



## News

### *DSM-5 released*

The fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has now been released by the American Psychiatric Association after more than a decade of development. Several new disorders have been added to the new edition, including binge eating disorder, disruptive mood dysregulation disorder and hoarding disorder. The bereavement exclusion of DSM-IV has also been removed from the diagnosis of major depressive disorder.

### *New treatment reduces alcohol use*

Nalmefene (Selincro), a selective opioid receptor ligand with antagonist activity at  $\mu$  and  $\delta$  receptors and partial agonist activity at the  $\kappa$  receptor, has been introduced as a treatment to help reduce alcohol intake.

Licensed for use in adults who are dependent on alcohol, its use is limited to those who continually consume more than 60g daily for men or more than 40g daily for women, and who do not have withdrawal symptoms or require immediate detoxification. It should only be prescribed in conjunction with continuous psychosocial support focused on treatment adherence and reducing alcohol consumption.

Nalmefene has been shown to reduce total alcohol consumption

and the number of heavy drinking days per month. At the recommended dose of 18mg daily, 28 days' treatment costs £84.84.

### *Mixed results for arbaclofen for autism*

Arbaclofen (STX209), an oral, selective, GABA<sub>B</sub> receptor agonist under development for the treatment of autism spectrum disorder (ASD), failed to achieve its primary endpoint of improving social withdrawal in a Phase IIb trial announced at the International Meeting for Autism Research (IMFAR) in San Sebastian/Donostia, Spain in May. However, it did improve secondary endpoints including measures of global severity and social functioning.

Manufacturer Seaside Therapeutics, founded to develop treatments for autism and intellectual disability, points out that autism spectrum disorder is a heterogeneous condition and the trial will improve understanding of who might respond to treatment with arbaclofen. A further trial in autism spectrum disorder is now underway; arbaclofen is also being evaluated in the treatment of fragile X syndrome.

### *Focus on medicines optimisation*

Medicines optimisation – individual intervention to increase the effectiveness and safety of medicines to improve outcomes – should be integrated into clinical practice, says the Royal Pharmaceutical Society in *Medicines Optimisation: Helping Patients to Make the Most of Medicines*, its new guidance on the subject ([www.rpharms.com](http://www.rpharms.com)).

The Society defines four principles: understand the patient's experience, base the choice of medicines on evidence, ensure medicines use is as safe as possible and make medicines optimisation part of routine practice. It cites

case studies including adherence to antipsychotic medication, polypharmacy including an antipsychotic and inappropriate administration of a mood stabiliser to illustrate the value of its initiative.

### *Clobazam liquid licensed*

Martindale Pharma has introduced a formulation of clobazam oral suspension (Tapclob) licensed for the short-term treatment of disabling anxiety and as adjunctive treatment in epilepsy.

Clobazam liquid was formerly a 'special' (manufactured in small batches to order), which cost NHS England over £3 million for 19 000 prescriptions in 2012. Tapclob is available as a suspension of 5mg per 5ml and 10mg per 5ml at a cost of £115.61 and £120.25 respectively for 150ml.

### *Antipsychotics mix-up*

The Medicines and Healthcare products Regulatory Agency has warned that similarities between drug names are contributing to prescribing errors (*Drug Safety Update* 2013;vol. 6(issue 9):H1).

Among the problems that have come to its attention is confusion between the depot formulation of the antipsychotic zuclopenthixol decanoate and the oral form zuclopenthixol acetate; there is also confusion between the antipsychotic risperidone and the dopamine agonist ropinirole.

### *Treatment for pseudobulbar affect coming to Europe*

A combination of dextromethorphan and quinidine (Nuedexta) has passed the first regulatory hurdle for European authorisation for the treatment of pseudobulbar affect (defined as sudden and uncontrollable bouts of laughing or crying unrelated or disproportionate to the emotional state).

The European Medicines Agency's Committee for Medicinal Products for Human Use has given a positive opinion for the treatment of adults and marketing approval normally follows. Nuedexta, marketed by Jenson Pharmaceutical Services, has been studied in patients with pseudobulbar affect in multiple sclerosis and amyotrophic lateral sclerosis (ALS).

