For patients with persistent asthma

Introducing the first multiple-strength inhaled corticosteroid with high topical anti-inflammatory activity

- B.i.d. convenience
- Multiple strengths to minimize the number of puffs per dose
- Relatively rapid onset of action
- Rare reports (<1%) of unpleasant taste

Maximum benefit may not be achieved for 1 to 2 weeks or longer after starting treatment. Onset of action and degree of symptom relief may vary.

FLOVENT is indicated for the maintenance treatment of asthma as prophylactic therapy for patients ≥12 years of age and for patients requiring oral corticosteroid therapy for asthma, many of whom may be able to reduce or eliminate their requirement for oral corticosteroids over time.

FLOVENT is NOT indicated for the relief of acute bronchospasm.

CAUTION: Adrenal insufficiency may occur when transferring patients from systemic steroids (see WARNINGS).


NEW Control made convenient
Flovent™ 44 mcg 110 mcg 220 mcg
(fluticasone propionate) Inhalation Aerosol
Custom-tailored treatment for starting, switching, and sparing

GlaxoWellcome
For Oral Inhalation

**BRIEF SUMMARY**
The following is a brief summary only; see full prescribing information for complete product information.

**CONTRAINDICATIONS:** Use is not recommended in the presence of status asthmaticus or other acute exacerbations of asthma where intensive measures are required.

**WARNINGS:**

- Particular care is needed for patients who are transferred from systemically active corticosteroids to FLOVENT Inhalation Aerosol because deaths due to adrenal insufficiency have occurred in asthmatics with abrupt withdrawal of systemic corticosteroids (including oral corticosteroids). After withdrawal from systemic corticosteroids, a number of months are required for recovery of adrenal function.

- Patients who have been previously maintained on 20 mg or more per day of prednisone (or its equiva-

- lent) should be tapered slowly over a period of several weeks. It should be treated with appropriate local or systemic (i.e., oral antihistamine) therapy while remaining on treatment with fluticasone propionate inhalation aerosol until control is achieved. Inhalated corticosteroids should be used with caution if at all in patients with active or quiescent tuberculosis infection of the respiratory tract; untreated systemic fungal, viral or parasitic infections; or latent tuberculosis infection.

Information for Patients:

Patients being treated with FLOVENT Inhalation Aerosol should receive the following information and instructions about the correct and safe use of the inhalation device. It is not a disclosure of all possible adverse or intended effects.

- Patients should use FLOVENT Inhalation Aerosol at regular intervals as directed. Results of clinical trials indicate that maximum effect may not be achieved until 1 to 2 months of treatment. Patient education should be reinforced by educational aids or videos of adequate dosage but should instruct the physician if symptoms do not improve or if the condition worsens.

- Patients should be warned to avoid exposure to chemicals or messies and if, they are exposed, to consult their physicians without delay.

For the proper use of FLOVENT Inhalation Aerosol and to obtain maximum improvement, the patient should read and follow carefully the Patient's Instructions for Use accompanying the product.

<table>
<thead>
<tr>
<th>Name</th>
<th>Phone</th>
<th>Address</th>
<th>City</th>
<th>State</th>
<th>Zip/Postal Code</th>
<th>Other (please specify)</th>
</tr>
</thead>
</table>

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Clinical Picture
Gary L. Darmstadt, MD; Walter W. Tunnessen, Jr, MD

LETTERS TO THE EDITOR

The SPIRITual History
H. E. Woodall, MD

In Reply
Todd A. Maugans, MD

Current Management of Acute Bronchitis in Ambulatory Care
David L. Hahn, MD
Donald Benz, MD

In Reply
Arch G. Mainous III, PhD; Roger J. Zoorob, MD, MPH; William J. Hueston, MD

ORIGINAL CONTRIBUTIONS

Violence, Mental Health, and Substance Abuse in Patients Who Are Seen in Primary Care Settings
Grace Wyshak, PhD; Geoffrey A. Modest, MD

What Influences Physician Practice Behavior? An Interview Study of Physicians Who Received Consultative Geriatric Assessment Recommendations
Rose C. Maly, MD, MSPH; Allan F. Abrahamse, PhD; Susan H. Hirsch, MPH; Janet C. Frank, DrPH; David B. Reuben, MD

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ZYRTEC: Efficacy you can count on

Excellent improvement in major symptom severity

<table>
<thead>
<tr>
<th>Period</th>
<th>Symptom Improvement</th>
<th>ZYRTEC 10 mg qd (n=67)</th>
<th>Claritin® 10 mg qd (n=67)</th>
<th>Placebo (n=68)</th>
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<td>I (0-5 hrs post-1st dose)</td>
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<tr>
<td>II (23-24 hrs post-1st dose)</td>
<td>Mean improvement</td>
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<td>III (0-4 hrs post-2nd dose)</td>
<td>Mean improvement</td>
<td>30</td>
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* p≤0.01 versus Claritin and placebo.

