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 SSRIs and bleeding Serotonin is released from platelets in response to vascular injury, promoting vasoconstriction and morphological changes in platelets that lead to aggregation.1 SSRIs inhibit the serotonin transporter, which is responsible for the uptake of serotonin into platelets (Table 3.19). The resultant depletion of platelet serotonin leads to a reduced ability to form clots and a subsequent increase in the risk of bleeding. Broadly speaking, the relative risk of any bleeding event compared with no use of SSRI/SNRI is around 1.4, with the absolute risk being between around 0.5% and 6%2 (depending on numerous factors). SSRIs may also increase gastric acid secretion and therefore may be indirectly irritant to the gastric mucosa,3 increasing the risk of peptic ulcer.4 The risk of abnormal bleeding of any kind with SSRIs is highest during the first 30 days of treatment.5,6 The effect on bleeding is probably related to the affinity of individual SSRIs for the serotonin transporter.7,8 Table 3.19 Antidepressants and degree of serotonin reuptake inhibition.6,9 Degree of serotonin reuptake inhibition Antidepressant Strong Sertraline, paroxetine, fluoxetine, duloxetine, clomipramine Intermediate Citalopram, escitalopram, fluvoxamine, vilazodone, vortioxetine, venlafaxine Amitriptyline, imipramine Weak or none Agomelatine, dosulepin, doxepin, lofepramine, mirtazapine, moclobemide, nortriptyline, reboxetine, mianserin Risk factors for

bleeding with SSRIs ■ ■Age, particularly those over 65 years ■ ■Alcohol misuse ■ ■Coronary artery disease ■ ■Drug misuse ■ ■Hypertension ■ ■History of GI bleed ■ ■History of stroke ■ ■History of major bleeding ■ ■Liver disease ■ ■Labile international normalised ratio (INR) ■ ■Medication predisposing to bleeding ■ ■Peptic ulcer ■ ■Renal disease ■ ■Smoking

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