

Colchicine Dosing and Interactions

Colchicine is a very old drug that has a history of serious safety issues. It has a narrow therapeutic index, is metabolized by the liver, and is excreted by the kidneys.^{1,2} Acute ingestion of less than ten times the daily dose has resulted in death.² About nine out of ten patients who take colchicine to treat a gout flare will have gastrointestinal symptoms, such as diarrhea and nausea, **before** they have pain relief.² Signs and symptoms of colchicine toxicity include gastrointestinal symptoms as well as organ failure (e.g., arrhythmias, myopathy, seizures, etc).² Colchicine dosing can be tricky, since there are differences depending on the indication, concomitant drug therapy, and liver and kidney function. We usually think of colchicine for gout. However, you may see low-dose colchicine used for its anti-inflammatory activity for some cardiac conditions. For example, colchicine can be used for three months (acute pericarditis) or six months (chronic pericarditis). Colchicine is dosed based on weight for pericarditis. Expect to see 0.6 mg once daily (<70 kg) or 0.6 mg twice daily ≥70 kg).¹⁰⁻¹² In addition, the effects of colchicine after a myocardial infarction (MI) were recently evaluated.⁸ This study suggests that adding colchicine 0.5 mg once daily to usual care prevents a recurrent cardiovascular event in about one in 63 post-MI patients treated for about two years compared to placebo.⁸ More data are needed before colchicine can be routinely recommended post-MI, due to study limitations (e.g., large dropout rate, limited generalizability, lack of impact on c-reactive protein).^{8,9} (Note that only the 0.6 mg strength is available in the U.S. and Canada.) The charts below review colchicine dosing for FDA- and Health Canada-approved indications and some significant drug-drug interactions. Note the drug-drug interactions listed are NOT all inclusive.

Abbreviations: BID = twice daily; CYP = cytochrome P450; FMF = Familial Mediterranean Fever (genetic disorder with recurrent fever and pain).

Dosing and Dose Adjustments for Colchicine		
Prophylaxis of gout flare (>16 years old) ^a	Treatment of gout flare (Adult only) ^a	Familial Mediterranean Fever (FMF) (>12 years old [see footnote c]) ^a
Normal dose (i.e., no significant drug-drug interactions, normal renal and hepatic function): ^{4,7}		
<ul style="list-style-type: none"> 0.6 mg once daily or BID Max dose: 1.2 mg/day 	<ul style="list-style-type: none"> 1.2 mg x1 dose at the first sign of a gout flare, then 0.6 mg one hour later Max dose: 1.8 mg in a one-hour period After acute treatment, wait <ul style="list-style-type: none"> 12 hours to resume prophylaxis. at least three days to repeat acute treatment. 	<ul style="list-style-type: none"> 1.2 to 2.4 mg/day Doses can be given once daily or divided BID. Increase doses in increments of 0.3 mg/day to the max dose based on patient's age.^c Decrease doses in increments of 0.3 mg/day if side effects are intolerable.

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Dosing and Dose Adjustments for Colchicine		
Prophylaxis of gout flare (>16 years old)^a	Treatment of gout flare (Adult only)^a	Familial Mediterranean Fever (FMF) (>12 years old [see footnote c])^a
Concurrent use (or use within 14 days) of strong CYP3A4 inhibitors (See the end of the document for a list of drugs.): ^{1,4,b} Avoid colchicine in patients with kidney or liver impairment. ^{1,4}		
<ul style="list-style-type: none"> 0.3 mg once daily if original dose was 0.6 mg BID 0.3 mg once every other day if original dose was 0.6 mg once a day 	<ul style="list-style-type: none"> 0.6 mg x1 dose then 0.3 mg one hour later Wait at least three days to repeat acute treatment. In the U.S. per product labeling: avoid colchicine for treatment if the patient is also taking colchicine for gout prophylaxis.¹ 	<ul style="list-style-type: none"> 0.6 mg once daily or 0.3 mg BID Max dose: 0.6 mg/day
Concurrent use (or use within 14 days) of moderate CYP3A4 inhibitors (See end of the document for a list of drugs.): ^{1,4,b}		
<ul style="list-style-type: none"> 0.3 mg BID or 0.6 mg once daily if original dose was 0.6 mg BID 0.3 mg once daily if original dose was 0.6 mg once daily 	<ul style="list-style-type: none"> 1.2 mg x1 dose Wait at least three days to repeat acute treatment. Per U.S. product labeling, avoid colchicine for treatment if the patient is already taking colchicine for gout prophylaxis.¹ 	<ul style="list-style-type: none"> 1.2 mg once daily or 0.6 mg BID Max dose: 1.2 mg/day
Concurrent use (or use within 14 days) of p-glycoprotein inhibitors (See end of the document for a list of drugs.): ^{1,4,b} Avoid colchicine in patients with kidney or liver impairment. ^{1,4}		
<ul style="list-style-type: none"> 0.3 mg once daily if original dose was 0.6 mg BID 0.3 mg once every other day if original dose was 0.6 mg once daily 	<ul style="list-style-type: none"> 0.6 mg x1 dose Wait at least three days to repeat acute treatment. 	<ul style="list-style-type: none"> 0.6 mg once daily or 0.3 mg BID Max dose: 0.6 mg/day
Use in Patients with creatinine clearance 30 to 80 mL/min: ^{4,7} Avoid colchicine in patients receiving strong CYP3A4 or p-glycoprotein inhibitors. ^{1,4}		
<ul style="list-style-type: none"> No dose adjustment required. Monitor for adverse effects. 	<ul style="list-style-type: none"> No dose adjustment required. Monitor for adverse effects. Per U.S. product labeling, avoid colchicine for treatment if the patient is already taking colchicine for prophylaxis of gout flares.¹ 	<ul style="list-style-type: none"> No dose adjustment required. Monitor for adverse effects. Dose adjustment may be needed.

