31 - Adverse effects1

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296 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 2 considered to be superior to carbamazepine in reducing suicidal behaviour,15 although data are not consistent16 and carbamazepine may have anti-suicidal properties.17 In the UK, NICE considers carbamazepine to be a third-line prophylactic agent5 and data emerging since this guidance support this positioning.18 Three small studies suggest the related oxcarbazepine may have some prophylactic efficacy when used in combination with other mood-stabilising drugs.19–21 There are data supporting the use of carbamazepine in the management of alcohol withdrawal symptoms,22 although the high initial doses required are often poorly tolerated. A Cochrane review did not consider the evidence strong enough to support the use of carbamazepine for this indication.23 Carbamazepine has also been used to manage aggressive behaviour in patients with schizophrenia;24 the quality of data is weak and the mode of action unknown. There are a number of case reports and open case series that report on the use of carbamazepine in various psychiatric illnesses such as panic disorder, borderline personality disorder and episodic dyscontrol syndrome. Plasma levels When carbamazepine is used as an antiseizure medication, the therapeutic range is generally considered to be 4–12mg/L, although the supporting evidence is not strong. In patients with affective illness, a dose of at least 600mg/day and a plasma level of at least 7mg/L may be required,25 although this is not a consistent finding.4,11,26 Levels above 12mg/L are associated with a higher adverse effect burden. Carbamazepine blood concentrations vary markedly within the dosage interval. It is therefore important to sample at a point in time where levels are likely to be reproducible for any given individual. The most appropriate way of monitoring is to take a trough level before the first dose of the day. Carbamazepine metabolism is genetically determined and so genetic testing may be helpful before starting carbamazepine.27 Carbamazepine is a hepatic enzyme inducer that induces its own metabolism as well as that of other drugs, including some antipsychotics.28 An initial plasma half-life of around 30 hours is reduced to around 12 hours on chronic dosing. For this reason, plasma levels should be checked 2–4 weeks after starting or after an increase in dose to ensure that the desired level is still being obtained. Most published clinical trials that demonstrated the efficacy of carbamazepine as a mood stabiliser used doses that are significantly higher (800–1200mg/day) than those commonly prescribed in UK clinical practice.29 Adverse effects1 The main adverse effects associated with carbamazepine therapy are dizziness, diplopia, drowsiness, ataxia, nausea and headaches. They can sometimes be avoided by starting with a low dose and increasing slowly. Avoiding high peak blood levels by splitting the dose throughout the day or using a controlled-release formulation may also help. Dry mouth, oedema and hyponatraemia are also common. Sexual dysfunction can occur, probably mediated through reduced testosterone levels.30 Around 3% of patients treated with carbamazepine develop a generalised erythematous rash. Serious exfoliative dermatological reactions can rarely occur and

vulnerability is genetically determined.31 The human lymphocyte antigen (HLA) variant B*15:02 has a sensitivity of around 70%

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