Warfarin + NSAIDs (Draft 1)

Non-steroidal anti-inflammatory drugs (NSAIDs) have antiplatelet effects which increase the bleeding risk when combined with oral anticoagulants such as warfarin. The antiplatelet effect of NSAIDs lasts only as long as the NSAID is present in the circulation, unlike aspirin's antiplatelet effect, which lasts for up to 2 weeks after aspirin is discontinued. NSAIDs also can cause peptic ulcers and most of the evidence for increased bleeding risk with NSAIDs plus warfarin is due to upper gastrointestinal bleeding (UGIB).

Is NSAID topical diclofenac?	Yes	No					
Is there a suitable alternative to the NSAID in this patient?		Yes	No				
Is patient on proton pump inhibitor or misoprostol?			Yes	No			
Does the patient have one or more of the following risk factors: - history of UGIB or peptic ulcer - > 65 years old				Yes		No	
Is patient also taking: - systemic corticosteroids - aldosterone antagonist - high dose or multiple NSAIDs				Yes	No	Yes	No
Not likely to increase risk of UGIB	○[1]						
Use alternative to NSAID		○[2]					
Possible increased risk of UGIB or other bleeding			■[3]				
Substantially increased risk of UGIB or other bleeding				◆[4,5]			
Increased risk of UGIB or other bleeding					◆[4]	◆[5]	◆

○ = No special precautions. ■ = Assess risk and take action if necessary. ◆ = Use only if benefit outweighs risk

Footnotes:

1. Topical diclofenac has relatively low systemic absorption; in one study a topical gel (16 g/day) produced about 6% of the absorption seen with systemic administration of 150 mg/day. A higher than recommended dose of topical gel (48 g/day) produced 20% of a systemic dose of diclofenac.
2. If the NSAID is being used as an analgesic or antipyretic, it would be prudent to use an alternative such as acetaminophen. In some people, acetaminophen can increase the anticoagulant effect of warfarin, so monitor the INR if acetaminophen is used in doses over 2 g/day for a few days. For more severe pain consider short-term opioids in place of the NSAID.
3. Proton pump inhibitors and misoprostol may reduce the risk of UGIB in patients receiving NSAIDs and warfarin.
4. Patients with a history of UGIB or peptic ulcer may have an increased risk of UGIB from this interaction. The extent to which older age is an independent risk factor for UGIB due to these interactions is not firmly established, but UGIB in general is known to increase with age.
5. Both corticosteroids and aldosterone antagonists have been shown to substantially increase the risk of UGIB in patients on NSAIDs, with relative risks of 12.8 and 11 respectively compared to a risk of 4.3 with NSAIDs alone (Masclee et al. *Gastroenterology* 2014;147:784-92.)

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