Results Sexual dysfunction is observed in 5 patients (3.7%) at 50 and 100 mg/d (2 and 3 patients, respectively) desvenlafaxine doses. Two patients (1.5%) have experimented more than one sexual side effect. Regarding gender differences, the most frequent sexual dysfunctions are diminished sexual desire (5.5%) and erectile dysfunction (5.5%) in men and orgasmic dysfunction (1.2%) in women (*P*-values are 0.034; 0.034 and 0.408, respectively). Discontinuation is decided in 60% of patients.
Conclusions Desvenlafaxine has a well-tolerated sexual side effect profile in general population. There are some gender-related differences both in presentation and perception, as it has been described with other drugs, and this should be taken into account by prescriptors.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.562

EW445

The novel antipsychotic cariprazine (RGH-188): State-of-the-art in the treatment of psychiatric disorders

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Introduction Cariprazine (RGH-188) is a novel antipsychotic drug that exerts partial agonism of dopamine D_2/D_3 receptors with preferential binding to D_3 receptor, antagonism of $5HT_{2B}$ receptors and partial agonism of $5HT_{1A}$. Currently, cariprazine is in late-stage clinical development (phase III clinical trials) in patients with schizophrenia (S) and in patients with bipolar disorder (BD), as well as an adjunctive treatment in patients with Major Depressive Disorder (MDD) and drug-resistant MDD.
Objectives Cariprazine has completed phase III trials for the acute treatment of schizophrenia and bipolar mania, phase II trials for the bipolar depression and MDD whilst it is undergoing phase III trials as an adjunct to antidepressants.
Aims The present review aims at proving a comprehensive summary of the current evidence on the safety, tolerability and efficacy of cariprazine in the treatment of schizophrenia, BD (manic/mixed/depressive episode) and MDD.
Methods A systematic search was conducted on PubMed/Medline/Scopus and the database on Clinical Trials from inception until April 2015 by typing a set of specified keywords.
Results Available evidence seems to support cariprazine efficacy in the treatment of cognitive and negative symptoms of schizophrenia. Preliminary findings suggest its antimanic activity whilst it is still under investigation its efficacy in the treatment of bipolar depression and MDD. Furthermore, the available data seems not to allow judgements about its antipsychotic potential in comparison with currently prescribed antipsychotics.
Conclusions Further studies should be carried out to better investigate its pharmacodynamic and clinical potential, particularly as alternative to current antipsychotic drugs.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.563

EW446

Use of inhaled loxapine in acute psychiatric agitation

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Objectives The aim of this work is to study the efficacy of loxapine inhalation powder on agitated patients in a psychiatric inpatient unit.
Methods Nineteen patients sample, with an average age of 39.4 years old, diagnosed with schizophrenia, bipolar disorder or schizoaffective disorder. Patients inhaled loxapine 10 mg, using the staccato system, when they suffered a psychomotor agitation. The clinical efficacy was measured as a change from baseline in the Positive and Negative Syndrome Scale-Excited Component (PANSS-EC) and in the Young Mania Rating Scale (YMRS) one hour after the administration of loxapine.
Results A mean of 9.8 points reduction (22.6 at baseline and 12.7 one hour after the administration) was found on the PANSS-EC (*t*-test, $P < .001$) and 68.4% of the patients were considered responders as they obtained a reduction of at least 40% of the basal score. On 10 of the total of the agitated patients showed an improvement of the psychomotor excitement, and this allowed the clinicians to remove the physical restraint; on 6 of the agitated patients the physical restraint could be avoided during the whole treatment; and 3 of the patients experienced a reduction of the excitement. The reduction on PANNS-EC on the latest group was not statistically significant (*t*-test, $P = .121$).
Conclusions Inhaled loxapine was a non-invasive, rapid and effective alternative treatment for acute agitation in a psychiatric inpatient unit. It resulted more effective on mild and moderate cases; not been significantly effective on the severe cases of agitation.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.564

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Which antidepressants are associated with increased risk of developing mania? A retrospective electronic case register cohort study

