patel, specialist paediatric HIV pharmacist at St Mary's Hospital, Imperial College Healthcare NHS Trust, London, told *The Journal* that the new product "will make a big difference" for certain paediatric patients.

"We have been waiting for its approval all year," he said. "It will allow children who have been through 'pill-school' — pill swallowing counselling — to switch away from bitter-tasting Kaletra liquid, which can alter sense of taste and put kids off their food," he pointed out. Mr Patel explained that the poor palatability of the liquid formulation was due to its ritonavir component.

"Kaletra liquid also has very high alcohol content — 42 per cent," he added.

□ **Tenofovir for hepatitis B** Antiretroviral medicine tenofovir disoproxil has had its licence extended to include treatment of hepatitis B.

The medicine is indicated for the treatment of chronic hepatitis B in adults with compensated liver disease, with evidence of active viral replication, persistently elevated serum alanine aminotransferase levels and histological evidence of active inflammation or fibrosis.

## Cases of drug-resistant tuberculosis on the increase in the UK

Changes in the population and ongoing migration have increased cases of drug-resistant tuberculosis in the UK, according to a new study (*BMJ Online First* www.bmj.com, 2 May).

Researchers used data from the national tuberculosis surveillance system, involving 28,620 confirmed cases of the disease, to present the latest trends in resistance to anti-tuberculosis drugs.

Overall, the proportion of cases resistant to any first-line drug had increased from 5.6 per cent in 1998 to 7.5 per cent in 2005 (with a peak of 7.9 per cent in 2004). The researchers report an increasing proportion of isoniazid resistance (6.9 per cent) and small increases in rifampicin resistance (1.0 to 1.2 per cent) and multidrug resistance (0.8 to 0.9 per cent).

The authors suggest that the rise in resistance to isoniazid outside London reflects the

increasing number of patients with tuberculosis who were not born in the UK.

In London, the rise in isoniazid resistance has been linked to an ongoing outbreak associated with imprisonment and drug misuse and includes mainly the UK-born population.

The researchers suggest that most cases of multidrug resistance result from problems with patient management rather than transmission within the UK.

# Views sought on dismantling blister packs in advance

Pharmacists are being asked whether professional guidelines should be changed to allow the removal of medicines from blister or foil packs in advance of them being dispensed to patients. The Royal Pharmaceutical Society is suggesting that the change be written into guidance which supports the profession's code of ethics because the current clause is out of step with the modern practices of robotic dispensing and monitored dosage systems (MDS).

The present standards and guidance for the sale or supply of medicines states that "medicines must be removed from the blister or foil packs only at the time of dispensing to assist an individual patient".

The Society, in its consultation document, says: "Developments such as robotic dispensing and MDS could require the de-blistering of products at some time prior to the actual supply. This is already happening with MDS cassettes which are routinely made up in one operation for supply on consecutive weeks."

In another consultation, pharmacists are asked whether the guidance should also be

changed to allow them to dispense out-of-date or returned medicines in the case of an influenza pandemic.

In this consultation document the Society points out that some medicines do not degrade once they reach their expiry date and could still be safely dispensed for a period of time.

In a national emergency, such as a flu pandemic, when community pharmacists may face shortages of medicines, allowing discretion on their continued supply after the expiry date could help ease the effect of such a shortage and benefit patients, provided that the patient had been informed and had consented to such a supply, the consultation suggests.

The Society is also recommending that, in the case of a national emergency, returned medicines could be dispensed if they are still in their original packaging and look fit for purpose.

Commenting on the consultations, the Society's head of professional ethics Priya Sejjal said: "During the review of the code of ethics the Society recognised the need to



Ed Phillips/Dreamstime.com

## Medicines could be removed from blister strips ahead of dispensing

provide more detailed standards separately to the code itself.

"As technology and practice develop so too might the standards and guidance documents."

The consultations, which can be accessed on the Society's website ([www.rpsgb.org](http://www.rpsgb.org)), close on 20 June.

