

Can I split my dose for better tolerance?

Yes, you can, especially if you are experiencing stomach cramping, abdominal pain, diarrhea or vomiting. The total dose may be taken once daily or divided into morning, noon and evening. Other options for minimizing the gastrointestinal effects of colchicine, are to temporarily reduce dairy intake, add antidiarrheal and spasmolytic agents, as well as a stomach protector (e.g. Omeprazole, Pepcid). If you are experiencing diarrhea episodes, please make sure to increase your intake of electrolyte fortified fluids (i.e. Gatorade, Pedialyte, etc).

For better tolerance, colchicine should be started at the lowest subtherapeutic dose, which can be achieved by splitting the 0.6mg dose in half, in case of severe intolerance. Colchicine should not be increased if the patient is already experiencing diarrhea, as there is often an adjustment period to tolerating the medication.

As soon as side effects subside, the dose can be increased incrementally by 0.6mg. Please allow several days before increasing the prescribed dose. Additionally, DO NOT increase the dose if it has not been recommended by your rheumatologist/immunologist or treating clinician.

The majority of adult FMF patients need approximately one month to reach the standard dose of 1.8mg, this is different for other diseases.

Are colchicine brands different?

Yes, patients have known for years that there are differences among the colchicine brands. Individual patients may tolerate or respond differently to the various preparations. This difference may be attributed to fillers and pharmacokinetic properties. If you do not tolerate a certain brand, your physician may prescribe an alternative for better efficacy and tolerability.

Can colchicine affect my liver?

Colchicine is primarily metabolized by the liver and excreted by the kidneys. Daily use in some patients can cause liver enzymes to be elevated.

For this reason, liver enzymes and complete blood count (CBC) should be monitored regularly in FMF/ autoinflammatory patients treated with colchicine or any other medication. This is particularly important in the first 3 months of use. If your liver enzymes are elevated greater than twice the normal upper limit, colchicine should be reduced or stopped, under medical supervision. If the patient cannot tolerate colchicine, other alternatives should be considered, including biologics such as IL-1 inhibitors.

I am on colchicine but still flaring.

The persistence of attacks or subclinical inflammation represents the need to increase your colchicine dose. Please consult with your physician as your dose may need to be adjusted. Certain patients may require a biological medication to achieve better symptom control.

Is it possible to overdose with colchicine? If so, what are the signs?

Yes, colchicine overdose is a serious complication. High concentrations may cause serious toxicity that can be life threatening. Ingesting higher than recommended doses may cause abdominal cramping, vomiting, or diarrhea. There are 3 stages of toxicity:

Stage 1 manifests with gastrointestinal symptoms with a cholera-like syndrome associated with dehydration, shock, acute renal failure, acute liver failure and even seizures.

Stage 2 develops 24–72 hours or may last several weeks and is dominated by multiorgan failure, including bone marrow failure, renal insufficiency, adult respiratory distress syndrome, arrhythmias, disseminated intravascular coagulation, neuromuscular disturbances, coma or death.

Stage 3 is characterized by recovery of bone marrow and rebound leukocytosis, resolution of organ failure and alopecia. If you have overdosed on colchicine, please seek medical assistance immediately.

Do MEFV carriers also need to take colchicine?

If the patient is symptomatic, regardless of carrier status (one/heterozygous, several or no variants), you require colchicine treatment from your physician. Symptom-free carriers DO NOT require treatment.

Main reference:

Ozen S, Demirkaya E, Erer B, et al. EULAR recommendations for the management of Familial Mediterranean Fever. *Annals of the Rheumatic Diseases* 2016;75:644-651.

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Familial Mediterranean Fever & Autoinflammatory Diseases

COLCHICINE



ENGLISH

What is colchicine?

Colchicine is an alkaloid extracted from autumn crocus (*Colchicum autumnale*), and its use dates back over 4000 years. Its therapeutic use has been well documented in gout and Familial Mediterranean Fever (FMF). It is also used to treat other conditions such as Behçet's disease (BD), amyloidosis, pericarditis, coronary artery disease, and other inflammatory and fibrotic conditions.

Colchicine is also broadly used for treating other autoinflammatory diseases such as HIDS, CAPS, TRAPS, PFAPA, etc. Colchicine has an analgesic and anti-inflammatory effect, and is effective on a variety of ulcers. Colchicine is available in the form of tablets, capsules, liquid (for children), and also intravenously in a hospital environment.

Why is colchicine important?

