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A New Approach...  
in Osteoarthritis (OA)

**Limbrel™**  
(flavocoxid) 250 mg/500 mg  
CAPSULES

Safety that Works... in OA

#### How soon will I feel an effect from Limbrel?

It varies depending on the severity of OA, individual differences in metabolizing concentrated flavonoid ingredients, and if you have recently stopped taking other OA prescription products prior to taking Limbrel. In clinical practice, physicians find that patients with mild to moderate OA feel an effect of Limbrel in 4-5 days after taking Limbrel, while others may feel an effect in 5-10 days or longer. Physicians may increase the loading strength of Limbrel to help patients feel an effect sooner.

#### What should I know about side effects?

Limbrel represents a whole new approach to managing osteoarthritis (OA) by addressing the dietary imbalances of the metabolic processes involved in the joint disease, rather than merely focusing on the symptoms of OA. The fact that Limbrel is neither a drug nor an alternative to any drugs is reassuring to many physicians and patients. (See *Limbrel's key ingredients* for its Generally Recognized As Safe or GRAS status.) Safe flavonoid ingredients combined with unique effects on dual inhibition and antioxidant action are the foundations of Limbrel's safety.

The side effects of Limbrel have generally been mild and infrequent including some nausea and diarrhea, occasional heartburn, skin rash, joint pain and, rarely, joint swelling. There has been no serious adverse events reported to-date in actual in-market usage of Limbrel.

If you experience any discomfort while taking Limbrel, inform your doctor immediately.

#### Who should not take Limbrel?

Limbrel is not intended for patients with hypersensitivity to flavonoids. Flavonoids are a family of beneficial ingredients generally found in colored vegetables, fruits, red wine and green tea. Limbrel has not been tested among pregnant or lactating women, pediatric patients, or patients with an active bleeding gastrointestinal ulcer.

#### How to take Limbrel?

Please follow physician's directions at all times when taking Limbrel. The recommended usage is 1 capsule (250 mg) every 12 hours, and may be increased to two or more capsules (250 mg) every 12 hours, as directed by a physician. Limbrel is also available in 500 mg capsules. Physicians have found that some OA patients may require a higher strength of Limbrel due to their OA severity or individual differences in metabolizing concentrated flavonoid ingredients. For some patients who have recently stopped using other OA prescription products, some physicians have reported good patient responses to taking Limbrel 500 mg every 12 hours, then slowly drop down to a 250 mg twice daily maintenance schedule.

#### What should I do if I forgot to take Limbrel?

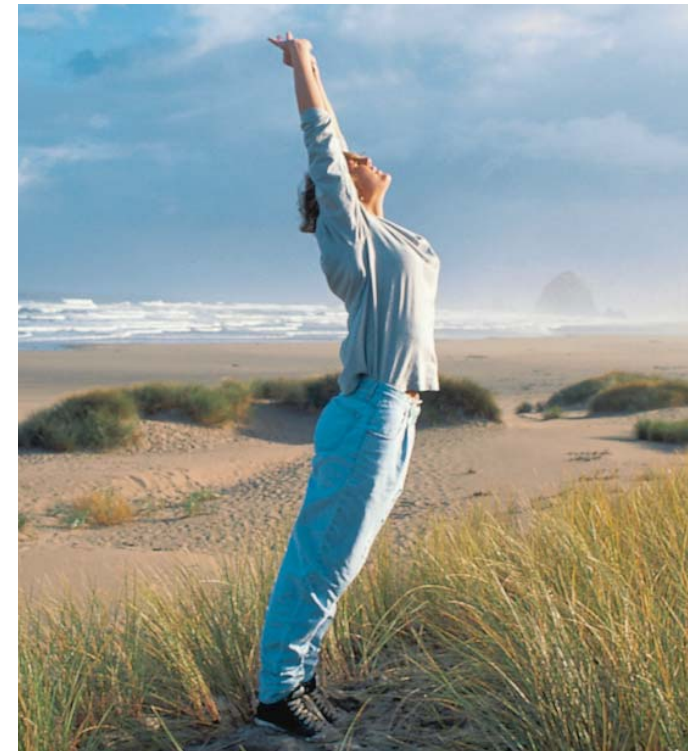
Take the prescribed number of capsules as soon as you remember, and resume the normal schedule as directed by a physician. There are no negative effects from missing a capsule of Limbrel.

#### Take with or without other foods?

Limbrel is safe to be taken with or without other foods. Taking Limbrel 1 hour before or after meals helps to moderately increase the absorption of its key ingredients into the blood stream. If any indigestion occurs, Limbrel is recommended to be taken with other foods.



Limbrel is a prescription medical food product for the safe clinical dietary management of the metabolic processes of osteoarthritis under a physician's supervision. Full prescribing information available at [www.limbrel.com](http://www.limbrel.com) or call 1-888-LIMBREL. © 2006 Primus Pharmaceuticals, Inc. All rights reserved. ISS. 0506 #10060



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### Is osteoarthritis (OA) a degenerative or a metabolic disease?