## Self care principles for health and social care

Seven core principles to support self care have been published by the Government. They are intended for use by the health and social care workforce in England to help people live independently and manage their own conditions.

Launching the 40-page document, health minister Ivan Lewis said: "Supporting self care is consistent with our policy of putting people first. People want control over their lives enabling them, their families and carers to maintain and improve their well-being and independence.

"The Common Core Principles to Support Self Care are intended to be a resource for reflection, challenge and practice change. Their purpose is to enable organisations and all those who work in health and social care, whether as commissioners, service providers or educators, to make personalised services, enablement and early intervention to promote independence a reality."

The seven principles are:

- Ensure individuals are able to make informed choices to manage their self care needs
- Communicate effectively to enable individuals to assess their needs, and develop and gain confidence to self care
- Support and enable individuals to access appropriate information to manage their self care needs
- Support and enable individuals to develop skills in self care
- Support and enable individuals to use technology to support self care
- Advise individuals how to access support networks and participate in the planning, development and evaluation of services
- Support and enable risk management and risk taking to maximise independence and choice

## Healthy Start vitamins to be supplied through community pharmacies in Scotland

Community pharmacies in Scotland are set to have a key role in supplying vitamins through the Healthy Start scheme.

The news comes in an update to the scheme published last week by the Scottish Government. It says: "We are funding a pilot project within NHS Tayside and Fife which aims to test distributing the vitamins via the community pharmacy route."

The Government states that community pharmacies are "likely to be a key mechanism in the distribution of Healthy Start vitamins" in future but that, until the pilots are complete, NHS boards should use other distribution routes. The vitamins, which are supplied to children and pregnant women on low incomes, are currently supplied through health centres and clinics.

## National Association of Women Pharmacists champions pharmacies as gateway for carers

Support for carers through a project initiated by the National Association of Women Pharmacists has been piloted in Wales. The project, launched in 12 pharmacies and 25 GP practices across Cardiff, followed a suggestion made by the Princess Royal at the NAWP centenary lunch in July 2005 that pharmacists could help the UK's six million carers.

Speaking at the NAWP annual conference in April, Anita White, who was instrumental in setting up the project, said that carers often fail to recognise themselves as such, so fail to ask for and benefit from available help. The aim of the project was therefore to identify both "hidden" and known carers and to evaluate the potential for pharmacies to act as a gateway for carers.

The project was promoted through the use of posters providing details of how carers can get help, including asking pharmacists. Cards were also made available for people to pick up and take away. For a period of six months each pharmacy was asked to attach a bright yellow sticker to repeat prescription bags saying: "Are you a carer? Do you need support? Ask us how . . ."

Although numbers of queries were low, the project has now been extended for a further six months across the 12 pharmacies. The aim is to roll the project out across all pharmacies in Cardiff and eventually to all 700 pharmacies in Wales. "We also hope to provide this service as one of the six services funded by the local health boards," said Mrs White.

# Trial hints at improved safety for novel psoriasis drug

ISA247, a novel calcineurin inhibitor, is safe and effective in the treatment of patients with moderate to severe psoriasis and may have an improved safety profile compared with ciclosporin, according to the authors of a phase III study published in *The Lancet* (2008;371:1337). However, an editorial warns that the two drugs need to be compared directly before conclusions can be drawn.

ISA247 differs from ciclosporin by a chemical modification of the functional group of the aminoacid-1 residue (see Panel).

The researchers conducted a study of 451 patients with plaque psoriasis involving at least 10 per cent of the body surface area.

## ISA247 and ciclosporin

The chemical modification of ISA247 means that it binds more tightly to calcineurin than does ciclosporin, leading to greater inhibition. In addition, the metabolism of ISA247 has been shifted away from aminoacid-1, resulting in faster elimination of metabolites and a lower drug and metabolite load after administration, leading to improved pharmacokinetic and pharmacodynamic predictability, say the researchers.

