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Antidepressants: relative adverse effects – a rough guide

446 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 3 Anxiety spectrum disorders Anxiety disorders can occur in isolation, be comorbid with other psychiatric disorders (particularly depression), be a consequence of physical illness such as thyrotoxicosis or be drug-induced (e.g. by caffeine). Comorbidity with other psychiatric disorders is very common. These disorders tend to be chronic and treatment is often only partially successful. People with anxiety disorders may be especially prone to adverse effects.1 High initial doses of SSRIs in particular may be poorly tolerated, for example. Benzodiazepines Benzodiazepines provide rapid symptomatic relief from acute anxiety states.2 Nearly all guidelines and consensus statements recommend that this group of drugs should be used only to treat anxiety that is severe, disabling or subjecting the individual to extreme distress. Because of their potential to cause physical dependence and withdrawal symptoms, these drugs should be used at the lowest effective dose for the shortest period of time (maximum 4 weeks), while longer-term treatment strategies are put in place. For the majority of patients these recommendations are sensible and should be followed. A very small number of patients with severely disabling anxiety may benefit from long- term treatment with a benzodiazepine and these patients should not normally be denied treatment. Benzodiazepines are, however, known to be over-prescribed in the long term for treatment of both anxiety3 and depression,4 perhaps especially in the USA, where attitudes to benzodiazepines differ markedly from other developed countries.5 In the UK, NICE recommends that benzodiazepines should not be used to treat panic disorder.6 In other countries, alprazolam is widely used for this indication. Benzodiazepines should be used with some care in post-traumatic stress disorder (PTSD).7 SSRIs/SNRIs When used to treat generalised anxiety disorder (GAD), SSRIs should initially be prescribed at half the normal starting dose and titrated to the normal antidepressant dosage range as tolerated (initial worsening of anxiety may be seen when treatment is started).8 The same advice applies to the use of venlafaxine and duloxetine. Modest benefit is usually seen within 6 weeks and continues to increase over time.9 The optimal duration of treatment has not been

determined but should probably be at least 1 year.10,11 Effective treatment of GAD may prevent the development of major depression.10 An early network meta-analysis suggested that fluoxetine is the most effective SSRI in GAD and sertraline the best tolerated.12 More recent analyses suggest that bupropion13 or agomelatine14 is the most effective drug in GAD. Neither analysis found clear effects over placebo for lorazepam or vortioxetine. When used to treat panic disorder, the same starting dose and dosage titration should be used as for GAD. Doses of clomipramine,15 citalopram16 and sertraline17 towards the bottom of the antidepressant range give the best balance between efficacy and adverse effects, whereas higher doses of paroxetine (≥40mg) may be required.18 Higher doses of

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