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Pharmacodynamic interactions2–4

Pharmacokinetics CHAPTER 11 Interactions of uncertain aetiology include increased blood alcohol concentrations in people who take verapamil and decreased metabolism of methylphenidate in people who consume alcohol. Alcohol may also, via various routes, impair the function of slow--release tablet mechanisms causing dose-dumping.17 Pharmacodynamic interactions2–4 Alcohol enhances inhibitory neurotransmission at gamma-aminobutyric acid A (GABA-A) receptors and reduces excitatory neurotransmission at glutamate N-methyl-D-aspartate (NMDA) receptors. It also increases dopamine release in the mesolimbic pathway and may have some effects on serotonin and opiate pathways. Given these actions, alcohol would be expected to cause sedation, amnesia and ataxia (Table 11.10) and give rise to feelings of pleasure (and/or worsen psychotic symptoms in vulnerable individuals). Table 11.9 (Continued) Substrates for enzyme (note: this is not an exhaustive list) Effects in an intoxicated patient Effects in a chronic, sober drinker CYP3A4 Alprazolam Aripiprazole Benzodiazepines Carbamazepine Clozapine Donepezil Galantamine Haloperidol Methadone Mirtazapine Quetiapine Risperidone Sildenafil Tricyclics Valproate Venlafaxine Z-hypnotics Competition between alcohol and drug leading to reduced rates of metabolism of both compounds. Increased plasma levels may lead to toxicity Increased rate of drug metabolism potentially leading to therapeutic failure Enzyme induction can last for several weeks after alcohol consumption ceases Table 11.10 Pharmacodynamic interactions with alcohol. Effect of alcohol Effect exacerbated by Potential consequences Sedation Other sedative drugs, e.g.: Antihistamines Antipsychotics Baclofen Benzodiazepines Lofexidine Opiates Tizanidine Tricyclics Z--hypnotics Increased CNS depression ranging from increased propensity to be involved in accidents through to respiratory depression and death (Continued)

898 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 11 Alcohol can cause or worsen psychotic symptoms by increasing dopamine release in mesolimbic pathways. The effect of antipsychotic drugs may be competitively antagonised, rendering them less effective. Electrolyte disturbances secondary to alcohol-related dehydration can be exacerbated by other drugs that cause electrolyte disturbances (e.g. diuretics). Heavy alcohol consumption can lead to hypoglycaemia in people with diabetes who take insulin or oral hypoglycaemics. Theoretically there is an increased risk of lactic acidosis in patients who take metformin with alcohol. Alcohol can also

increase blood pressure. Chronic alcohol drinkers are particularly susceptible to the gastrointestinal irritant effects of aspirin and non-steroidal anti-inflammatory drugs. In the presence of pharmacokinetic interactions, pharmacodynamic interactions may be more marked. For example, in a chronic heavy drinker who is sober, enzyme induction will increase the metabolism of diazepam, which may lead to increased levels of anxiety (treatment failure). If the same patient becomes intoxicated with alcohol, the metabolism of diazepam will be greatly reduced as it will have to compete with alcohol for the metabolic capacity of CYP3A4. Plasma levels of alcohol and diazepam will rise (toxicity). As both alcohol and diazepam are sedative (via GABA-A affinity), loss of consciousness and respiratory depression may occur. Table 11.11 lists drugs that are safe and those that should be avoided in patients who continue drinking. Table 11.10 (Continued) Effect of alcohol Effect exacerbated by Potential consequences Amnesia Other amnesic drugs, e.g.: Barbiturates Benzodiazepines Z-hypnotics Increased amnesic effects ranging from mild memory loss to total amnesia. Usually anterograde amnesia: loss of memory of events after the effects of alcohol begin Ataxia ACE inhibitors Beta-blockers Calcium channel blockers Nitrates Adrenergic alpha receptor antagonists, e.g.: Clozapine Risperidone Tricyclics Increased unsteadiness and falls ACE, angiotensin-converting enzyme; CNS, central nervous system.

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