

Frequently Asked Questions

What ingredients are in Limbrel?

Limbrel contains flavocoxid, a natural proprietary blend of flavonoids, baicalin and catechin, from the plants *scutellaria baicalensis* and *acacia catechu* respectively. Flavonoids are a family of healthful nutrients generally found in colored vegetables, fruits, red wine, dark chocolate, and green tea. Baicalin and catechin have been studied extensively and are recognized for their anti-inflammatory and antioxidant properties, as well as their safety profile.

Who should not take Limbrel?

Limbrel is not intended for patients with hypersensitivity to flavonoids. If you are taking the form of Limbrel with citrated zinc bisglycinate, zinc sensitivities should be considered. Limbrel has not been tested among pregnant or lactating women, pediatric patients, or patients with an active bleeding gastrointestinal ulcer. If you experience any discomfort while taking Limbrel, please inform your doctor immediately.

What should I know about side effects?

Because of its natural ingredients, Limbrel has an excellent safety profile with a low incidence of side effects. The most common side effects reported are nausea, diarrhea, and flatulence; which are often mild and do not require discontinued use. Many patients find relief from any stomach upset by taking Limbrel with food. If you experience any discomfort, please inform your physician immediately.

There are two types of Limbrel products. One with flavocoxid alone, and one with flavocoxid and citrated zinc bisglycinate. Some people have difficulty tolerating high dose concentrated flavonoids. For many, zinc chelate may help manage the initial response to the high dose of flavonoids in Limbrel. If you experience mild stomach upset, check with your doctor if Limbrel with zinc may be better choice for you.

As with all anti-inflammatory agents, Limbrel may occasionally cause elevations of liver function tests. Your doctor should monitor for this as per his/her usual procedures.

Is Limbrel safe for your stomach?

Limbrel is well tolerated by people with a high risk or history of gastrointestinal (GI) upset.^{3,5} In post market studies, Limbrel has shown a lack of serious upper GI reactions like ulcers.⁶

Are there drug interactions?

Tests suggest no major drug interactions with Limbrel. If any drug interaction is suspected, inform your doctor immediately.

Can patients take Limbrel and be on warfarin (Coumadin®)?

Limbrel has been shown to be safe for patients who are also taking warfarin⁷. However, following usual clinical practice, physicians are advised to check prothrombin time one to two weeks after starting Limbrel and then intermittently, in patient's anticoagulated with warfarin.

Limbrel 500
(flavocoxid and citrated zinc bisglycinate) 500 mg/50 mg

Limbrel 500
(flavocoxid and citrated zinc bisglycinate) 500 mg/50 mg

Tough on Osteoarthritis Easy on Your Stomach



Limbrel is as effective as naproxen with a superior GI safety profile

- Safe and effective for long-term management of osteoarthritis symptoms
- Unlike traditional NSAIDs, Limbrel works on underlying metabolic causes of joint discomfort

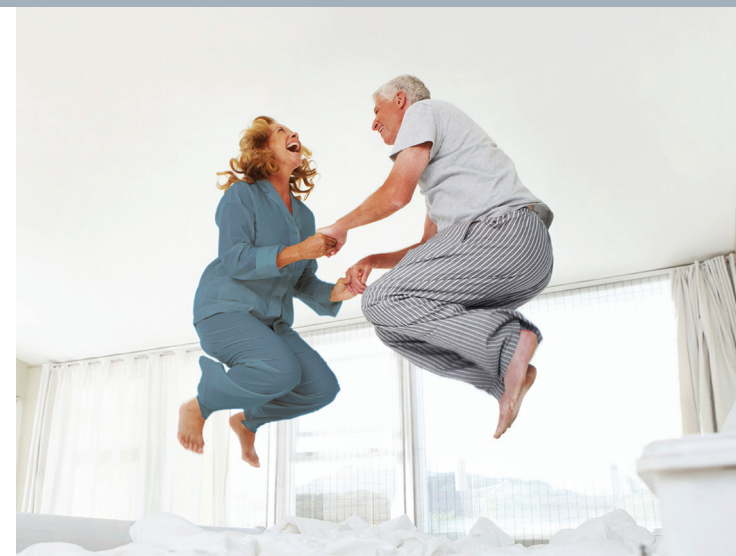


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Call **1-888-LIMBREL** or **1-888-546-2735**

Limbrel is a prescription Medical Food product for the clinical dietary management of the metabolic processes of osteoarthritis under a physician's supervision. Full prescribing information is available at www.limbrel.com. © 2015 Primus Pharmaceuticals, Inc. All rights reserved. ISS. 0115 #10073



Tough on Osteoarthritis, Easy on Your Stomach.



Now you can safely and effectively manage your osteoarthritis (OA) with Limbrel®

Osteoarthritis (OA)

Osteoarthritis is traditionally known as a degenerative joint disease caused either by trauma or wear and tear. OA is a chronic condition and is characterized by cartilage breakdown in the joints leading to discomfort and stiffness. However, after initial damage, metabolic imbalances which regulate the body's inflammatory process lead progressively to chronic disease.

