

<b>Interacting Drug</b>	<b>Effect</b>	<b>Clinical Comment</b>
<b>ACE Inhibitors and Angiotensin II Receptor Blockers</b>	Decreased antihypertensive effect since NSAIDs can increase BP. Additive risk of hyperkalemia. NSAID-induced inhibition of renal prostaglandins decreases potassium excretion and maintenance of renal blood flow. Additive risk of renal failure, especially in patients with poor renal perfusion or if diuretics are used concurrently.	Monitor BP, potassium levels and renal function.
<b>Beta-adrenergic Blockers</b>	Decreased antihypertensive effect since NSAIDs can increase BP.	Monitor BP.
<b>Cholestyramine</b>	Decreased oral absorption of NSAID.	Space doses or avoid. Spacing doses will not prevent the interaction with NSAIDs that undergo enterohepatic recirculation (indomethacin, meloxicam, piroxicam, sulindac).
<b>Corticosteroids</b>	Increased risk of gastrointestinal bleeding.	Consider gastroprotection in patients at risk.
<b>Cyclosporine</b>	Additive risk of renal failure.	Monitor renal function.
<b>CYP2C9 Inhibitors (fluconazole, voriconazole)</b>	Increased levels and toxicity of NSAIDs that are metabolized by CYP2C9.	Many NSAIDs are metabolized by CYP2C9. Reduce dose of NSAID.
<b>CYP2D6 Substrates (amitriptyline, codeine, metoprolol)</b>	Inhibition of CYP2D6 (celecoxib only).	Consider alternate therapy or monitor for altered response/adverse effects.
<b>Digoxin</b>	Increased digoxin levels with some NSAIDs.	Diclofenac, etodolac, ibuprofen and indomethacin may interact with digoxin. Lack of interaction has been found with ketoprofen, meloxicam, piroxicam and tenoxicam.
<b>Diuretics (loop, thiazide and potassium-sparing)</b>	Antagonism of therapeutic effect of diuretic and increased risk of renal failure; additive risk of hyperkalemia with potassium-sparing diuretics. Mechanism involves sodium and water retention by NSAIDs plus decreased potassium excretion.	Monitor BP and potassium levels.
<b>Drugs that increase the risk of bleeding (anticoagulants, antiplatelet drugs, heparin, low-molecular-weight heparins and SSRIs)</b>	Additive bleeding risk: NSAIDs inhibit platelet aggregation. Severe bleeding and increased PT have been reported when NSAIDs, including celecoxib, have been combined with anticoagulants.	Monitor INR in patients taking anticoagulants, although bleeding has occurred without a change in INR. ASA has a prolonged effect on platelet aggregation, and high doses should be avoided with anticoagulants. Low-dose ASA is used with warfarin for therapeutic effect.
<b>Lithium</b>	Increased lithium levels possibly due to decreased renal clearance.	Most NSAIDs can increase lithium levels. ASA does not interact. Monitor lithium levels when starting and stopping NSAIDs other than ASA.
<b>Methotrexate (MTX)</b>	Increased methotrexate levels and toxicity with antineoplastic doses, possibly due to decreased renal tubular secretion.	Avoid combining antineoplastic doses of MTX with NSAIDs if possible. Monitor renal function and CBC. Risk is considered less with low methotrexate doses used for arthritis.
<b>NSAIDs</b>	Additive risk of toxicity when multiple NSAIDs are consumed.	Avoid combining two NSAIDs. Risk of gastrointestinal bleeding increases, even when low doses of ASA are combined with other NSAIDs. Ibuprofen and mefenamic acid may decrease the cardioprotective effect of ASA by binding to the active site on COX; give ASA 2 h before ibuprofen.
<b>Potassium Supplements</b>	Additive risk of hyperkalemia.	Monitor potassium levels.
<b>Probenecid</b>	Increased levels of some NSAIDs.	Diflunisal, indomethacin, ketoprofen, ketorolac, naproxen and tenoxicam interact. Monitor for NSAID toxicity.

Source: Canadian Pharmacists Association: Compendium of Pharmaceuticals and Specialties, online version (e-CPS), accessed on May 10, 2013