Participants were randomised to receive placebo or ISA247 at 0.2mg/kg, 0.3mg/kg or 0.4mg/kg orally twice daily for 12 weeks. The primary endpoint was a 75 per cent reduction in the psoriasis area and severity index (PASI75) score at week 12.

PASI75 scores were achieved in 16 per cent of the 0.2mg/kg group (95 per cent confidence interval 9–24), 25 per cent of the 0.3mg/kg group (17–24;  $P=0.0085$ ), and 47 per cent of the 0.4mg/kg group (27–57;  $P<0.0001$ ) compared with 4 per cent of the placebo group (0–8).

Adverse events were reported by 368 (82 per cent) of 451 patients, with headache, nasopharyngitis and upper respiratory tract infections the most frequent. Mild to moderate reductions in glomerular filtration rate were seen in eight (2 per cent) patients — one in the ISA247 0.3mg/kg group and seven in the ISA247 0.4mg/kg group.

This contrasts with the 10–27 per cent of patients who developed 30 per cent or more reductions in renal function when given ciclosporin in a previous study, say the researchers.

“Pharmacokinetic data show a strong correlation between response and drug concentra-



Tracy Hebbden/Dreamstime.com

Plaque psoriasis improved with ISA247

tions, raising the potential for precise titration of dosing in clinical practice,” say the researchers. They add that ISA247 could therefore provide effective immunosuppression without many of the dose-limiting side effects associated with other calcineurin inhibitors.

However, the author of an accompanying editorial (ibid, p1311) says that the claim that ISA247 is safer than ciclosporin should be viewed cautiously because it is based on external comparisons.

# Corticosteroids do not improve infant survival in bacterial meningitis

Using adjuvant corticosteroids to treat bacterial meningitis does not reduce the risk of infected children dying, a study published this week in *JAMA* shows (2008;299:2048).

The researchers say that the use of corticosteroids in addition to primary therapy for bacterial meningitis reduces mortality in adults. However, in children, studies reveal conflicting results and the potential benefit of adjuvant corticosteroids remains unclear.

In a multicentre, observational study, Jillian Mongelluzzo, of the Children's Hospital of Philadelphia, and colleagues analysed data for 2,780 children, with a mean age of 3.4 years, discharged from hospital with bacterial meningitis. *Streptococcus pneumoniae* was the most commonly identified cause.

Adjuvant corticosteroids (most commonly dexamethasone) were administered to 248 of the children (8.9 per cent). The overall mortality rate was found to be 4.2 per cent (95 per cent confidence interval, 3.5–5 per cent); cumulative mortality rates were 2.2 per cent and 3.1 per cent at seven days and 28 days, respectively, after admis-

sion. There were 15 deaths (6.0 per cent) in children who received corticosteroids and 102 deaths (4.0 per cent) in children who did not receive corticosteroids (relative risk 1.50; CI 0.89–2.54).

The researchers conclude that use of adjuvant corticosteroids was not associated with survival, length of hospital stay or infecting organism in children regardless of age. They say that the results may differ from those of adult studies for several reasons. “First, adults may have different predisposing factors for meningitis or a different inflammatory response, either of which may alter the course of disease compared with children,” they say. Secondly, the case fatality rate in pneumococcal meningitis in children is lower compared with that in adults (4.2 per cent vs 34 per cent, respectively) — the current study could have been underpowered to determine a difference in mortality, they add.

The researchers say that adjuvant corticosteroid use in bacterial meningitis appears to be increasing and may improve the long-term quality of life in some children. However, a randomised trial is warranted before such corticosteroid use becomes routine.

# Metformin safe and effective to treat diabetes that develops in pregnancy, say researchers

Metformin is a safe and effective treatment for women with gestational diabetes mellitus, a study published this week in *The New England Journal of Medicine* confirms (2008;358:2003).

Researchers randomly assigned 751 women with gestational diabetes at 20 to 33 weeks of pregnancy to receive open treatment with metformin (with supplemental insulin if required) or insulin. They found that metformin, alone or in conjunction with supplemental insulin, was not associated with an increase in neonatal complications compared with insulin.

