

SCHIP Short 10 Votes, Negotiations Start Again

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Congress and the Bush administration headed back to the negotiating table in mid-October after the House of Representatives failed to override President Bush's veto of the State Children's Health Insurance Program reauthorization legislation.

The House voted 273-156 to override the President's SCHIP veto, but that was

10 votes short of the needed two-thirds majority.

The House vote was split down party lines, with 229 Democrats and 44 Republicans voting in favor of the SCHIP veto override, and 154 Republicans and 2 Democrats voting against.

SCHIP expired on Sept. 30, but a continuing resolution ensures that the program is funded through Nov. 16.

House Speaker Nancy Pelosi (D-Calif.) has said she aims to bring a new version

of the SCHIP legislation to the floor for a vote ahead of that deadline, Ron Pollack, executive director of Families USA, said in an interview.

Mr. Pollack predicted that compromises would be crafted around the issues that concern the White House, which he calls "myths."

Among those that he noted are: that the law would cover children in families earning up to \$83,000 a year, and that illegal immigrants would be eligible for

coverage. These issues led a majority of House Republicans to vote in line with President Bush, he said.

Dr. Jay E. Berkelhamer, president of the American Academy of Pediatrics, said in a statement that "the rhetoric of those who opposed the legislation to reauthorize SCHIP demonstrated a fundamental misunderstanding of the bill."

Dr. Berkelhamer noted that the legislation would have blocked enrollment of many adults and children the White House has considered not eligible for the program, "while still providing states flexibility and financial support for enrollment of up to 4 million low-income eligible children."

The White House claimed victory after the House failed to override the veto.

"As it is clear that this legislation lacks sufficient support to become law, now is the time for Congress to stop playing politics and to join the President in finding common ground to reauthorize this vital program," according to a White House statement.

Rep. Charles Rangel (D-N.Y.) blasted the Bush administration, saying that the White House was out of touch with the American people. "It is appalling that the administration would declare victory after denying health care to 10 million of the neediest children in America."

The White House said it had appointed a team to negotiate with Congress to make sure at least 500,000 children who currently are eligible for SCHIP, but not receiving benefits, would be enrolled in the program. "If enrolling these children requires more than the 20% funding increase proposed by the President, we will work with Congress to find the necessary money," according to a statement from the White House.

About 6 million children are currently enrolled in SCHIP. The congressional proposal would have increased funding by about \$7 billion a year, adding as many as 4 million children to the SCHIP rolls.

The American College of Physicians said it would push for passage of a new bill, but one that would ensure coverage for those additional children. "The current SCHIP formula does not go far enough," said Dr. David C. Dale, ACP president, in a statement.

Similarly, the American Medical Association said it was committed to expanding coverage. "The number of uninsured kids has increased by nearly 1 million over the past 2 years, and action must be taken to reverse this growing trend," said Dr. Edward Langston, AMA board chair, in a statement.

XYZAL®

(levocetirizine dihydrochloride)

5 mg tablets

Rx only

Brief Summary of Prescribing Information

INDICATIONS AND USAGE

Allergic Rhinitis – XYZAL® is indicated for the relief of symptoms associated with allergic rhinitis (seasonal and perennial) in adults and children 6 years of age and older.

Chronic Idiopathic Urticaria – XYZAL is indicated for the treatment of the uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older.

DOSAGE AND ADMINISTRATION

XYZAL is available as 5 mg breakable (scored) tablets, allowing for the administration of 2.5 mg, if needed. XYZAL can be taken without regard to food consumption.

Adults and Children 12 Years of Age and Older – The recommended dose of XYZAL is 5 mg once daily in the evening. Some patients may be adequately controlled by 2.5 mg once daily in the evening.

Children 6 to 11 Years of Age – The recommended dose of XYZAL is 2.5 mg (1/2 tablet) once daily in the evening. The 2.5 mg dose should not be exceeded because the systemic exposure with 5 mg is approximately twice that of adults (see CLINICAL PHARMACOLOGY, Pharmacokinetics in Full Prescribing Information).

