# 07 - Sedatives in hepatic impairment

# Sedatives in hepatic impairment

760 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 8 Stimulants in hepatic impairment6,7,82 Recommendations for the use of stimulant medications in hepatic impairment are outlined in Table 8.4. Sedatives in hepatic impairment Table 8.5 summarises recommended sedatives in hepatic impairment. Table 8.5 Sedatives in hepatic impairment. Drug Comments Benzodiazepines Extensively hepatically metabolised. Prolonged duration of effect particularly for drugs with active metabolites (diazepam, midazolam, clonazepam). Lorazepam, oxazepam and temazepam do not have active metabolites and are preferred. Lorazepam is considered the best tolerated in advanced liver disease28 and is commonly used in alcohol withdrawal. Liver enzyme elevations are uncommon and liver injury very rare.28 Melatonin7,89 Complex handling of melatonin in liver impairment. Reduced clearance and prolonged half-life contribute to higher circulating levels of endogenous melatonin in daytime hours; negative feedback and accumulation of toxic products results in reduced endogenous production. Relevance to dosing of exogenous melatonin is unclear, although toxicity of melatonin is minimal. Manufacturer advises avoiding in moderate or severe liver disease. Rarely associated with changes in liver function tests (LFTs). Promethazine7 Extensive hepatic metabolism. Manufacturers advise caution in liver impairment. Jaundice reported with high doses. Despite widespread use, no reports of LFT abnormalities or toxicity with lower doses.28 Z drugs7,90,91 Hepatically metabolised, but all have a relatively short half-life. Reduce initial doses in mild to moderate impairment (use zopiclone 3.75mg, zolpidem 5mg, zaleplon 5mg). Avoid in severe impairment. Manufacturers warn that benzodiazepines as a class may precipitate encephalopathy. Zaleplon is subject to significant first-pass metabolism and zolpidem plasma concentrations and half-life are significantly increased in hepatic impairment. These agents should be used with caution.92 Although zopiclone has the longer half-life, this may not be clinically relevant except in severe disease.90 Zopiclone and zaleplon have not been associated with hepatotoxicity. There are rare reports of abnormal LFTs and a single case of liver injury with zolpidem.28 There is one case of acute liver injury with eszopiclone (a zopiclone isomer).93 Table 8.4 Stimulants in hepatic impairment. Drug Comments Atomoxetine83 Reduce initial and target dose by 50% in moderate impairment, and by 75% in severe impairment. Very rare reports of liver toxicity, manifested by elevated hepatic enzymes, and raised bilirubin with jaundice. Manufacturer states ‘discontinue in patients with jaundice or laboratory evidence of liver

injury, and do not restart’. Dexamfetamine/ lisdexamfetamine84,85 Little experience in liver disease. Manufacturers recommend cautious dose titration. Very rarely associated with abnormal liver function, two case reports of hepatotoxicity.86,87 Methylphenidate88 Mild and transient elevations in liver enzymes have been reported. Rare reports of liver dysfunction and hypersensitivity reactions. Limited experience in liver disease.

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