Rates of neonatal hypoglycaemia were similar in each group, but severe hypoglycaemia ( $<1.6$ mmol of glucose per litre) occurred significantly less in infants of women taking metformin. However, the frequency of preterm birth was found to be higher in the metformin group. The difference could be due to chance or to an unrecognised effect of metformin on the labour process, the researchers suggest.

Overall, metformin was reported to be a more acceptable treatment than insulin but the researchers comment: “Clinicians may re-

main circumspect about using metformin until follow-up data for offspring are available.”

Recent guidance from the National Institute for Health and Clinical Excellence says that hypoglycaemic therapy for women with gestational diabetes — which may include regular insulin, rapid-acting insulin analogues (aspart and lispro) and/or the oral hypoglycaemic agents metformin and glibenclamide — should be tailored to the glycaemic profile of, and acceptability to, the individual woman.

# Cilostazol as effective as aspirin

Cilostazol, an investigational antiplatelet drug, is as effective as aspirin for the secondary prevention of ischaemic stroke and is associated with fewer bleeding events, according to a study in China (published online in *The Lancet Neurology*, 5 May, www.thelancet.com). However, a larger study is needed to confirm the findings, say the researchers.

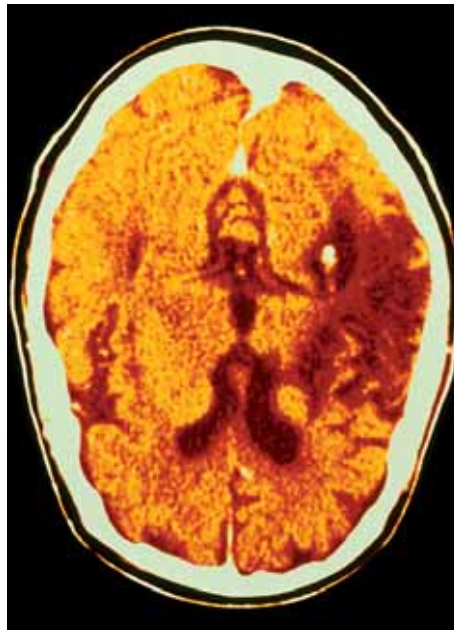
Cilostazol is a phosphodiesterase-3 inhibitor and so works via a different mechanism to aspirin. It prevents inactivation of the intracellular second messenger cyclic AMP and irreversibly inhibits platelet aggregation and vasodilation.

The study included 720 patients who had experienced an ischaemic stroke within the past one to six months. Participants were randomised to receive cilostazol 100mg twice a day or aspirin 100mg a day for 12 to 18 months. The primary endpoint was recurrence of stroke — ischaemic, haemorrhagic or subarachnoid.

The researchers found no difference in the recurrence of stroke between the two groups (12 patients in the cilostazol group versus 20 in the aspirin group, hazard ratio 0.62, 95 per cent confidence interval 0.3–1.26;  $P=0.185$ ). However, more patients in the aspirin group experienced symptomatic cerebral haemorrhage (five versus one) and asymptomatic cerebral haematoma (four versus one). Bleeding events occurred more frequently in the aspirin group than in the cilostazol group (seven versus one;  $P=0.034$ ).

The researchers say that cilostazol had similar effects to aspirin in the prevention of stroke during the first six months after starting treatment but was more effective after that. They believe that the difference did not reach statistical significance due to the small sample size and short follow-up period of the study.

The incidence of cerebral haemorrhage and other bleeding events is higher in the



Coloured computed tomography scan of the brain after stroke

Mehar Kulkarni/Science Photo Library

Chinese population than in other ethnic groups so the prevention of cerebral haemorrhage is crucial in preventing stroke in these patients, the researchers note.

They conclude that the lower rates of ischaemic and haemorrhagic stroke in the cilostazol group suggest that it might be a more effective and safer alternative to aspirin for Chinese patients with ischaemic stroke. However, phase III trials are needed to confirm this result, they add.

