# Iroko's ZORVOLEX™ Now Available

## *First NSAID Using SoluMatrix Fine Particle Technology™ Available for the Treatment of Mild to Moderate Acute Pain in Adults*

PHILADELPHIA, JANUARY 3, 2014 — Iroko Pharmaceuticals, LLC, a global specialty pharmaceutical company dedicated to advancing the science of analgesia, announced today that ZORVOLEX™ (diclofenac) capsules, a nonsteroidal anti-inflammatory drug (NSAID), is now available in 18 mg and 35 mg dosage strengths at pharmacies across the United States. ZORVOLEX was approved by the U.S. Food and Drug Administration (FDA) in October 2013 for the treatment of mild to moderate acute pain in adults[1].

"We are pleased that ZORVOLEX is now available in U.S. pharmacies, as we are able to provide a lower dose NSAID option to prescribers and patients," said John Vavricka, President and CEO of Iroko Pharmaceuticals. "ZORVOLEX is approved by the FDA at dosage strengths that are 20 percent lower than other currently available diclofenac products, filling an important market need for additional treatment options in pain management."

Systematic reviews of observational studies have shown that serious NSAID adverse events, including cardiovascular thrombotic events, myocardial infarction, stroke, gastrointestinal ulcers, gastrointestinal bleeds[2] and renal events such as acute renal failure[3] are dose related[4]. As such, the FDA and professional medical organizations including the American Heart Association, American Gastroenterological Association, and The American College of Rheumatology, recommend that NSAIDs be used at the lowest effective dose for the shortest possible duration of time consistent with individual patient treatment goals[5].

**About ZORVOLEX**

ZORVOLEX is the first and only FDA-approved NSAID developed using proprietary SoluMatrix Fine Particle Technology™. ZORVOLEX contains diclofenac as submicron particles that are approximately 20 times smaller than their original size. The reduction in particle size provides an increased surface area, leading to faster dissolution. ZORVOLEX was developed to align with recommendations from FDA and other professional medical organizations that NSAIDs be used at the lowest effective dose for the

shortest possible duration of time consistent with individual patient treatment goals. For more information, visit www.zorvolex.com.

**ZORVOLEX is indicated for the treatment of mild to moderate acute pain in adults.**

**Important Safety Information about ZORVOLEX**

**Cardiovascular Risk**

**Nonsteroidal anti-inflammatory drugs (NSAIDs) may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.**

**ZORVOLEX is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.**

**Gastrointestinal Risk**

**NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.**

ZORVOLEX is contraindicated in patients with: a known hypersensitivity to diclofenac or its inactive ingredients; a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs.

ZORVOLEX should be used at the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Elevation of one or more liver tests may occur during therapy with ZORVOLEX. Physicians should measure transaminases (ALT and AST) periodically in patients receiving long-term therapy with ZORVOLEX. ZORVOLEX should be discontinued immediately if abnormal liver tests persist or worsen.

NSAIDS, including ZORVOLEX, can lead to the new onset or worsening of existing hypertension which may contribute to the increased incidence of cardiovascular events. Blood pressure should be monitored closely during treatment with ZORVOLEX. NSAIDs may diminish the antihypertensive activity of thiazides, loop diuretics, ACE inhibitors and angiotensin II antagonists.

Fluid retention and edema have been observed in some patients taking NSAIDs. ZORVOLEX should be used with caution in patients with fluid retention or heart failure.

Long-term administration of NSAIDs can result in renal papillary necrosis and other renal injury. ZORVOLEX should be used with caution in patients at greatest risk of this reaction, including the elderly, those with impaired renal function, heart failure, liver dysfunction, and those taking diuretics and ACE inhibitors.

Treatment with ZORVOLEX in patients with advanced renal disease is not recommended.

Anaphylactoid reactions may occur in patients with the aspirin triad or in patients without prior exposure to ZORVOLEX and should be discontinued immediately if an anaphylactoid reaction occurs.

NSAIDs can cause serious skin adverse events such as exfoliative dermatitis, Stevens – Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. ZORVOLEX should be discontinued if rash or other signs of local skin reaction occur.

Starting at 30 weeks gestation, ZORVOLEX and other NSAIDs should be avoided by pregnant women as premature closure of the ductus arteriosus in the fetus may occur.

Concomitant administration of diclofenac and aspirin or anticoagulants is not generally recommended because of the risk of increased GI bleeding higher than users of either drug alone.

Most common adverse reactions in clinical trials (incidence ≥2%) include: edema, nausea, headache, dizziness, vomiting, constipation, pruritus, flatulence, pain in extremity, and dyspepsia.

ZORVOLEX capsules do not result in an equivalent systemic exposure to diclofenac as other oral formulations. Therefore, do not substitute similar dosing strengths of other diclofenac products for ZORVOLEX.

Please see full **Prescribing Information** for additional important safety and dosing information.

**About Iroko Pharmaceuticals, LLC**

Iroko is a global specialty pharmaceutical company, based in Philadelphia, dedicated to advancing the science of analgesia. The company develops and globally commercializes pharmaceutical products. In addition to the Iroko products that are marketed worldwide, the company has a robust pipeline of investigational lower dose NSAID products being developed using iCeutica Pty Ltd's proprietary SoluMatrix Fine Particle Technology™. For more information, visit **www.iroko.com**.

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[1] ZORVOLEX Prescribing Information

[2] Rahme E et. al. (2001 Aug). Cost of prescribed NSAID-related gastrointestinal adverse events in elderly patients. Br J Clin Pharmacol. 52(2): 185-192.

[3] Annual Review of Medicine, Nonsteroidal Antiinflammatory Drugs and Renal Function. Vol. 35: 411-428. DOI: 10.1146/annurev.med.35.020184.002211.

[4] Risser A. (2009 Dec). NSAID Prescribing Precautions. Am Fam Physician. 80(12):1371-1378.

[5] U.S. Food and Drug Administration. Public Health Advisory - FDA Announces Important Changes and Additional Warnings for COX-2 Selective and Non-Selective Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).