ZYRTEC significantly improved seasonal allergic rhinitis symptoms

In a controlled environmental exposure unit, 202 patients who tested positive to ragweed pollen received either ZYRTEC 10 mg/day, Claritin 10 mg/day, or placebo to control symptoms of seasonal allergic rhinitis. Patients were exposed to ragweed pollen for two 5-hour periods over 2 days in a "classroom-type" setting in which the pollen was delivered to a large seating area at a controlled rate. While fans circulated air, particle counters measured pollen levels throughout the seating area to control exposure level. Major symptom complex included: runny nose, sniffles, itchy nose, nose blows, sneezes, and watery eyes. Baseline severity, assessed by patients, was comparable for all groups. (Data on file.)

ZYRTEC relieved symptoms rapidly

In a separate study by Meltzer et al comparing Zyrtec 10 mg/day and Claritin 10 mg/day in 279 patients with seasonal allergic rhinitis, ZYRTEC's fast-acting, effective relief was confirmed.

Significant relief beginning at 1 hour

<table>
<thead>
<tr>
<th>Hours</th>
<th>ZYRTEC 10 mg qd (n=67)</th>
<th>Claritin 10 mg qd (n=67)</th>
<th>Placebo (n=68)</th>
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<td>0</td>
<td>Mean improvement</td>
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<tr>
<td>1</td>
<td>Mean improvement</td>
<td>30</td>
<td>40</td>
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* p≤0.05 versus Claritin and placebo.
| Hours | 1.5 | 2   | 2.5 | 3   | 3.5 | 4   | 4.5 | 5   | 6   | 7   | 8   | 9   | 10  | 11  | 12  | 13  | 14  | 15  | 16  | 17  | 18  | 19  | 20  | 21  | 22  | 23  | 24  |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Mean improvement | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   | ↑   |

* p≤0.05 versus Claritin and placebo.
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</table>

* p≤0.05 versus placebo.

Please see reference section for available clinical literature on cetirizine and loratadine.

Once-a-day Zyrtec (cetirizine HCl) tablets

FOR EFFECTIVE ALLERGY RELIEF
ZYRTEC (cetirizine HCl) tablets

For Effective Allergy Relief

2. billion patient-days of use*

- No clinically significant drug-drug interactions seen in concomitant mild to moderate asthma
- Most patients started at 10 mg
- No clinically significant increases in QTc
- Choose ZYRTEC for an excellent safety profile

ZYRTEC® is well tolerated. Side effects were mild or moderate. The incidence of somnolence was dose related (6% on placebo, 11% at 5 mg, and 14% at 10 mg). Discontinuations due to somnolence were not significantly different from placebo (1% vs. 0.6% on placebo). Other side effects included fatigue (5.9% vs. 2.6% on placebo) and dry mouth (5.0% vs. 2.3% on placebo).

*Based on Total Sector USB S.A. sales tracking of ZYRTEC 10 mg standard daily doses (1 x 10 mg tablet), which constitutes days of use from January 1988-March 1996. Total Sector is defined as all 94 countries in which ZYRTEC was sold during the stated period.

References:

BRIEF SUMMARY

ZYRTEC (cetirizine hydrochloride) Tablets

For Oral Use

(Data For Prescribing Information, Consult Package Insert)

INDICATIONS AND USAGE: Seasonal Allergic Rhinitis: ZYRTEC is indicated for the relief of symptoms associated with seasonal allergic rhinitis due to allergic reactions such as sneezing, runny nose, and congestion in adults and children 12 years of age and older. ZYRTEC is indicated for the relief of symptoms associated with perennial allergic rhinitis due to allergies such as dust mites, animal dander and molds in adults and children 12 years of age and older. ZYRTEC treated subjects experienced improved rhinitis, rhinorrhea, postnasal discharge, nasal pruritus, ocular pruritus and tearing.

