

NEW INDICATION

Asenapine for pediatric bipolar disorder

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Asenapine, an atypical antipsychotic sold under the brand name Saphris, was granted a second, pediatric indication by the FDA in March 2015 as monotherapy for acute treatment of manic or mixed episodes of bipolar I disorder in children and adolescents age 10 to 17 (*Table 1*).¹ (Asenapine was first approved in August 2009 as monotherapy or adjunctive therapy to lithium or valproate in adults for schizophrenia and bipolar I disorder.^{1,2})

Dosage and administration

Asenapine is available as 2.5-, 5-, and 10-mg sublingual tablets, the only atypical antipsychotic with this formulation.¹ The recommended dosage for the new indication is 2.5 mg twice daily for 3 days, titrated to 5 mg twice daily, titrated again to 10 mg twice daily after 3 days.³ In a phase I study, pediatric patients appeared to be more sensitive to dystonia when the recommended dosage escalation schedule was not followed.³

In clinical trials, drinking water 2 to 5 minutes after taking asenapine decreased exposure to the drug. Instruct patients not to swallow the tablet and to avoid eating and drinking for 10 minutes after administration.³

For full prescribing information for pediatric and adult patients, see Reference 3.

Safety and efficacy

In a 3-week, placebo-controlled, double-blind trial of 403 patients, 302 children and adolescents age 10 to 17 received asenapine at fixed dosages of 2.5 to 10 mg twice daily; the remainder were given placebo. The Young Mania Rating Scale (YMRS)

Table 1

Asenapine: Fast facts

Brand name: Saphris
Class: Atypical antipsychotic
New indication: Bipolar I disorder in children and adolescents (age 10 to 17)
FDA approval date: March 13, 2015
Manufacturer: Forest Pharmaceuticals
Doses: 2.5 mg, 5, mg, and 10 mg sublingual tablets
Recommended dosing: 2.5 mg twice daily titrated to 10 mg twice daily
Source: Reference 1

total score and Clinical Global Impressions Severity of Illness scores of patients who received asenapine improved significantly compared with those who received placebo, as measured by change from baseline to week 3 (*Table 2*).¹

The safety and efficacy of asenapine has not been evaluated in pediatric bipolar disorder patients age ≤10 or pediatric schizophrenia patients age ≤12, or as an adjunctive therapy in pediatric bipolar disorder patients.

Asenapine was not shown to be effective in pediatric patients with schizophrenia in an 8-week, placebo-controlled, double-blind trial.

The pharmacokinetics of asenapine in pediatric patients are similar to those seen in adults.

Adverse effects

In pediatric patients, the most common reported adverse effects of asenapine are:

- dizziness
- dysgeusia



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Table 2

YMRS total score changes in pediatric bipolar disorder patients

Treatment group	Mean baseline score (SD)	LS mean change from baseline	Placebo-subtracted difference (95% CI)
Asenapine, 2.5 mg twice daily	29.5 (5.7)	-12.8 (0.8)	-3.2 (-5.6, -0.8)
Asenapine, 5 mg twice daily	30.4 (5.9)	-14.9 (0.8)	-5.3 (7.7, -2.9)
Asenapine, 10 mg twice daily	30.1 (5.7)	-15.8 (0.9)	-6.2 (-8.6, -3.8)
Placebo	30.1 (5.7)	-9.6 (0.9)	--

CI: confidence interval; LS: least-square mean; SD: standard deviation; YMRS: Young Mania Rating Scale
Source: Reference 1

Table 3

Common adverse effects of asenapine used as monotherapy for bipolar disorder^a

Adverse effect	Incidence	
	Children and adolescents	Adults
Oral hypoesthesia/paresthesia	27%	4%
Somnolence	24%	24%
Headache	9%	9%
Fatigue	9%	4%
Increased appetite	8%	4%
Dizziness	7%	11%
Dysgeusia	6%	3%
Insomnia	3%	6%
Increased weight	3%	5%
Akathisia	2%	4%
Extrapyramidal symptoms ^b	1%	7%
Dyspnea	1%	4%

^aPediatric dosages: 2.5 mg, 5 mg, 10 mg; adult dosages: 5 mg, 10 mg
^bParkinsonism is a common symptom; the rate of Parkinson-like symptoms in adults is unavailable, however
Source: Reference 3

- fatigue
- increased appetite
- increased weight
- nausea
- oral paresthesia
- somnolence.

Similar adverse effects were reported in the pediatric bipolar disorder and adult bipolar disorder clinical trials (Table 3).³ A complete list of reported adverse effects is given in the package insert.³

When treating pediatric patients, monitor the child’s weight gain against expected normal weight gain.

Asenapine is contraindicated in patients with hepatic impairment and those who have a hypersensitivity to asenapine or any components in its formulation.³

References

1. Actavis receives FDA approval of Saphris for pediatric patients with bipolar I disorder. Drugs.com. <http://www.drugs.com/newdrugs/actavis-receives-fda-approval-saphris-pediatric-patients-bipolar-disorder-4188.html>. Published March 2015. Accessed June 19, 2015.
2. Lincoln J, Preskon S. Asenapine for schizophrenia and bipolar I disorder. *Current Psychiatry*. 2009;12(8): 75-76,83-85.
3. Saphris [package insert]. St. Louis, MO: Forest Pharmaceuticals; 2015.

Clinical Point

The YMRS total scores of patients who received asenapine improved significantly compared with those who received placebo