

## Flavocoxid (Limbrel®) manages osteoarthritis through modification of multiple inflammatory pathways: a review

Bruce P. Burnett\* and Robert M. Levy

Primus Pharmaceuticals, Inc., 4725 N. Scottsdale Road, Suite 200, Scottsdale, AZ 85251

\*Corresponding Author: Bruce P. Burnett, PhD, Primus Pharmaceuticals, Inc., 4725 N. Scottsdale Road, Suite 200, Scottsdale, AZ 85251, USA

Submission date: September 16, 2012, Acceptance date: November 1, 2012; Publication date: November 3, 2012

### ABSTRACT:

Limbrel (flavocoxid) is marketed as an FDA-regulated medical food for the clinical dietary management of osteoarthritis (OA) to be used under physician supervision. Flavocoxid is composed of a >90% mixture of baicalin and catechin and represents a non-targeted anti-inflammatory which works differently than non-steroidal anti-inflammatory drugs (NSAIDs) that bind to and only inhibit the *cyclooxygenase* moieties of COX-1 and COX-2. Flavocoxid binds to and weakly modulates the *peroxidase* activity of the COX enzymes permitting low level expression of prostaglandins (PGs), prostacyclin (PGI<sub>2</sub>) and thromboxane (TxA<sub>2</sub>). In addition, flavocoxid weakly inhibits phospholipase A<sub>2</sub> (PLA<sub>2</sub>) and 5-lipoxygenase (5-LOX) as well as increases IκBα and prevents nuclear factor kappa B (NFκB) activation/induction of inflammatory genes such as tumor necrosis factor-alpha (TNFα), interleukin-1β (IL-1 β), IL-6, COX-2, inducible nitric oxide synthase (iNOS) and 5-LOX. In clinical studies, flavocoxid shows equivalent efficacy to naproxen with statistically fewer renal (edema) and upper gastrointestinal (GI) side effects, does not affect platelet function and bleeding times, does not change international normalized ratio (INR) in warfarinized patients, is well-tolerated in patients with previous NSAID-induced GI side effects, and decreases or eliminates the use of gastroprotective medications in patients who previously required them to tolerate NSAIDs. With its broad, non-targeted and multiple weak activities which result in fewer side effects compared to NSAIDs, flavocoxid represents a different way managing OA by working on the underlying and multiple causes of cartilage degradation as well as joint inflammation.

**Keywords:** Flavocoxid, Limbrel, osteoarthritis, inflammatory pathways, and medical foods