COVENTRY AND WARWICKSHIRE PARTNERSHIP TRUST
Evidence for the unlicensed use of
Oxcarbazepine in the treatment of Bipolar Affective Disorder (BPAD)

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1 Background

• Licensed pharmacological approaches for the treatment of BPAD include (in alphabetical order) aripiprazole, carbamazepine, lithium, olanzapine.

1.1 The pharmacological basis for the use of oxcarbazepine: oxcarbazepine is a derivative of carbamazepine, with similar actions to carbamazepine.

• Evidence for the use of oxcarbazepine:
A Cochrane review of the published literature in 2008 concluded that there was insufficient evidence on which to base any recommendations on the use of oxcarbazepine in the maintenance treatment of bipolar disorder, either in monotherapy or as an adjunctive treatment. A review of the literature by Mazza et al stated that there was a lack of double-blind, placebo controlled studies; that recently published studies had small numbers of patients, insufficient follow-up and methodological weaknesses. The authors suggested that oxcarbazepine may be useful as an add-on treatment in those where previous treatments have failed, or in patients who have difficulty tolerating adequate dosages of standard approved treatment. A separate review by Pratoomsri et al draws a similar conclusion.

British Association for Psychopharmacology (BAP) guidelines recommend that lithium is considered for long term treatment of bipolar disorder; if lithium is ineffective or poorly tolerated, treatment with carbamazepine would be an option. The guidelines add that oxcarbazepine may be considered instead of carbamazepine because of a lower potential for pharmacokinetic interaction.

Interaction potential: oxcarbazepine, has less potent enzyme inducing properties than carbamazepine. At high doses, it does act as an inhibitor of CYP2C19. Stockley says that the situation is unclear when considering an interaction potential with lamotrigine. In one study, lamotrigine appeared to decrease the metabolism of oxcarbazepine but another study found no interaction.

1.2 Dose: in one retrospective study (involving 15 patients), the daily dose of oxcarbazepine ranged from 150mg to 2100mg (mean dose 775mg/day (±556mg)).

1.3 Side effects: Common side effects include nausea, vomiting, constipation, diarrhoea, abdominal pain, dizziness, headache, drowsiness, agitation, amnesia, asthenia, ataxia, confusion, impaired concentration, depression, tremor, hyponatraemia, acne, alopecia, rash, nystagmus, visual disorders including diplopia.

1.4 Prescribers considering prescribing oxcarbazepine for the treatment of BPAD should follow the Medicines Policy Guidance for prescribing unlicensed medicines and ensure that they:
• Exclude licensed alternatives
• Ensure familiarity with the evidence base
• Consider the contraindications and precautions for use (as listed in the SPC)
• Consider and document the potential risks and benefits — sharing the risk assessment with the patient and carers if applicable.
• Monitor for efficacy and side-effects

References:
7 Pratoomsri W, Yatham LN, Sohn CH et al. Oxcarbazepine add-on in the treatment of refractory bipolar disorder. Bipolar Disorders, 2005: 7(5); 37-52