Treatment with selective serotonin reuptake inhibitors (SSRI) increases the risk of gastrointestinal bleeding. The combination with non-steroidal anti-inflammatory drugs (NSAIDs) further augments this hazard. Particular precaution is also necessary in patients on platelet aggregation inhibitors, with a known bleeding disorder or preceding gastrointestinal lesions. The incidence of bleeding events apart from the gastrointestinal tract, e.g. intracerebral hemorrhages, is not cumulated under SSRI treatment. This also applies for the combination of SSRI and coumarin or aspirin. Prescribing doctors have to be aware of the bleeding risks of SSRI and should explain this to their patients. High-risk patients have to be followed up closely and an SSRI with a low potential for drug interaction should be used. The prescription of gastroprotective agents and a change of the antidepressant should be considered in particular cases. We provide a literature survey and recommendations for the clinical routine.