## *NICE guide for implementing guidance*

The National Institute for Health and Clinical Excellence has published a guide to help health and social care providers to implement its guidance and quality standards (<http://publications.nice.org.uk>). Intended for almost anyone involved in service planning or delivery, *Using NICE Guidance and Quality Standards to Improve Practice* suggests ways to implement and assess NICE advice, and how to plug gaps in provision.

## *NICE quality standards for social care*

NICE has published two new quality standards for social care, covering support to help people with dementia live well and improving the health and social, educational and emotional wellbeing of looked-after children and young people in care ([www.nice.org.uk/guidance](http://www.nice.org.uk/guidance)).

QS30, *Supporting People to Live Well with Dementia*, will help people with dementia, with the involvement of their carers, to exercise choice and control in decisions affecting their care and support, and to participate in a review of their needs and preferences when their circumstances change. NICE's responsibilities were extended to social care on 1 April by the Health and Social Care Act 2012.

## *What to expect from your doctor*

The General Medical Council has published new guidance for patients on how their doctor should behave.

*What to Expect from Your Doctor* ([www.gmc-uk.org](http://www.gmc-uk.org)) is based on the GMC's fifth edition of *Good Medical Practice*. It states that doctors have a duty to be honest and open if things go wrong and to make patient care their first concern, it emphasises the importance of dignity and respect in the patient-doctor relationship and describes the standard of conduct, knowledge and skills that patients should receive.

## *NICE summarises evidence for zonisamide and lisdexamfetamine*

NICE's Evidence Summaries: New Medicines (ESNMs) review the key evidence for products of significance to the NHS. They are intended to summarise information for those working on the managed entry of new medicines for the NHS but they do not constitute NICE guidance (see [www.nice.org.uk/mpc/evidencesummariesnewmedicines](http://www.nice.org.uk/mpc/evidencesummariesnewmedicines)).

NICE has published a summary of the key evidence underlying the use of zonisamide (Zonegran) for its recent licence extension as monotherapy for treating partial-onset seizures, with or without secondary generalisation, in adults with newly diagnosed epilepsy (ESNM17). Noting that it appears to be slightly less effective than carbamazepine but equally well tolerated, NICE concludes that 'zonisamide could offer an alternative to other antiepileptic drugs in some people because of its different mechanism of action, once-daily dosing, and adverse event and interaction profiles' though it is more expensive than the alternatives.

In its summary of lisdexamfetamine dimesylate (Elvanse) for the treatment of ADHD in children and young people (ESNM19), NICE concludes that evidence of efficacy is limited to a single clinical trial and the adverse effect pro-

file appears similar to other stimulants. Theoretical advantages in terms of improved adherence and reduced abuse potential need further evaluation in clinical practice. Lisdexamfetamine dimesylate costs more than dexamfetamine and current NICE guidance on ADHD recommends prescribing the least expensive treatment option that is appropriate.

## *Mental health trusts first up for new CQC approach*

The Care Quality Commission (CQC; [www.cqc.org.uk](http://www.cqc.org.uk)) has explained how it plans to inspect and regulate health and social care services in 2013-2016. These changes will affect NHS hospitals and mental health trusts first because, the CQC says, there is an urgent need for more effective inspection and regulation of these services.

In future, specialised inspectors will lead teams of individuals with experience of care to assess services according to five standards: safe, effective, caring, well led and responsive to people's needs. There will be in-depth reviews, closer attention to what service users say and a quicker response. The CQC also plans to strengthen the protection of people whose rights are restricted under the Mental Health Act.

## *MS treatments underused?*

Only 40 per cent of people with multiple sclerosis who are eligible for treatment currently receive a disease-modifying drug, according to a survey by the Multiple Sclerosis Society ([www.mssociety.org.uk](http://www.mssociety.org.uk)).

*A Lottery of Treatment and Care: MS services across the UK* included 10 500 respondents across the UK. It found that use of disease-modifying therapy varied more than two-fold between Northern Ireland (68 per cent of patients) and Wales (30

per cent). Uptake among eligible patients was 29 per cent for natalizumab and only 5 per cent for fingolimod. The UK ranks 25th out of 27 European countries for drug prescription rates, with only Poland and Romania below it.

The Multiple Sclerosis Society has now launched Stop the MS Lottery, a campaign to increase access to treatment by promoting personalised management plans for all patients, twice-yearly reviews and integrated commissioning of multidisciplinary care.