Dose Adjustment for Renal and Hepatic Impairment – In adults and children 12 years of age and older with:

- Mild renal impairment (creatinine clearance [CL_{CR}] = 50-80 mL/min): a dose of 2.5 mg once daily is recommended;
- Moderate renal impairment (CL_{CR} = 30-50 mL/min): a dose of 2.5 mg once every other day is recommended;
- Severe renal impairment (CL_{CR} = 10-30 mL/min): a dose of 2.5 mg twice weekly (administered once every 3-4 days) is recommended;
- End-stage renal disease patients (CL_{CR} < 10 mL/min) and patients undergoing hemodialysis should not receive XYZAL.

No dose adjustment is needed in patients with solely hepatic impairment. In patients with both hepatic impairment and renal impairment, adjustment of the dose is recommended.

CONTRAINDICATIONS

The use of XYZAL is contraindicated in:

- Patients with known hypersensitivity to levocetirizine or any of the ingredients of XYZAL, or to cetirizine. Observed reactions range from urticaria to anaphylaxis (see ADVERSE REACTIONS, Post-Marketing Experience).
- Patients with end-stage renal disease (CL_{CR} < 10 mL/min) and patients undergoing hemodialysis.
- Pediatric patients 6 to 11 years of age with impaired renal function (see USE IN SPECIFIC POPULATIONS, Pediatric Use).

WARNINGS AND PRECAUTIONS

Activities Requiring Mental Alertness – In clinical trials the occurrence of somnolence, fatigue, and asthenia has been reported in some patients under therapy with XYZAL. Patients should be cautioned against engaging in hazardous occupations requiring complete mental alertness, and motor coordination such as operating machinery or driving a motor vehicle after ingestion of XYZAL. Concurrent use of XYZAL with alcohol or other central nervous system depressants should be avoided because additional reductions in alertness and additional impairment of central nervous system performance may occur.

ADVERSE REACTIONS

Use of XYZAL has been associated with somnolence, fatigue, and asthenia (see WARNINGS AND PRECAUTIONS, Activities Requiring Mental Alertness).

Clinical Trials Experience – The safety data described below reflect exposure to XYZAL in 2549 patients with seasonal or perennial allergic rhinitis and chronic idiopathic urticaria in 12 controlled clinical trials of 1 week to 6 months duration. The short-term (exposure up to 6 weeks) safety data for adults and adolescents are based upon eight clinical trials in which 1896 patients (825 males and 1071 females aged 12 years and older) were treated with XYZAL 2.5, 5, or 10 mg once daily in the evening. The short-term safety data from pediatric patients are based upon two clinical trials in which 243 children with seasonal or perennial allergic rhinitis (162 males and 81 females 6 to 12 years of age) were treated with XYZAL 5 mg once daily for 4 to 6 weeks. The long-term (exposure of 4 or 6 months) safety data are based upon two clinical trials in adults and adolescents in which 428 patients (190 males and 238 females) with allergic rhinitis were exposed to treatment with XYZAL 5 mg once daily. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trial of another drug and may not reflect the rates observed in practice.

Adults and Adolescents 12 years of Age and Older – In studies up to 6 weeks in duration, the mean age of the adult and adolescent patients was 32 years, 44% of the patients were men and 56% were women, and the large majority (more than 90%) was Caucasian.

In these trials 43% and 42% of the subjects in the XYZAL 2.5 mg and 5 mg groups, respectively, had at least one adverse event compared to 43% in the placebo group.

In placebo-controlled trials of 1-6 weeks in duration, the most common adverse reactions were somnolence, nasopharyngitis, fatigue, dry mouth, and pharyngitis, and most were mild to moderate in intensity. Somnolence with XYZAL showed dose ordering between tested doses of 2.5, 5 and 10 mg and was the most common adverse reaction leading to discontinuation (0.5%).

Table 1 lists adverse reactions that were reported in greater than or equal to 2% of subjects aged 12 years and older exposed to XYZAL 2.5 mg or 5 mg in eight placebo-controlled clinical trials and that were more common with XYZAL than placebo.