Chronic Urticaria: ZYRTEC is indicated for the treatment of the uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 12 years of age and older. ZYRTEC significantly reduces the occurrence, severity and duration of hives and significantly reduces pruritus.

CONTRAINDICATIONS: ZYRTEC is contraindicated in patients with a known hypersensitivity to it or any of its ingredients or hydroxyzine.

PRECAUTIONS: Activities Requiring Mental Alertness: In clinical trials, the occurrence of somnolence has been reported in 3% of patients treated with ZYRTEC due to oral or nasal decongestants, cromolyn sodium, sympathomimetic agents, caffeine, sedatives, hypnotics, or other CNS depressants should be avoided because additional reductions in alertness and the additional CNS depressant effect of ZYRTEC performance may occur. Drug-drug Interactions: No clinically significant drug interactions have been found with theophylline at a low dose, diazepam, propranolol, lidocaine, or erythromycin. There was a small increase in the clearance of tetrahydrozoline caused by a 400 mg dose of ZYRTEC at a single dose. It is possible that larger theophylline dosages could have a greater effect. Carcinogenesis, Mutagenesis and Impairment of Fertility: No evidence of carcinogenicity was observed in rats and mice treated with cetirizine at oral doses up to 20 mg/kg/day (10 times the maximum recommended human dose on a mg/m2/day basis). An increased incidence of benign liver tumors was found in a 2-year carcinogenicity study in male mice at a dietary dose of 15 mg/kg/day (6 times the maximum recommended human dose on a mg/m2/day basis). The clinical significance of these findings for long-term use of ZYRTEC is not known. Cetirizine was not mutagenic in the Ames test, and not clastogenic in the human lymphocyte assay, the mouse lymphoma assay, and the in vitro recombinant test in rats. No impairment of fertility was found in a fertility and general reproductive performance study in rats at a dietary dose of 64 mg/kg/day (26 times the maximum recommended human dose on a mg/m2/day basis). Pregnancy Category B: Cetirizine was not teratogenic in mice, rats and rabbits at doses up to 96, 225, and 130 mg/kg/day (40, 183, and 216 times the maximum recommended human dose on a mg/m2/day basis). There are no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, ZYRTEC should be used in pregnancy only if clearly needed. Nursing Mothers: There was no evidence of excretion of cetirizine or its metabolites in breast milk. In a multiple dose study, a single dose of 20 mg/day of ZYRTEC in lactating mothers did not lead to any decreases in breast milk. Use of ZYRTEC in nursing mothers is not recommended.

Geriatric Use: In placebo-controlled trials, 196 patients age 65 to 94 years received doses of 5 to 20 mg of ZYRTEC per day. Adverse events were similar in this group to patients under age 65. Substantially fewer studies in this group were not done. Pediatric Use: Safety and effectiveness in children under 12 years of age has not been established.

ADVERSE REACTIONS: Controlled and uncontrolled clinical trials conducted in the United States and Canada included 186 patients treated at doses up to 20 mg/day of ZYRTEC at least once during the treatment. The duration of treatment ranged from 1 week to 6 months, with a mean exposure of 30 days. Most adverse reactions reported during therapy with ZYRTEC were mild or moderate. In placebo-controlled trials, the incidence of discontinuations due to adverse reactions in patients receiving ZYRTEC 5 mg or 10 mg was not significantly different from placebo (2.9% vs. 2.4%, respectively). The most common adverse reaction that occurred more frequently on cetirizine than placebo was somnolence. The incidence of somnolence associated with ZYRTEC 5 mg is 3.0% (5/167) at 5 mg and 11% at 10 mg. Discontinuations due to somnolence for ZYRTEC were uncommon (1.0% on ZYRTEC vs. 0.6% on placebo). Fatigue and dry mouth also appeared to be treatment-related adverse reactions. There were no differences by age, race, gender or by body weight with regard to incidence of adverse reactions.

Table 1 lists adverse experiences which were reported for ZYRTEC 5 mg and 10 mg in clinical trials in the United States and that were more common with ZYRTEC than placebo.