In an accompanying comment, Graeme Hankey, department of neurology, Royal Perth Hospital, Australia, says: "The implications of these results for clinicians are that they offer hope for a safer antiplatelet drug that is at least as effective as aspirin for use in patients with ischaemic stroke."

## Drug development

### Tarenflurbil mixed success in AD

Tarenflurbil has shown some benefit in the mild stages of Alzheimer's disease in a phase II study, published online in *The Lancet Neurology* (30 April, www.thelancet.com). In the 210-patient trial, patients with mild disease taking 800mg of the drug experienced slower rates of decline in daily living activities ( $P=0.033$ ), but not in cognitive function, than those on placebo. Patients with moderate disease did not benefit from treatment. Tarenflurbil selectively lowers the amyloid- $\beta$  peptide  $A\beta_{42}$ , thought to be responsible for starting the process of amyloid- $\beta$  deposition in the brain in Alzheimer's disease.

### HIV research

Researchers have shown that *in vitro* inhibition of a cellular protein, inducible T-cell kinase (ITK), can block HIV replication at multiple steps: HIV gene transcription, viral entry and viral particle production and release (*Proceedings of the National Academy of Sciences*, 28 April, www.pnas.org). "Our results suggest that ITK inhibition provides a model for the study of cellular protein targets that affect HIV infection, which may be useful as part of a multidrug regimen directed against HIV," they say.

### Everolimus stent shows promise

Use of everolimus — an experimental macrolide immunosuppressant — in drug-eluting stents, has been tested in a 1,002-patient trial, reported recently in *JAMA* (2008;299:1903). Patients with coronary artery disease had either an everolimus-eluting stent or a paclitaxel-eluting stent implanted during percutaneous coronary intervention. The everolimus stent, compared with the paclitaxel stent, resulted in less in-segment late loss (an angiographic measure of restenosis) at 240 days ( $P\leq 0.004$ ), non-inferior rates of failure of the target vessel at nine months ( $P\leq 0.001$ ) and fewer major cardiac events at nine months ( $P=0.03$ ) and at 12 months ( $P=0.02$ ).

### Potential metastatic cancer strategy

Combination of bortezomib with MD5-1 — a tumour necrosis factor-related apoptosis-inducing ligand (TRAIL) receptor agonist monoclonal antibody — could be a useful strategy for treating metastatic solid tumours, the authors of a new study suggest (*Journal of the National Cancer Institute*, 29 April, www.jnci.oxfordjournals.org). Mice given the combination treatment had fewer lung metastases after 18 days and survived for longer than those given either agent alone, without obvious signs of toxicity.

# Fluoxetine could benefit patients with multiple sclerosis

Fluoxetine has a tendency to reduce the formation of new brain lesions over time in patients with multiple sclerosis (MS), preliminary research published online reveals (*Journal of Neurology, Neurosurgery and Psychiatry*, 1 May, http://jnnp.bmj.com).

In a double-blind, placebo-controlled exploratory study researchers randomly assigned 40 non-depressed patients with relapsing remitting or relapsing secondary progressive MS to fluoxetine 20mg or placebo daily for 24 weeks. MRI scans of the brain were performed at four, eight, 16 and 24 weeks.

The fluoxetine group showed a trend towards a reduction in the cumulative volume of new gadolinium-enhancing lesions, the number of scans with gadolinium-enhancing lesions and increase of lesion load. No differences in MRI outcome measures were seen

up to the first eight weeks of treatment. However, during the last 16 weeks the number of patients with no new gadolinium-enhancing lesions was 63 per cent in the fluoxetine group compared with 26 per cent in the placebo group ( $P=0.02$ ).

The researchers conclude that the results are sufficiently encouraging to justify further studies with fluoxetine in patients with MS. Higher doses and combination treatment with immunomodulatory drugs should be considered. They say that an interesting aspect of considering fluoxetine as a candidate for the treatment of MS is its additional mechanisms of action, including the production of neurotrophic factors by astrocytes. However, conclusions from the study "must be made with caution because of the small sample size and exploratory design," they say.