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Dosing and Dose Adjustments for Colchicine		
Use in Patients with creatinine clearance <30 mL/min : ^{4,7}		
Avoid colchicine in patients receiving strong CYP3A4 or p-glycoprotein inhibitors. ^{1,4}		
Prophylaxis of gout flare (>16 years old) ^a	Treatment of gout flare (Adult only) ^a	Familial Mediterranean Fever (FMF) (>12 years old [see footnote c]) ^a
<ul style="list-style-type: none"> • Start with 0.3 mg once daily. Only increase dose with close monitoring.¹ (In Canada, 0.3 mg once daily.⁴) • Monitor for adverse effects. 	<ul style="list-style-type: none"> • No dose adjustment required. • Wait at least two weeks to repeat acute treatment. • Per U.S. product labeling, avoid colchicine for treatment if the patient is already taking colchicine for prophylaxis of gout flares.¹ 	<ul style="list-style-type: none"> • Start with 0.3 mg once daily. Only increase dose with close monitoring.¹ (In Canada, 0.3 mg once daily.⁴) • Monitor for adverse effects.
Use in patients receiving dialysis: ^{4,7}		
Avoid colchicine in patients receiving strong CYP3A4 or P-glycoprotein inhibitors. ^{1,4}		
<ul style="list-style-type: none"> • Start with 0.3 mg twice per week. • Monitor closely for adverse effects. 	<ul style="list-style-type: none"> • 0.6 mg x1 dose • Wait at least two weeks to repeat acute treatment. • Per U.S. product labeling, avoid colchicine for treatment if the patient is already taking colchicine for prophylaxis of gout flares.¹ 	<ul style="list-style-type: none"> • Start with 0.3 mg once daily. Only increase dose with close monitoring.¹ (In Canada, 0.3 mg once daily.⁴) • Monitor for adverse effects.
Use in Patients with mild to moderate liver impairment : ^{4,7}		
Avoid colchicine in patients receiving strong CYP3A4 or P-glycoprotein inhibitors. ^{1,4}		
<ul style="list-style-type: none"> • No dose adjustment required. • Monitor for adverse effects. 	<ul style="list-style-type: none"> • No dose adjustment required. • Monitor for adverse effects. • Per U.S. product labeling, avoid colchicine for treatment if the patient is already taking colchicine for prophylaxis of gout flares.¹ 	<ul style="list-style-type: none"> • No dose adjustment required. • Monitor for adverse effects.

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Dosing and Dose Adjustments for Colchicine		
Use in patients with severe liver impairment: ^{4,7}		
Avoid colchicine in patients receiving strong CYP3A4 or P-glycoprotein inhibitors. ^{1,4}		
Prophylaxis of gout flare (>16 years old) ^a	Treatment of gout flare (Adult only) ^a	Familial Mediterranean Fever (FMF) (>12 years old [see footnote c]) ^a
<ul style="list-style-type: none"> Consider dose reduction. 	<ul style="list-style-type: none"> No dose adjustment required.⁷ (Consider dose reduction [Canada].)⁴ Per U.S. product labeling:¹ <ul style="list-style-type: none"> Wait at least two weeks to repeat acute treatment. Avoid colchicine for treatment if the patient is already taking colchicine for prophylaxis of gout flares. 	<ul style="list-style-type: none"> Consider dose reduction.