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Introduction The symptoms of bipolar disorder are sometimes misrecognised for unipolar depression and inappropriately treated with antidepressants. This may be associated with increased risk of

https://doi.org/10.1016/j.eurpsy.2016.01.565 Published online by Cambridge University Press

developing mania. However, the extent to which this depends on what type of antidepressant is prescribed remains unclear.
Aims To investigate the association between different classes of antidepressants and subsequent onset of mania/bipolar disorder in a real-world clinical setting.
Methods Data on prior antidepressant therapy were extracted from 21,012 adults with unipolar depression receiving care from the South London and Maudsley NHS Foundation Trust (SLaM). multivariable Cox regression analysis (with age and gender as covariates) was used to investigate the association of antidepressant therapy with risk of developing mania/bipolar disorder.
Results In total, 91,110 person-years of follow-up data were analysed (mean follow-up: 4.3 years). The overall incidence rate of mania/bipolar disorder was 10.9 per 1000 person-years. The peak incidence of mania/bipolar disorder was seen in patients aged between 26 and 35 years (12.3 per 1000 person-years). The most frequently prescribed antidepressants were SSRIs (35.5%), mirtazapine (9.4%), venlafaxine (5.6%) and TCAs (4.7%). Prior antidepressant treatment was associated with an increased incidence of mania/bipolar disorder ranging from 13.1 to 19.1 per 1000 person-years. Multivariable analysis indicated a significant association with SSRIs (hazard ratio 1.34, 95% CI 1.18–1.52) and venlafaxine (1.35, 1.07–1.70).
Conclusions In people with unipolar depression, antidepressant treatment is associated with an increased risk of subsequent mania/bipolar disorder. These findings highlight the importance of considering risk factors for mania when treating people with depression.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.565

EW448

Characterization of agomelatine-induced liver injury, incidence and risk factors: A pooled analysis of 7605 treated patients

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Introduction/objective The hepatic safety of agomelatine was assessed in 49 phase II and III studies. The aim was to analyze the characteristics of patients who developed an increase in transaminases whilst taking agomelatine.
Method A retrospective pooled analysis of changes in serum transaminase in 7605 patients treated with agomelatine (25 mg or 50 mg/day) from 49 completed studies was undertaken. A significant increase in serum transaminase was defined as > 3-fold the upper limit of normal (> 3 ULN). Final causality was determined in a case-by-case review by five academic experts.
Results Transaminase increased to > 3 ULN in 1.3% and 2.5% of patients treated with 25 mg and 50 mg of agomelatine respectively, compared to 0.5% for placebo. The onset of increased transaminases occurred at < 12 weeks in 64% of patients. The median time to recovery (to ≤ 2ULN) was 14 days following treatment withdrawal. Liver function tests recovered in 36.1% patients despite the continuation of agomelatine, suggesting the presence of a liver adaptive mechanism. Patients with elevated transaminases at baseline, secondary to obesity and fatty liver disease (NAFLD), had an equally increased risk of developing further elevations of transaminases with agomelatine and placebo. This reflects the widespread fluctuations of serum transaminases in patients with NAFLD.
Conclusions The overall incidence of abnormal transaminases was low and dose dependent. No specific population was identified regarding potential risk factors. Withdrawal of agomelatine led to rapid recovery, and some patients exhibited an adaptive phenomenon. The liver profile of agomelatine seems safe when serum transaminases are monitored.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.566

EW449

Hospital admissions and direct costs: A comparative study between paliperidone palmitate and oral antipsychotics

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Introduction The total costs of schizophrenia increased to 2576 million Euros in 2013 in Spain, or 2.7% of the annual cost of health services. The hospitalizations, along with other intermediate resources, such as Day Hospital, etc., significantly contribute to the increase of economic burden. In Spain, the average hospital stay of schizophrenic patients is 18.24 days, totalling to an average cost of 6,753 Euros/patient (370.23 Euros/patient/day).
Material and methods The sample selected included patients from both sexes, aged between 18 and 65 years old, with diagnostic criteria of schizophrenia (according to DSM-IV and ICD-10), admitted in the Mental Health Hospital Unit (MHHU), Úbeda between 2012 and 2013, with registered visits of at least 2 outpatient visits or 1 hospitalization related to the schizophrenia diagnosis ($n = 48$).
Results After the start of treatment with the injectable antipsychotic drug of prolonged duration, the number of patients that required hospitalization for any psychiatric motive went from 24 patients (49.7%) to 11 patients (22.4%; $P < 0.001$). The patients who started treatment with PAP during hospitalization had an average stay of 15.7 days, as compared to 18.24 days of average hospital stay due to schizophrenia in Spain. The direct costs of hospitalization stays due to psychiatric reasons decreased from 162,071.88 Euros to 74,282.95 Euros ($P < 0.001$).
Conclusions This observational study shows us that the treatment with PAP reduced the average length of the hospital stay, and resulted in a decreased percentage of re-admissions as compared to oral treatments for schizophrenia. These data led to savings of more than 50% of the direct costs of hospitalization.
Disclosure of interest The authors have not supplied their declaration of competing interest.

http://dx.doi.org/10.1016/j.eurpsy.2016.01.567