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).


Please consult Brief Summary of Prescribing Information on adjacent page.

NEW
Control made convenient

Flovent™ 44 mcg 110 mcg 220 mcg
(fluticasone propionate)
Inhalation Aerosol

Custom-tailored treatment for starting, switching, and sparing

GlaxoWellcome
daily inhalation dose based on mcg/kg) for 78 weeks in the mouse or inhalation of up to 57 mcg/kg (approximately 1/4 the maximum human daily inhalation dose based on mcg/kg) for 104 weeks in the rat.

Fluticasone propionate did not induce gene mutation in prokaryotic or eukaryotic cells in vitro. No significant clastogenic effect was seen in cultured human peripheral lymphocytes in vitro or in the mouse micronucleus test when administered at high doses by the oral or subcutaneous routes. Furthermore, no evidence of teratogenic activity was noted in rats.

The following possible adverse effects have been reported during clinical trials with fluticasone propionate inhalation aerosol: Headache; Angina; Asthma attack; Infected tooth; Hiccups; Nasopharyngitis; Cough; Nasal congestion; Upper respiratory tract infection; Lower respiratory tract infection; Pneumonia; Rhinosinusitis; Upper respiratory tract hemorrhage; Urticaria; Rash; Pruritis.

Inhalation in overdose: No specific antidote is known. Treatment of overexposure consists of removal of the patient from the source of the exposure and institutional treatment for symptoms. Short-term, high-dose inhalations of fluticasone propionate (up to 1 mg) have resulted in elevations of systemic cortisol levels without evidence of systemic effects. The appropriate treatment of accidental overdose is supportive and symptomatic.
Persistent Facial Swelling in a Patient With Rosacea
L. Scerri, MD, MRCP; E. M. Saihan, MD, MRCP

Clinical Trial of Wax-Matrix Sustained-Release Niacin in a Russian Population With Hypercholesterolemia
David M. Aronov, MD, PhD; Joseph M. Keenan, MD; Nadir M. Akhmedzhanov, MD, PhD; Natalia V. Perova, MD, PhD; Raphael Y. Oganov, MD, PhD; Natalia Y. Kiseleva, MD, PhD

A Cost-benefit Analysis of Colposcopy for Cervical Squamous Intraepithelial Lesions Found on Papanicolaou Smear
Marcia J. Chesbro, MD; W. Douglas Everett, MD, MPH

Colposcopy for Cervical Squamous Intraepithelial Lesions Found on Papanicolaou Smear
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11. Herbert V, Memoli D, McAleer E, Coleman N. What is normal variation from the individual’s norm for granulocyte lobe average and holo-transcobalamin II (holo-TC II) diagnoses vitamin B12 deficiency before variation from the laboratory norm. Clin Res. 1986;34:718. Abstract.
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Come experience the new synergy. Plan now to attend. To register call 800 AMA-3211 and ask for the Department of Organized Medical Staff Services.

* The AMA is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

The AMA designates this continuing medical education activity for up to 3 credit hours in Category 1 of the Physician's Recognition Award.
Dosage and Administration

Taken With the First Bite of Each Main Meal

Initial dosage: 25 mg tid (half of 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

PRECOSE® (carbozyme tablets)

INDICATIONS AND USAGE

PRECOSE® as monotherapy, is 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. PRECOSE® may also be used in combination with a sulfonylurea or an oral anti-diabetic agent when plus either PRECOSE® or a sulfonylurea results in inadequate glycemic control. The effect of PRECOSE® to enhance glycemic control is additive to that of sulfonylureas when used in combination, presumably because its mechanism of action is different.

In initiating treatment for NIDDM, diet should be emphasized as the primary form of treatment. Caloric restriction and weight loss are essential in the obese diabetic patient. Proper dietary management alone may be effective in controlling blood glucose levels and symptoms. The importance of regular physical activity when appropriate should also be stressed. If this treatment program fails to result in adequate glycemic control, the use of PRECOSE® should be considered. The use of PRECOSE® must be viewed by both the physician and patient as a treatment in addition to diet, and not as a substitute for diet or as a convenient mechanism for avoiding dietary restraint.

CONTRAINDICATIONS

PRECOSE® is contraindicated in patients with known hypersensitivity to the drug and in patients with diabetic ketoacidosis or coma. PRECOSE® is also contraindicated in patients with inflammatory bowel disease, ulcerative colitis, partial intestinal obstruction, or in patients predisposed to intestinal obstruction.

