

# 24 - Interactions with other drugs

## Interactions with other drugs

292 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 2 Use in women of child-bearing age Valproate is an established human teratogen. NICE recommends that alternative antiseizure medications are preferred in women with epilepsy<sup>59</sup> and that valproate should not be used to treat bipolar illness in women of child-bearing age.<sup>29</sup> The teratogenic potential of valproate is not widely appreciated and in the past many women of child-bearing age were not advised of the need for contraception or prophylactic folate.<sup>60,61</sup> Valproate may also cause impaired cognitive function in children exposed to valproate in utero.<sup>62</sup> Valproate is now contraindicated in women of child-bearing potential in many countries (see Chapter 7). Interactions with other drugs Valproate is highly protein bound and can be displaced by other protein bound drugs such as aspirin, leading to toxicity. Aspirin also inhibits the metabolism of valproate; a dose of at least 300mg aspirin is required.<sup>63</sup> Other, less strongly protein bound drugs such as warfarin can be displaced by valproate, leading to higher free levels and toxicity. Valproate is hepatically metabolised; drugs that inhibit CYP enzymes can increase valproate levels (e.g. erythromycin, fluoxetine and cimetidine). Valproate can increase the plasma levels of some drugs by inhibition of glucuronidation. Examples include tricyclic antidepressants (TCAs; particularly clomipramine<sup>64</sup>), lamotrigine,<sup>65</sup> quetiapine,<sup>66</sup> warfarin<sup>67</sup> and phenobarbital. Valproate may also significantly lower plasma olanzapine concentrations although the mechanism is unknown.<sup>68</sup> Pharmacodynamic interactions also occur. The anticonvulsant effect of valproate is antagonised by drugs that lower the seizure threshold (e.g. antipsychotics). Weight gain can be exacerbated by other drugs such as clozapine and olanzapine. Table 2.3 summarises the prescribing and monitoring of valproate.

Table 2.3 Valproate: prescribing and monitoring. Indications Mania, hypomania, bipolar depression and prophylaxis of bipolar affective disorder. May reduce aggression in a range of psychiatric disorders (although data are weak). Pre-valproate work-up FBC and LFTs. Baseline measure of weight desirable. Prescribing Titrate dose upwards against response and adverse effects. Loading doses can be used and are generally well tolerated. Modified-release sodium valproate (Epilim Chrono6) can be given once daily. All other formulations must be administered at least twice daily. Plasma levels can be used to assure adequate dosing and treatment compliance. Blood should be taken immediately before the next dose. Monitoring FBC and LFTs if clinically indicated. Weight (or body mass index). Stopping Reduce slowly over at least 1 month, preferably longer.