In addition, headache and nausea occurred in more than 2% of the patients, but were more common in placebo patients. The following events were observed infrequently (less than 2%), in 382 patients who received ZYRTEC in U.S. trials, including an open study of six months duration: a causal relationship with ZYRTEC administration has not been established: Autoimmune System Anemia; anaemia, urinary retention, flushing, increased salivation. Cardiovacular: palpitations, tachycardia, hypertension, cardiac failure. Central and Peripheral Nervous System: headache. Respiratory System: epistaxis, rhinitis. Metabolic/Nutritional: thirst. Reproductive: dysmenorrhea, female breast pain, intermenstrual bleeding, leukorrhoea, vaginitis. Respiratory system: dyspnoea, laryngitis, nocturnal coughing, rhinitis. Skin: photosensitivity. Stomach: nausea, vomiting, diarrhoea, weight loss, constipation, flatulence. Urinary System: dysuria, pyuria. Vision: blurred vision.

DRUG ABUSE AND DEPENDENCE: There is no information to indicate that abuse or dependence occurs with cetirizine HCl.

OVERDOSAGE: Overdose has been reported with ZYRTEC. In one patient who took 150 mg of ZYRTEC, the patient was somnolent but did not display any other clinical signs or abnormal blood chemistry or hematology results. Should overdose occur, symptomatic and supportive measures should be employed. Cetirizine is not removed by hemodialysis. There is no known specific antidote to ZYRTEC. If ZYRTEC is not effectively removed by dialysis, and death is inevitable without an identifiable cause, the ZYRTEC level should be determined. There is no known specific antidote to ZYRTEC. If ZYRTEC is not effectively removed by dialysis, and death is inevitable without an identifiable cause, the ZYRTEC level should be determined.

Table 1. Adverse Experiences Reported in Placebo-Controlled United States ZYRTEC Trials (Maximum Dose of 10 mg at Rates of 2% or Greater (Percent Incidence)

<table>
<thead>
<tr>
<th>Adverse Experience</th>
<th>ZYRTEC (N=2043)</th>
<th>Placebo (N=1612)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somnolence</td>
<td>9.7</td>
<td>6.3</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5.9</td>
<td>2.6</td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>5.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>2.2</td>
<td>1.9</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2.0</td>
<td>1.2</td>
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<th>Regular</th>
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</thead>
<tbody>
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<td>$160</td>
</tr>
<tr>
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<td>$130</td>
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<tr>
<td>Archives of Internal Medicine (22 issues)</td>
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<td>$145</td>
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<tr>
<td>Archives of Neurology (12 issues)</td>
<td>$160</td>
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<tr>
<td>Archives of Ophthalmology (12 issues)</td>
<td>$120</td>
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Dosage and Administration

Taken With the First Bite of Each Main Meal

Initial dosage: 25 mg tid (all or a scored 50-mg tablet tid)

Alternate Initial Dosage to Minimize GI Side Effects

Initial dosage: 25 mg once daily (taken with the first bite of the main meal)

Gradually titrate to: 25 mg tid

Titrated to: 50 mg tid

Maintenance dosage: 50 mg tid to 100 mg tid

Maximum dosages: 50 mg tid for patients ≤ 132 lb

100 mg tid for patients > 132 lb

BRIEF SUMMARY

CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

P2500088S

INDICATIONS AND USAGE

PRECODE® is a non-insulin therapy, indicated as an adjunct to diet to lower blood glucose in patients with non-insulin-dependent diabetes mellitus (NIDDM) whose hyperglycemia cannot be managed on diet alone. PRECODE® may also be used in combination with sulfonylureas when diet plus either PRECODE® or a sulfonylurea fails to achieve an adequate glucose control. PRECODE® is intended for use in NIDDM patients who may require improvement in glycemic control. Patients with a prior history of hypoglycemia are at risk for potentially significant episodes of hypoglycemia. Particular emphasis should be placed on the recognition of the clinical signs of hypoglycemia, and appropriate therapy should be readily available.

PRECODE® is contraindicated in patients with known hypersensitivity to the drug and in patients with a prior history of hypoglycemia. PRECODE® is also contraindicated in patients with anaphylactic bowel disease, exacerbation of pre-existing partial intestinal obstruction, or patients predisposed to intestinal obstruction. In addition, PRECODE® is contraindicated in patients who have chronic intestinal diseases associated with marked derangements of digestion or absorption and in patients who have conditions that may deteriorate as a result of increased gas formation in the intestine.

