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16. References

Depression and anxiety disorders CHAPTER 3 (lumateperone and ziprasidone) and drugs of misuse such as MDMA (3,4-methylene dioxymethamphetamine). ■ ■prevent the destruction of other monoamine neurotransmitters (e.g. catecholamines). Co-prescription with sympathomimetic drugs that raise blood pressure (e.g. psychostimulants) can cause hypertensive crises. MAOIs also prevent the breakdown of dietary tyramine (high levels present in aged and fermented foods), which acts as a catecholamine-releasing agent leading to similar hypertensive reactions. References

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Cardiac effects of antidepressants – summary The cardiac effects of antidepressants are summarised in Table 3.13. Table 3.13 Cardiac effects of antidepressants. Drug Heart rate Blood pressure QTc Arrhythmia Conduction disturbance Licensed restrictions post-MI Comments Agomelatine1,2 No changes reported No changes reported Single case of QTc prolongation No arrhythmia reported Unclear No specific contra-indication Cautiously recommended Bupropion1,3,4 Slight increase Slight increases in blood pressure but can sometimes be significant. Rarely postural hypotension. QTc shortening, but prolongation has been reported in cases of overdose5 No effect. Rare reports in overdose. None Well tolerated for smoking cessation in post-MI patients Be aware of interaction potential. Monitor blood pressure Brexanolone6–8 One case of tachycardia reported in trials Small reduction in blood pressure possible No effect on QTc interval No arrythmia reported None No specific contraindication Minimal effect on cardiac parameters in trial data Citalopram1,9–12 (assume same for escitalopram) Small decrease in heart rate Slight drop in systolic blood pressure Dose-related increase in QTc Torsade de Pointes reported, mainly in overdose None Caution in patients with recent MI or uncompensated heart failure. But some evidence of safety in CVD. Minor metabolite which increases QTc interval. No clear evidence of increased risk of arrhythmia at any licensed dose. Dextromethorphan

- bupropion13 As per bupropion As per bupropion As per bupropion. QTc prolongation in dextromethorphan overdose.14 As per bupropion As per bupropion No specific contraindication As per bupropion Duloxetine1,15–17 Slight increase Important effect (see

SPC). Caution in hypertension. Isolated reports of QT prolongation Isolated reports of toxicity Isolated reports of toxicity Caution in patients ‘whose conditions could be compromised by an increased heart rate or by an increase in blood pressure’ Not recommended in cardiac disease

Fluoxetine12,18–20 Small decrease in mean heart rate Minimal effect on blood pressure No effect on QTc interval None None Caution in patients with acute MI or heart failure Evidence of safety post MI Fluvoxamine21,22 Minimal effect on heart rate Small drop in systolic blood pressure No significant effect on QTc None None Caution Limited changes in ECG have been observed Levomilnacipran23–25 Slight increase Small increase No effect on QTc interval* Pre-existing tachyar rhythmias should be treated before initiating treatment None Caution in patients with cardiac disease Monitor heart rate and blood pressure Lofepramine26,27 Modest increase in heart rate Less decrease in postural blood pressure than other TCAs May prolong QTc interval at higher doses May occur at higher doses, but rare Unclear Coronary insufficiency in patients with recent MI Less cardiotoxic than other TCAs. Reasons unclear MAOIs26,28 Decrease in heart rate Postural hypotension. Risk of hypertensive crisis. Unclear but may shorten QTc interval May cause arrhythmia and decrease LVF No clear effect on cardiac conduction Use with caution in patients with CVD Not recommended in CVD Milnacipran1,29 Slight increase in heart rate (c.10bpm) Small increases in systolic and diastolic BP No effect on QTc None None Caution Avoid in hypertension and heart failure Mirtazapine1,30 Minimal change in heart rate Minimal effect on BP No effect on QTc None None Caution in patients with recent MI Evidence of safety post MI. Good alternative to SSRIs. Moclobemide31–33 Marginal decrease in heart rate Minimal effect on blood pressure. Isolated cases of hypertensive episodes. No effect on QTc interval in normal doses. Prolongation in overdose. None None General caution in patients with a history of cardiac disorders Possibly arrhythmogenic in overdose Paroxetine12,34,35 Small decrease in mean heart rate Minimal effect on BP No effect on QTc interval None None General caution in patients with cardiac disease Probably safe post MI Reboxetine36–38 Significant increase in heart rate Marginal increase in both systolic and diastolic BP. Postural decrease at higher doses. No effect on QTc Rhythm abnormalities may occur Atrial and ventricular ectopic beats, especially in the elderly Caution in patients with cardiac disease Probably best avoided in IHD (Continued)

Sertraline12,39–42 Minimal effect on heart rate Minimal effect on BP No effect on QTc interval at standard doses. Small increase (<10ms) at 400mg/day.43 None None Drug of choice post MI but formal labelling acknowledges effect on QT and cautions against use in patients with additional risk factors for QTc prolongation Safe post MI and in heart failure Trazodone26,44–46 Decrease in heart rate more common, although increase can also occur Can cause significant postural hypotension Can prolong QTc interval Several case reports of prolonged QT and arrhythmia Unclear Contraindicated in patients with acute MI May be arrhythmogenic in patients with pre-existing cardiac disease Tricyclics26,47,48 Increase in heart rate Postural hypotension Prolongation of QTc interval† and QRS interval Ventricular arrhythmia common in overdose. Torsade de Pointes reported. Slows cardiac conduction; blocks cardiac Na/K channels Contraindicated in patients with recent MI TCAs affect cardiac contractility. Some TCAs linked to IHD and sudden cardiac death. Avoid in IHD. Venlafaxine15,49–53 (assume same for desvenlafaxine) Marginally increased Some increase in postural blood pressure. At higher doses increase in BP. Possible prolongation in overdose, but very rare Rare reports of cardiac arrhythmia in overdose Rare reports of conduction abnormalities Has not been evaluated in post-MI patients. Caution advised. Evidence for arrhythmogenic potential is slim, but avoid in IHD Vilazodone54–56 Increased in overdose

Increased in overdose No effect, even in overdose No reports, even in overdose No effect No specific contraindications Probably no effect on CV function in clinical doses Vortioxetine57–59 No effect No effect No effect No effect No effect No specific contraindications Trial data suggest no effect on QTc or on coagulation parameters * Small increase in QTc reported when using Bazett’s correction formula but not with Fridericia’s. † Possibly the result of overestimation that can occur when using Bazett’s correction formula at high resting heart rates. CV, cardiovascular; CVD, cardiovascular disease; IHD, ischaemic heart disease; LVF, left ventricular function; MI, myocardial infarction; SPC, summary of product characteristics. Table 3.13 (Continued) Drug Heart rate Blood pressure QTc Arrhythmia Conduction disturbance Licensed restrictions post-MI Comments

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