## Research

### Psychiatric disorders

Studies of the pharmacology of antipsychotics have found that the effects of aripiprazole on cognitive function and frontal metabolic function correlate with greater striatal D<sub>2</sub> receptor occupancy (*Psychopharmacology* 2013;227:221-9).

Japanese investigators say that atypical antipsychotics affect the QT<sub>c</sub> interval differently in men and women: in women, quetiapine and olanzapine increased the QT<sub>c</sub> interval significantly more than risperidone or aripiprazole, but these differences were not statistically significant in men (*Hum Psychopharmacol* 2013;doi:10.1002/hup.2309). However, in a *post hoc* analysis, only olanzapine increased the QT<sub>c</sub> interval significantly more in women than in men.

In clinical studies, French investigators report that the six-month clinical response among previously untreated patients with schizophrenia is heterogeneous and can be divided into five types: a rapid response, a gradual response, patients who remain mildly ill, patients who remain very ill, and patients with an unsustained response (*Acta Psychiatr Scand* 2013;doi:10.111/acps.12135).

A behavioural weight loss programme can significantly reduce

weight over a period of 18 months in overweight or obese people with psychosis, a US study has shown (*New Engl J Med* 2013;368:594-1602). Mean weight loss was 3.2kg compared with placebo.

Folic acid plus vitamin B<sub>12</sub> supplementation seemed to improve negative symptoms in people with schizophrenia taking an antipsychotic in a multicentre trial – although the response appeared to depend on genetically determined folate absorption (*JAMA Psychiatry* 2013;70:481-9).

Calcitonin has been shown in preliminary trials to reduce agitation in patients with acute mania; however, in a trial of people with treatment-resistant mania, calcitonin nasal spray did not improve manic symptoms, say Canadian researchers (*Bipolar Dis* 2013;doi:10.1111/bdi.12062).

Several recent studies have identified an increased risk of autism spectrum disorder after *in utero* exposure to valproate (*JAMA* 2013;309:1696-1703; *J Neurol Neurosurg Psychiatry* 2013;84:637-43) and to SSRIs and tricyclic antidepressants (*BMJ* 2013;346:f2059).

A retrospective study of 530 416 patients in 375 US hospitals has linked perioperative use of an SSRI with a slightly increased risk of in-hospital mortality, bleeding and readmission (*JAMA Intern Med* 2013;doi:10.1001/jamainternmed.2013.714).

### Neurological disorders

The severity of Parkinson's disease motor symptoms, as measured by the United Parkinson's Disease Rating Scale (UPDRS) correlates inversely with serum vitamin D concentrations, a US study suggests – in particular, with balance (*Movement Dis* 2013;doi:10.1002/mds.25405).

A dry powder inhaler of apomorphine has been shown to

reverse 'off' periods in patients with Parkinson's disease: rapid absorption means the effects were apparent within 10 minutes and this route of administration may even replace subcutaneous injection in the future (*Acta Neurol Scand* 2013;doi:10.1111/ane.12107).

Preladenant, a novel adenosine A<sub>2A</sub>-receptor antagonist appeared to be safe and well tolerated as an adjunct to levodopa in patients with fluctuating Parkinson's disease, reducing 'off' time and increasing 'on' time in a 36-week Phase II trial (*Movement Dis* 2013;doi:10.1002/mds.25395).

Neurologists in Germany have reported outcomes for 15 patients with multiple sclerosis who developed progressive multifocal leukoencephalopathy (PML) after treatment with natalizumab (*J Neurol Neurosurg Psychiatry* 2013;doi:10.1136/jnnp-2013-304897). They found that eight patients developed seizures during the acute phase, half of whom were not seizure free one year later. However, the clinical outcome was better in these patients than in those with HIV-associated PML.

People with pain associated with multiple sclerosis will be interested in a US study in healthy volunteers reporting that oral dronabinol (tetrahydrocannabinol) may be more effective than smoking marijuana, offering longer lasting analgesia and possibly having a lower risk of dependence (*Neuropharmacology* 2013;doi:10.1038/npp.2013.97).

A meta-analysis from China has concluded that steroids are safe and effective as prophylaxis of moderate to severe migraine headache when added to acute treatment – not something recommended in the current British Association for the Study of Headache (BASH) guideline (*Eur J Neurol* 2013;doi:10.1111/ene.12155).