Colchicine is the mainstay of treatment for patients with Familial Mediterranean Fever (FMF) given that it reduces the frequency, duration and severity of the flares. It also prevents the development of amyloidosis. For colchicine to be effective, it needs to be taken daily, and not just during a flare. Colchicine toxicity is uncommon, unless combined with other medications or in the case of overdose. Once a patient's appropriate dose is established for symptom control, it should NOT be reduced.

How much colchicine is it safe to take?

Colchicine may be increased up to a daily dose of 2mg in children and 3mg in adults, or the maximum tolerated dose by the patient.

How do I know if my doctor should be increasing my colchicine dose?

The persistence of symptoms, flares or subclinical inflammation, represents an indication to increase your colchicine dose. Please contact your doctor to discuss breakthrough symptoms and request a dose increase. DO NOT increase your dose without your doctor's approval.

Food & Alcohol interactions with colchicine

Grapefruit may interfere with your body's ability to process colchicine by increasing the levels in your body, resulting in additional side effects.

If you regularly consume alcohol while on colchicine, it is recommended you speak with your physician to ensure there are no interactions or associated risks.

What medications are contraindicated with colchicine?

Colchicine SHOULD NOT be taken together with certain antibiotics and other drugs such as:

- Clarithromycin, Erythromycin or Telithromycin (antibiotics)
- Ritonavir, Atazanavir, Nelfinavir, Saquinavir or Indinavir (for HIV infection)
- Cyclosporine (for immune suppression and in a variety of autoimmune diseases)
- Fluconazole, Ketoconazole or Itraconazole (for the treatment of fungal infections)
- Verapamil, diltiazem (used for hypertension or angina pectoris)
- Aprepitant (for the prevention of acute nausea and vomiting)
- Quinidine, Amiodarone (for the treatment of cardiac arrhythmias)
- Nefazodone (antidepressant)

→ If you are taking other types of medications, including supplements, in addition to colchicine, please check with your pharmacist with regards to any possible interactions.

Can patients be resistant or intolerant to colchicine?

Yes, approximately 5 to 10% of patients are considered to be resistant or intolerant to colchicine. Resistant patients will not have any improvement or worsening of symptoms regardless of colchicine dose. Intolerant patients tend to have adverse reactions that will be a cause for discontinuation of treatment.

Key factors in assessing colchicine resistance include flare frequency and severity, levels of acute phase reactants, colchicine dosage and composition, and treatment compliance. Promising clinical results have been obtained with biologics targeting interleukin-1 in colchicine-resistant or -intolerant patients with FMF.

Is it safe to take colchicine during pregnancy and breastfeeding?

Yes, colchicine may be safely used during conception, pregnancy and breastfeeding. Many studies on large cohorts have proven that colchicine is safe for mother and unborn baby. Colchicine SHOULD NOT be discontinued as it may lead to premature contractions, early delivery or abortion.

Breastfeeding while taking colchicine is safe for both mother and baby.

What labs should be monitored when on colchicine?

Laboratory tests are recommended to monitor liver enzymes, complete cell blood count, kidney function, creatinine phosphokinase (CPK), and to identify proteinuria. The preferred acute phase reactants (APR) are CRP, ESR, and SAA protein (Serum Amyloid A).

Monitoring CRP, ESR and SAA at least every 3 months is required during dose escalation in patients with active disease, to determine the necessary colchicine dose. Disease severity and frequency of flares must be considered when deciding on an individualized colchicine dose.

Does colchicine also help with chronic arthritis?

FMF patients with chronic arthritis may need colchicine and additional medications such as DMARDs and biologics (IL-1 inhibitors), to have effective symptom control. The joint pain afflicting FMF patients often resembles spondyloarthritis with sacroiliitis, peripheral monoarthritis or oligoarthritis.

What if I forget to take my colchicine?

If you forget to take a dose, take it as soon as you remember unless it is nearly time for your next dose, in which case, leave out the missed dose. Do not take two doses together to make up for a forgotten dose.

Do men need to stop colchicine prior to conception?

In general, men do not need to stop colchicine prior to conception. However, in the rare case of azoospermia or oligospermia, proven to be related to colchicine by your doctor, temporary dose reduction or discontinuation may be required. If colchicine is discontinued, anti-IL-1 treatment may be used for about 3 months allowing recovery of the testes and symptom management. Colchicine can then be resumed after successful conception.

Do children metabolize colchicine faster?

Yes, they do. The doses for children and adults are fairly similar due to children metabolizing the medication very efficiently. Thus, doses can be the same. However, often children are given a lower dose to commence treatment.

Is my baby too young for colchicine?

The answer is NO. Colchicine is a safe drug, even in infancy.