GI side effects from NSAIDs

NSAIDs (nonsteroidal anti-inflammatory drug) are very often prescribed for osteoarthritis because they are effective in reducing symptoms like joint discomfort and swelling. Patients need to be aware that NSAIDs, both prescription and over-the-counter brands, can cause side effects in some people who take them. The most common are GI (gastrointestinal) side effects, from mild stomach upset to life-threatening gastric ulcers. If you have these related side effects with other OA medications, or are concerned about long-term GI side effects, Limbrel may be a better alternative for you.



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Unique way that Limbrel works

Limbrel is a non-NSAID prescription made with natural ingredients that is safe and effective for the long-term management of osteoarthritis symptoms. Unlike traditional chronic OA pain medications that treat the symptoms (like NSAIDs), Limbrel works on underlying metabolic causes of joint discomfort.¹



Limbrel is a medical food, which is regulated by the FDA, but in a unique class separate from drugs and dietary supplements. Limbrel contains only ingredients that have been designated as GRAS (Generally Recognized As Safe)

for wide populations, a strict safety standard set by the FDA. Medical foods are intended for the dietary management of a disease, and must be used under a physician's supervision.

Medical foods are prescribed for people with ongoing chronic diseases. Limbrel is indicated for the dietary management of osteoarthritis, rebalancing metabolic processes that are specific to OA.

What to expect

Limbrel has a gradual onset of action and it might take up to 4 weeks for initial results, and you may continue to see improvement for up to 90 days.¹ Because Limbrel works metabolically, and builds up in the system gradually, the full therapeutic effect takes time. In order to obtain the intended results of Limbrel, be sure to take the full dose of your medication daily as prescribed by your physician.



In clinical trials, Limbrel works for the majority of people who use it at the recommended dose of 2x a day for a minimum of 30 days. The effect of Limbrel can depend on individual differences in metabolism, nutritional status, use of certain vitamins or supplements, and the severity of the osteoarthritis. Unlike traditional NSAIDs, it does not cause GI ulceration or have black box safety warnings about extended use. If you haven't seen signs of improvement after the first month, then discuss with your physician if Limbrel is the right choice for you.

How to take Limbrel

Take one capsule about every 12 hours, or as directed by your physician. Limbrel is safe to be taken with or without food. Taking Limbrel 1 hour before or after meals helps to moderately increase the absorption. If any indigestion occurs, taking with food is recommended. Limbrel can be taken with over-the-counter & prescription NSAID pain relievers for short periods of time (7-10 days) as needed, however combining NSAIDs and any selective COX-2 inhibitors with Limbrel will inhibit its effectiveness.



If you forget to take your Limbrel, then resume your normal number of capsules on your regular schedule as prescribed.

Visit www.limbrel.com
Call 1-888-LIMBREL or 1-888-546-2735

References: 1. Burnett BP, Bitto A, Sqadrito F, Levy RM, Pillai L. 2011. Flavocoxid Inhibits Phospholipase A2, Peroxidase Moieties of the Cyclooxygenases (COX), 5-Lipoxygenase, Modifies COX-2 Gene Expression and Acts as an Antioxidant. *Mediators Inflamm.* 2011;385780, published online June 22, doi: 10.1155/2011/385780. 2. Levy R, Saikovskiy R, Schmidt E, Khokhlov A, Burnett BP. 2009. Efficacy of flavocoxid compared with naproxen in subjects with osteoarthritis of the knee: a randomized, double-blind pilot study. *Nutr Res.* 29(5):298-304. 3. Levy R, Khokhlov A, Kopenkin S, Bart B, Ermolova T, Kantemirova R, Mazurov V, Bell M, Caldron P, Pillai L, Burnett BP. Efficacy and safety of flavocoxid, a novel therapeutic, compared with naproxen: a randomized multicenter controlled trial in subjects with osteoarthritis of the knee. *Advances in Therapy.* 2010; 27:731-42. 4. Levy RM, Khokhlov A, Kopenkin S, Bart B, Ermolova T, Kantemirova R, Mazurov V, Bell M, Caldron P, Pillai L, Burnett BP. 2010b. Efficacy and safety of flavocoxid compared with naproxen in subjects with osteoarthritis of the knee—a subset analysis. *Adv Ther.* 27(12):953-62. 5. Pillai L, Burnett BP, Levy RM for the GOAL Study Cooperative Group. Open-label, post-marketing study of flavocoxid, a novel dual pathway inhibitor anti-inflammatory agent of botanical origin: the GOAL study. *Current Medical Research and Opinion.* 2010; 26(5):1055-1063. 6. Data on file, post marketing surveillance report, June 2014. 7. Pillai L, Levy R, Yimam M, Zhao Y, Jia Q, Burnett BP. Flavocoxid, an anti-inflammatory agent of botanical origin, does not affect coagulation or interact with anticoagulation therapies. *Advances in Therapy.* 2010; 27(6):400-11