Table 1 Adverse Reactions Reported in $\geq 2\%$ of Subjects Aged 12 Years and Older Exposed to XYZAL 2.5 mg or 5 mg in Placebo-Controlled Clinical Trials 1-6 Weeks in Duration

Adverse Reactions	XYZAL 2.5 mg (n = 421)	XYZAL 5 mg (n = 1070)	Placebo (n = 912)
Somnolence	22 (5%)	61 (6%)	16 (2%)
Nasopharyngitis	25 (6%)	40 (4%)	28 (3%)
Fatigue	5 (1%)	46 (4%)	20 (2%)
Dry Mouth	12 (3%)	26 (2%)	11 (1%)
Pharyngitis	10 (2%)	12 (1%)	9 (1%)

*Rounded to the closest unit percentage

Additional adverse reactions of medical significance observed at a higher incidence than in placebo in adults and adolescents aged 12 years and older exposed to XYZAL are syncope (0.2%) and weight increased (0.5%).

Pediatric Patients 6 to 12 Years of Age – A total of 243 pediatric patients 6 to 12 years of age received XYZAL 5 mg once daily in two short-term placebo controlled double-blind trials. The mean age of the patients was 9.8 years, 79 (32%) were between 6-8 years of age, and 50% were Caucasian. Table 2 lists adverse reactions that were reported in greater than or equal to 2% of subjects aged 6-12 years exposed to XYZAL 5 mg in placebo-controlled clinical trials and that were more common with XYZAL than placebo.

Table 2 Adverse Reactions in Subjects Aged 6-12 Years Reported in $\geq 2\%$ for XYZAL 5 mg in Placebo-Controlled Clinical Trials 4 and 6 Weeks in Duration

Adverse Reactions	XYZAL 5 mg/day (n = 243)	Placebo (n = 240)
Pyrexia	10 (4%)	5 (2%)
Cough	8 (3%)	2 (<1%)
Somnolence	7 (3%)	1 (<1%)
Epistaxis	6 (2%)	1 (<1%)

*Rounded to the closest unit percentage

Long-Term Clinical Trials Experience – In two controlled clinical trials, 428 patients (190 males and 238 females) aged 12 years and older were treated with XYZAL 5 mg once daily for 4 or 6 months. The patient characteristics and the safety profile were similar to that seen in the short-term studies. Ten (2.3%) patients treated with XYZAL discontinued because of somnolence, fatigue or asthenia compared to 2 (<1%) in the placebo group.

Laboratory Test Abnormalities – Elevations of blood bilirubin and transaminases were reported in <1% of patients in the clinical trials. The elevations were transient and did not lead to discontinuation in any patient.

Post-Marketing Experience – In addition to the adverse reactions reported during clinical trials and listed above, adverse events have also been identified during post-approval use of XYZAL in other countries. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Adverse events of hypersensitivity and anaphylaxis, angioneurotic edema, fixed drug eruption, pruritus, rash, and urticaria, convulsion, aggression and agitation, visual disturbances, palpitations, dyspnea, nausea, hepatitis, and myalgia have been reported.

Besides these events reported under treatment with XYZAL, other potentially severe adverse events have been reported from the post-marketing experience with cetirizine. Since levocetirizine is the principal pharmacologically active component of cetirizine, one should take into account the fact that the following adverse events could also potentially occur under treatment with XYZAL: hallucinations, suicidal ideation, orofacial dyskinesia, severe hypotension, cholestasis, glomerulonephritis, and still birth.

DRUG INTERACTIONS

In vitro data indicate that levocetirizine is unlikely to produce pharmacokinetic interactions through inhibition or induction of liver drug-metabolizing enzymes. No *in vivo* drug-drug interaction studies have been performed with levocetirizine. Drug interaction studies have been performed with racemic cetirizine.

Antipyrine, Azithromycin, Cimetidine, Erythromycin, Ketoconazole, Theophylline, and Pseudoephedrine – Pharmacokinetic interaction studies performed with racemic cetirizine demonstrated that cetirizine did not interact with antipyrine, pseudoephedrine, erythromycin, azithromycin, ketoconazole, and cimetidine. There was a small decrease (~16%) in the clearance of cetirizine caused by a 400 mg dose of theophylline. It is possible that higher theophylline doses could have a greater effect.

Ritonavir – Ritonavir increased the plasma AUC of cetirizine by about 42% accompanied by an increase in half-life (53%) and a decrease in clearance (29%) of cetirizine. The disposition of ritonavir was not altered by concomitant cetirizine administration.