It is both. Osteoarthritis (OA) is traditionally known as a degenerative joint disease caused by traumatic injury or wear and tear. OA is characterized by the breakdown of cartilage in the joints, leading to discomfort, stiffness and loss of movement. However, after the initial damage, the progression of OA generally is worsened by metabolic imbalances of arachidonic acid derived fatty acids which regulate the inflammatory processes in the body. Arachidonic acid is essential to build membranes in the body, but it is also inflammatory when in excess and could lead to further deterioration of cartilage over time. OA is the most common type of arthritis, and it can affect any joint, especially weight-bearing joints such as knees, hips, feet or back.

### How does Limbrel work?

Limbrel works through dietary management to restore the underlying metabolic balance of inflammatory fatty acids in OA, rather than “treating symptoms” as drugs do. Limbrel’s dietary management approach to OA ultimately results in dual inhibition as well as antioxidant action, and both effects are important to managing OA.

*Dual Inhibition* refers to inhibition of COX (cyclooxygenase) and LOX (lipoxygenase) enzyme systems, two major inflammatory pathways involved in OA that process arachidonic acid into inflammatory metabolites. Limbrel is the first and only marketed prescription product that balances COX-1 & COX-2 metabolism by inhibiting both enzymes equally, in addition to a relatively equal inhibition of 5-LOX. Limbrel is not a selective COX-2 inhibitor. The COX & LOX dual inhibition action of Limbrel helps to minimize systemic side effects while effectively manages the metabolic imbalances of OA.

*Antioxidant Action* refers to the “absorption” of free radicals (or reactive oxygen species). Free radicals in the joints have been found to directly break down cartilage over time and trigger other inflammatory processes in OA. Limbrel is a potent antioxidant that helps to “absorb” free radicals in the joints. The antioxidant potency score of Limbrel is higher than many well-known antioxidants such as Vitamin C and E, as well as concentrated sources of antioxidants such as blueberry juice.

### What are Limbrel’s key ingredients?

Limbrel consists of flavocoxid, a proprietary blend of natural flavonoids from two plants called *Scutellaria baicalensis* and *Acacia catechu*. These plants have been used in foods and medicinal products for thousands of years in other countries, especially in Japan and China.

The two key flavonoids, baicalin and catechin, in Limbrel have been studied extensively around the world and are recognized for their anti-inflammatory and antioxidant properties, as well as their exceptional safety profile. Limbrel’s ingredients have achieved GRAS (Generally Recognized As Safe) status, a strict food safety standard set by the FDA.

Flavonoids in general are the healthful ingredients that give color to vegetables, fruits, cocoa, red wine and green tea. However, a simple change in diet would not provide enough flavonoids needed to manage the metabolic processes of OA. In practical terms, an OA patient would need to consume 3 or 4 pounds of fruits and vegetables daily in order to obtain the high concentration levels of flavonoids in the body that Limbrel provides.

### Is Limbrel a drug or dietary supplement?

Limbrel is neither a drug nor a dietary supplement. Limbrel is a prescription medical food product. Medical foods are also regulated by the FDA, but are in a unique class separate from drugs and dietary supplements. The effectiveness of a medical food must be proven by acknowledged sound laboratory and clinical science. A medical food is intended for the dietary (metabolic) management of a disease and must be used under physician (MD or DO) supervision. Although the term “food” sounds deceptively common, it actually speaks to the safety of medical food products because they must contain only ingredients that have been designated as GRAS (Generally Recognized As Safe).



## PATIENT FREQUENTLY ASKED QUESTIONS

### Can Limbrel be taken with NSAIDs?

Limbrel should not be taken together with NSAIDs such as naproxen, ibuprofen, aspirin (except baby aspirin for cardio-protection), or with any selective COX-2 inhibitors on a chronic basis. NSAIDs and selective COX-2 inhibitors will destroy Limbrel’s “balancing” effect on the COX and LOX pathways and lead to serious side effects. Limbrel may be used while taking acetaminophen since acetaminophen is not a NSAID and does not impact the COX and LOX pathways.

### Drug interactions?

Preclinical test results suggest no major drug interactions with Limbrel. Limbrel has been taken by patients for over 2 years, and there has been no drug interactions reported to date.

If any drug interaction is suspected, inform your doctor immediately.

### Food allergies?

Limbrel contains primarily two flavonoids (baicalin and catechin). Other (or “inactive”) ingredients of Limbrel are magnesium stearate, microcrystalline cellulose, Maltodextrin NF, gelatin (as the capsule material), and FD&C Blue #1 and Green #3 (approved food colorings). Limbrel does not contain fructose, glucose, sucrose, lactose, gluten or flavors. Limbrel does not contain any parts or ingredients of nuts, soy, corn, wheat, sugar, or any fruits and vegetables.

Patients with hypersensitivity to flavonoids should not take Limbrel. Some patients may experience indigestion while taking Limbrel, perhaps because the flavonoids in each capsule of Limbrel are in such high concentration levels, equivalent of almost 3 or 4 pounds of fruits and vegetables.

If you experience any discomfort while taking Limbrel, please inform your doctor immediately.

### Why not available OTC if Limbrel is so safe?

Limbrel is only available by prescription, and not available over-the-counter (OTC). Limbrel is regulated by the FDA as a medical food product, which must be used under physician supervision according to federal regulations. Therefore, Limbrel is only available by prescription to prevent possible use without physician supervision.

Continued...

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