PRECAUTIONS

General

Hypoglycemia: Because of its mechanism of action, PRECODE® when administered alone should not cause hypoglycemia in the fasted or postprandial state. Sulfonylureas may cause hypoglycemia. Because PRECODE® given in combination with a sulfonylurea will cause a further lowering of blood glucose, it may increase the hypoglycemic potential of the sulfonylurea. Oral glucose (dextrose), whose absorption is not inhibited by PRECODE®, should therefore be used instead of sucrose (cane sugar) in the treatment of mild to moderate hypoglycemia. Sucrose, whose hydrolysis to glucose and fructose is inhibited by PRECODE®, is unsuitable for the rapid correction of hypoglycemia. Severe hypoglycemia may require the use of either intravenous glucose infusion or glucagon injection.

Elevated Serum Transaminase Levels: In clinical trials, at doses of 50 mg t.i.d. and 100 mg t.i.d., the incidence of serum transaminase elevations with PRECODE® was the same as with placebo. In long-term studies (up to 12 months, and including PRECODE® at doses up to 200 mg t.i.d.) conducted in the United States, treatment-emergent elevations of serum transaminases (AST and/or ALT) occurred in 15% of PRECODE®-treated patients as compared to 10% of placebo patients. These serum transaminase elevations appear to be dose-related. At doses greater than 100 mg t.i.d., the incidence of serum transaminase elevations greater than twice the upper limit of normal was two to three times higher in the PRECODE® group than in the placebo group. These elevations were asymptomatic, reversible, more common in females, and, in general, were not associated with other evidence of liver dysfunction.

Information for Patients: Patients should be told to take PRECODE® truly three times a day at the start (with the first bite of each main meal). It is important that patients continue to adhere to dietary instructions, a regular exercise program, and regular testing of urine and/or blood glucose.

PRECODE® itself does not cause hypoglycemia. When administered to patients in the fasted state, sulfonylureas, drugs and insulin, however, can lower blood sugar levels enough to cause symptoms or sometimes life-threatening hypoglycemia. Because PRECODE® given in combination with a sulfonylurea or insulin will cause a further lowering of blood glucose levels, patients should be instructed to notify their physician if they have a history of hypoglycemic episodes.

Loss of Control of Blood Glucose: When diabetic patients are exposed to stress such as fever, trauma, infection, or surgery, a temporary loss of control of blood glucose may occur. At such times, temporary insulin therapy may be necessary.

Information for Patients: Patients should be told to take PRECODE® really three times a day at the start (with the first bite of each main meal). It is important that patients continue to adhere to dietary instructions, a regular exercise program, and regular testing of urine and/or blood glucose.

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Lab Data: Therapeutic response to PRECODE® should be monitored by periodic blood glucose tests. Measurement of glycosylated hemoglobin levels is recommended for the monitoring of long-term glycemic control.

PRECODE®, particularly at doses in excess of 50 mg t.i.d., may give rise to elevations of serum transaminases and, in rare instances, hyperbilirubinemia. It is recommended that serum transaminase levels be checked every 3 months during the first year of treatment with PRECODE® and periodically thereafter. If elevated transaminases are observed, a reduction in dosage or withdrawal of therapy may be indicated, particularly if the elevations persist.

Laboratory Tests: Therapeutic response to PRECODE® should be monitored by periodic blood glucose tests. Measurement of glycosylated hemoglobin levels is recommended for the monitoring of long-term glycemic control.

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Laboratory Tests: Therapeutic response to PRECODE® should be monitored by periodic blood glucose tests. Measurement of glycosylated hemoglobin levels is recommended for the monitoring of long-term glycemic control.
Unique,
Non-systemic
Mode of Action¹

Lowers blood glucose as an
adjunct to diet — alone or with
a sulfonylurea² when glycemic
control cannot be achieved.

Majority of side effects in clinical
trials were GI in nature (abdominal
pain, diarrhea, and flatulence),
related to the mode of action,
and generally diminished after
4 to 8 weeks due to adaptation of
small intestine enzyme activity.²

Precose is contraindicated in
patients with diabetic ketoacidosis,
cirrhosis, inflammatory bowel
disease, colonic ulceration, or
partial intestinal obstruction.

Because efficacy is similar across
dosages ≥ 100 mg tid, and dosages
> 100 mg tid may be associated
with an increased risk of elevated
serum transaminase levels, dosages
> 100 mg tid are not recommended.

* Non-insulin-dependent diabetes mellitus.

† Precose itself does not cause hypoglycemia.
When used in combination with sulfonylureas,
it may increase their hypoglycemic potential.
Oral glucose, whose absorption is not inhibited
by Precose, should be used instead of sucrose in
the treatment of mild to moderate hypoglycemia.