USE IN SPECIFIC POPULATIONS

Pregnancy – Teratogenic Effects: Pregnancy Category B

In rats and rabbits, levocetirizine was not teratogenic at oral doses up to 200 and 120 mg/kg, respectively (approximately 320 and 390 times the maximum recommended daily oral dose in adults on a mg/m² basis). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, XYZAL should be used during pregnancy only if clearly needed.

Nursing Mothers – No peri- and post-natal animal studies have been conducted with levocetirizine. In mice, cetirizine caused retarded pup weight gain during lactation at an oral dose in dams of 96 mg/kg (approximately 40 times the maximum recommended daily oral dose in adults on a mg/m² basis). Studies in beagle dogs indicated that approximately 3% of the dose of cetirizine was excreted in milk. Cetirizine has been reported to be excreted in human breast milk. Because levocetirizine is also expected to be excreted in human milk, use of XYZAL in nursing mothers is not recommended.

Pediatric Use – The safety and effectiveness of XYZAL in pediatric patients under 6 years of age have not been established. The recommended dose of XYZAL for the treatment of the uncomplicated skin manifestations of chronic idiopathic urticaria in patients 12 to 17 years of age is based on extrapolation of efficacy from adults 18 years of age and older (see CLINICAL STUDIES in Full Prescribing Information).

The recommended dose of XYZAL in patients 6 to 11 years of age for the treatment of the symptoms of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria is based on cross-study comparison of the systemic exposure of XYZAL in adults and pediatric patients and on the safety profile of XYZAL in both adult and pediatric patients at doses equal to or higher than the recommended dose for patients 6 to 11 years of age.

The safety of XYZAL 5 mg once daily was evaluated in 243 pediatric patients 6 to 12 years of age in two placebo-controlled clinical trials lasting 4 and 6 weeks (see ADVERSE REACTIONS, Clinical Trials Experience). The effectiveness of XYZAL 2.5 mg once daily for the treatment of the symptoms of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria in children 6 to 11 years of age is supported by the extrapolation of demonstrated efficacy of XYZAL 5 mg once daily in patients 12 years of age and older and by the pharmacokinetic comparison in adults and children.

Cross-study comparisons indicate that administration of a 5 mg dose of XYZAL to 6-12 year old pediatric seasonal allergic rhinitis patients resulted in about 2-fold the systemic exposure (AUC) observed when 5 mg of XYZAL was administered to healthy adults. Therefore, in children 6 to 11 years of age the recommended dose of 2.5 mg once daily should not be exceeded (see DOSAGE AND ADMINISTRATION, Children 6 to 11 Years of Age; CLINICAL STUDIES in Full Prescribing Information and CLINICAL PHARMACOLOGY, Pharmacokinetics in Full Prescribing Information).

Geriatric Use – Clinical studies of XYZAL for each approved indication did not include sufficient numbers of patients aged 65 years and older to determine whether they respond differently than younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.

Renal Impairment – XYZAL is known to be substantially excreted by the kidneys and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it may be useful to monitor renal function (see DOSAGE AND ADMINISTRATION and Clinical Pharmacology, Pharmacokinetics in Full Prescribing Information).

Hepatic Impairment – As levocetirizine is mainly excreted unchanged by the kidneys, it is unlikely that the clearance of levocetirizine is significantly decreased in patients with solely hepatic impairment (see CLINICAL PHARMACOLOGY, Pharmacokinetics in Full Prescribing Information).

OVERDOSAGE

Overdosage has been reported with XYZAL.

Symptoms of overdose may include drowsiness in adults and initially agitation and restlessness, followed by drowsiness in children. There is no known specific antidote to XYZAL. Should overdose occur, symptomatic or supportive treatment is recommended. XYZAL is not effectively removed by dialysis, and dialysis will be ineffective unless a dialyzable agent has been concomitantly ingested.

The acute maximal non-lethal oral dose of levocetirizine was 240 mg/kg in mice (approximately 200 times the maximum recommended daily oral dose in adults and approximately 230 times the maximum recommended daily oral dose in children) on a mg/m² basis. In rats the maximal non-lethal oral dose was 240 mg/kg (approximately 390 times the maximum recommended daily oral dose in adults and approximately 460 times the maximum recommended daily oral dose in children on a mg/m² basis).



sanofi aventis

Manufactured for:

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