- a. In the U.S., only brand colchicine tablets (*Colcrys*) are FDA-approved for all three indications (**prophylaxis/treatment** of acute gout flares and Familial Mediterranean Fever). Colchicine oral solution (*Gloperba*) and colchicine capsules (*Mitigare*) are only FDA-approved for **prophylaxis** of gout flares.^{1,5,6}
- b. In the U.S., per *Mitigare* and *Gloperba* product labeling, avoid coadministration of colchicine with CYP3A4 and p-glycoprotein inhibitors. If coadministration is unavoidable, colchicine doses may need to be reduced or interrupted. Monitor for adverse effects.^{5,6}
- c. Consult product labeling for dosing in children (≤12 years old) being treated for Familial Mediterranean Fever.¹

NOTE: Drugs in the following chart are specifically mentioned in the *Colcrys* product labeling.¹ This listing is not meant to imply that these are the only CYP3A4 or P-glycoprotein inhibitors that will interact with colchicine.^{1,3,4} Go to our charts, *Cytochrome P450 Drug Interactions* and *P-glycoprotein Drug Interactions*, for a more extensive list of drugs that inhibit CYP3A4 and p-glycoprotein.

Select Drug Interactions with Colchicine ¹	
Interacting Drug	Mechanism for Interaction*
Aprepitant (e.g., <i>Emend</i>)	Moderate CYP3A4 inhibition
Atazanavir (e.g., <i>Reyataz</i>)	Strong CYP3A4 inhibition
Clarithromycin (e.g., <i>Biaxin</i>)	Strong CYP3A4 inhibition
Cyclosporine (<i>Neoral</i> , etc)	P-glycoprotein inhibition
Darunavir (e.g., <i>Prezista</i>) alone or WITH ritonavir	Strong CYP3A4 inhibition
Digoxin	P-glycoprotein substrate**
Diltiazem	Moderate CYP3A4 inhibition
Erythromycin	Moderate CYP3A4 inhibition
Fibrates (e.g., fenofibrate, gemfibrozil)	Pharmacokinetic/pharmacodynamic interaction**
Fluconazole (e.g., <i>Diflucan</i>)	Moderate CYP3A4 inhibition

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Select Drug Interactions with Colchicine¹	
Interacting Drug	Mechanism for Interaction*
Fosamprenavir (e.g., <i>Lexiva</i> [U.S.], <i>Telzir</i> [Canada])	Moderate CYP3A4 inhibition
Fosamprenavir (e.g., <i>Lexiva</i> [U.S.], <i>Telzir</i> [Canada]) WITH ritonavir	Strong CYP3A4 inhibition
Grapefruit and Grapefruit juice***	Moderate CYP3A4 inhibition
Indinavir (<i>Crixivan</i> [U.S.])	Strong CYP3A4 inhibition
Itraconazole (e.g., <i>Sporanox</i>)	Strong CYP3A4 inhibition
Ketoconazole	Strong CYP3A4 inhibition
Lopinavir/Ritonavir (e.g., <i>Kaletra</i>)	Strong CYP3A4 inhibition
Nefazodone (e.g., <i>Serzone</i> [discontinued], generics [U.S.])	Strong CYP3A4 inhibition
Nelfinavir (<i>Viracept</i>)	Strong CYP3A4 inhibition
Ranolazine (e.g., <i>Ranexa</i> [U.S.])	P-glycoprotein inhibition
Ritonavir (e.g., <i>Norvir</i>)	Strong CYP3A4 inhibition
Saquinavir (<i>Invirase</i>) alone or WITH ritonavir	Strong CYP3A4 inhibition
Statins (e.g., atorvastatin, simvastatin, lovastatin, pravastatin, fluvastatin)	Pharmacokinetic/pharmacodynamic interaction**
Telithromycin (<i>Ketek</i>)	Strong CYP3A4 inhibition
Tipranavir (<i>Aptivus</i>) alone or WITH ritonavir	Strong CYP3A4 inhibition
Verapamil	Moderate CYP3A4 inhibition

*Dose colchicine according to corresponding category in *Dosing and Dose Adjustments for Colchicine* section.

**Increased risk for myopathy and rhabdomyolysis. Monitor patients for muscle pain, tenderness, or weakness.^{1,5,6}

***Should not be consumed while taking colchicine.^{1,4} If grapefruit (including juice) is consumed during treatment with colchicine, monitor patients closely for adverse effects.⁴

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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