

order in adults.

Eli Lilly presented the results of a short-term study of 107 patients aged 13-17 with schizophrenia, comparing 2.5 mg to 20 mg per day of olanzapine to placebo over 4 weeks. The primary efficacy end point—the changes in the Brief Psychiatric Rating Scale-for Chil-

dren (BPRS-C) total score from baseline to end point—found a significantly greater effect among those on olanzapine, with an effect size comparable to that seen in adult studies, according to the company.

In another study of 161 patients aged 13-17 years with bipolar disorder who were in an acute manic or mixed episode, those who received 2.5 mg to 20 mg per day of olanzapine had reductions in the Young Mania Rating Scale (YMRS) total score (the primary efficacy end point) that were significantly greater than the reductions seen

among those on placebo, after 3 weeks of treatment.

In the two studies combined, sedation-related events were the most common adverse events associated with treatment (44% among those on olanzapine, compared with 9% of those on placebo), followed by increases in weight (almost 30%, compared with almost 6%, respectively), and increased appetite (24%, compared with 5.6%, respectively). Among those on olanzapine, 8% had elevated liver enzymes, compared with 1% of those on placebo.

The differences in these adverse events

were all significantly greater among the patients who were taking olanzapine.

In addition to weight gain, increases in fasting glucose, fasting total cholesterol, fasting triglycerides, and prolactin levels have been documented in adolescents treated with olanzapine for 12 weeks or less, and for longer durations, according to Eli Lilly.

The increased risks of weight gain, hyperlipidemia, hyperglycemia, and hyperprolactinemia associated with olanzapine use in adolescents are included in the drug's label, even though the drug has not been approved for this age group. ■

## Votes Mixed on Ziprasidone for Pediatric Bipolar

ADELPHI, MD. — The atypical antipsychotic ziprasidone is effective for the treatment of manic or mixed episodes associated with bipolar disorder in patients aged 10-17 years, a Food and Drug Administration panel advised.

At a meeting in June, the Psychopharmacologic Drugs Advisory Committee voted 12-2 on ziprasidone's efficacy, with 4 abstentions. However, many on the 18-member panel abstained from voting on whether the data had shown the drug was acceptably safe in treating this population. Eight panel members voted in favor of safety, and one panelist voted no on this question. Among the reasons the nine panelists cited for abstaining was that a large number of patients were lost to follow-up in the study.

They also cited ambiguous data on an increase in QTc intervals among children treated with the drug, and the need for more data overall. Study data were presented by Pfizer, which manufactures ziprasidone (Geodon). The drug is already approved for treating schizophrenia and bipolar disorder in adults.

The panel was not asked specifically to rule on whether to recommend approval for treatment of the pediatric population. The FDA usually follows the recommendations of its advisory panels.

At the meeting, study results were presented on 238 patients, aged 10-17 years, with bipolar disorder (manic or mixed episodes) treated with placebo or ziprasidone (40-80 mg/day for those under 45 kg; 80-160 mg/day for those 45 kg or more). Based on the primary efficacy end point—change from baseline in the Young Mania Rating Scale after 4 weeks—there was a highly significant treatment effect similar to the changes observed in studies of adults, according to Pfizer.

Ziprasidone was generally well tolerated over 4 weeks, and for up to 26 weeks in an open-label study. The adverse event profile was similar to that seen in adults, with the exception of sedation and somnolence, which were more common in the pediatric population.

The rate of extrapyramidal symptoms was 24% among those on ziprasidone, compared with almost 8% among placebo. There were no completed suicides, and no increase in suicidality among those on ziprasidone.

In the short-term pediatric study, 3.6% of those on ziprasidone had a QTc interval increase of more than 450 msec vs. 1.2% of those on placebo, Pfizer said.

—Elizabeth Mechatie

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DUE TO MINOR STRAINS, SPRAINS, AND CONTUSIONS

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- A unique way of delivering the proven efficacy of diclofenac in a patch that provides minimal systemic exposure<sup>1,2</sup>
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- Dispensed in boxes of 30 patches
- 2 weeks of therapy = 1 box
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FLECTOR® Patch is indicated for the topical treatment of acute pain due to minor strains, sprains, and contusions.

Carefully consider the potential benefits and risks of FLECTOR® Patch and other treatment options before deciding to use FLECTOR® Patch. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

**Important Safety Information**

**Cardiovascular (CV) risk**

- NSAIDs may cause an increased risk of serious CV thrombotic events, myocardial infarction, and stroke, which can be fatal. This risk may increase with duration of use. Patients with CV disease or risk factors for CV disease may be at greater risk
- FLECTOR® Patch is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery

**Gastrointestinal (GI) risk**

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

FLECTOR® Patch is contraindicated in patients with known hypersensitivity to diclofenac. FLECTOR® Patch should not be given to patients who have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs. Severe, rarely fatal, anaphylactic-like reactions to NSAIDs have been reported in such patients.

FLECTOR® Patch should not be applied to non-intact or damaged skin resulting from any etiology, e.g., exudative dermatitis, eczema, infected lesion, burns or wounds.

NSAIDs, including FLECTOR® Patch, can lead to new onset or worsening of hypertension, contributing to increased incidence of CV events. Fluid retention and edema have been observed in some patients taking NSAIDs. Use with caution in patients with hypertension, fluid retention or heart failure.

A patient with symptoms and/or signs of liver dysfunction, or with a history of an abnormal liver test, should be monitored for a more severe hepatic reaction and therapy stopped. Anemia is sometimes seen in patients receiving NSAIDs and platelet inhibition has been shown to prolong bleeding times.

Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. Renal toxicity has also been seen in patients in whom renal prostaglandins have a compensatory role in maintaining renal perfusion. FLECTOR® Patch is not recommended in patients with advanced renal disease.

NSAIDs, including FLECTOR® Patch, can cause serious skin adverse events without warning such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Overall, the most common adverse events associated with FLECTOR® Patch were skin reactions (pruritus, dermatitis, burning, etc.) at the site of treatment and gastrointestinal disorders (nausea, dysgeusia, dyspepsia, etc.) and nervous system disorders (headache, paresthesia, somnolence, etc.).

In late pregnancy, as with other NSAIDs, FLECTOR® Patch should be avoided because it may cause premature closure of the ductus arteriosus. FLECTOR® Patch is in Pregnancy Category C. Safety and effectiveness in pediatric patients have not been established.

**Please see Brief Summary of full Prescribing Information, including boxed warning, on adjacent page.**

**For more information, please visit [www.FlectorPatch.com](http://www.FlectorPatch.com) or [www.KingPharm.com](http://www.KingPharm.com).**

References: 1. Data on file. King Pharmaceuticals®, Inc. 2. Flector Patch [package insert]. Piscataway, NJ: Alpharma Pharmaceuticals LLC; 2008.





(diclofenac epolamine topical patch) 1.3%

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