PRECAUTIONS

General

Hypoglycemia: Because of its mechanism of action, PRECOSE® when administered alone should not cause hypoglycemia in the fasted or postprandial state. Sulfonylurea agents may cause hypoglycemia. Because PRECOSE® given in combination with a sulfonylurea will cause a further lowering of blood glucose, the increase may be greater than expected. Oral glucose (dextrose), whose absorption is not inhibited by PRECOSE®, should 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 PRECOSE®, 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 PRECOSE® was the same as with placebo. In long-term studies (up to 12 months, and including PRECOSE® doses up to 300 mg t.i.d.) conducted in the United States, treatment-emergent elevations of serum transaminases (AST and/or ALT) occurred in 15% of PRECOSE®-treated patients and in 8% of placebo-treated 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 in patients greater than 65 years of age with the finding of hepatic abnormality was higher in the PRECOSE® 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.

In international post-marketing experience with over 500,000 patients, 18 cases of serum transaminase elevations > 500 IU/L (12 of which were associated with jaundice) have been reported. Fifteen of these 18 cases received treatment with 100 mg t.i.d. or greater and 13 of 16 patients for whom weight was reported had a body weight > 60 kg. In five cases where follow-up was recorded, hepatic abnormalities improved or resolved upon discontinuation of PRECOSE®.

Use of Care in Skeletal Metabolism: 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 PRECOSE® orally 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 or blood glucose.

PRECOSE® itself does not cause hypoglycemia even when administered to patients in the fasted state. Sulfonylureas and insulin, however, can lower blood sugar levels enough to cause symptoms or sometimes life-threatening hypoglycemia. Because PRECOSE® given in combination with a sulfonylurea or an insulin agent can lower blood sugar levels even further, the risk of hypoglycemia is increased in such patients. The risk of hypoglycemia, its symptoms and treatment, and conditions that predispose to its development should be well understood by the patient and his family members. Because PRECOSE® prevents the breakdown of table sugar, patients should have a readily available source of glucose (dextrose). Glucose tablets are a source of low blood sugar when taking PRECOSE® in combination with a sulfonylurea or insulin.

If side effects occur with PRECOSE®, they usually develop during the first few weeks of treatment. They are most common during the initial treatment. Adverse gastrointestinal symptoms such as flatulence, diarrhea, or abdominal discomfort and generally diminish in frequency and intensity with time.

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

PRECOSE®, particularly at doses in excess of 50 mg t.i.d., may give rise to elevations of serum transaminase levels, particularly in non-insulin-dependent diabetics, in whom they may not be associated with clinical symptoms. In clinical studies, these enzyme levels were checked every 3 months during the first year of treatment with PRECOSE® and periodically thereafter. If elevated transaminases are observed, a reduction in dosage or withdrawal of therapy may be indicated, particularly if the elevations persist.

Renal Impairment: Plasma concentrations of PRECOSE® in renal impaired volunteers were proportionally increased relative to the degree of renal dysfunction. Long-term clinical trials in diabetic patients with significant renal dysfunction (serum creatinine >2.0 mg/dL) have not been conducted. Therefore, treatment of these patients with PRECOSE® is not recommended.

Drug Interactions: Certain drugs tend to produce hypoglycemia and may lead to loss of blood glucose control. These drugs include the thiazides and other diuretics, corticosteroids, phenothiazines, thyroid preparations, estrogens, non-steroidal anti-inflammatory agents, monoamine oxidase inhibitors, and other psychotropic drugs. Calcium channel-blocking drugs, and insulin. When such drugs are administered to a patient receiving PRECOSE®, the patient should be closely observed for loss of blood glucose control. When such drugs are withdrawn from patients receiving PRECOSE® in combination with sulfonylureas or insulin, patients should be observed closely for any evidence of hypoglycemia.

Intestinal adrenergics (e.g., choline) and digestive enzyme preparations containing carbohydrate-splitting enzymes (e.g., amylase, pancreatin) may reduce the effect of PRECOSE® and should not be taken concomitantly.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: Nine chronic toxicological/carcinogenicity studies were conducted in three animal species (rat, hamster, dog) including two rat strains (Sprague-Dawley and Wistar).

In the first rat study, Sprague-Dawley rats received acarbose in feed at high doses, i.p., up to approximately 500 mg/kg (body weight) for 104 weeks. Acarbose treatment resulted in a significant increase in the incidence of renal tumors (adenomas and adenocarcinomas) and benign Leydig cell tumors. This study was repeated with a similar outcome. Further studies were performed to separate direct carcinogenic effects of acarbose from indirect effects resulting from the carbohydrate malabsorption induced by the large doses of acarbose employed in the studies. In one study using Sprague-Dawley rats, acarbose was mixed with feed but carbohydrate deprivation was prevented by the addition of glucose to the diet. In a 26-month study of Sprague-Dawley rats, acarbose was administered by daily p.o. p.o. for postnatal gavage so as to avoid the pharmacologic effects of the drug. In both of these studies, the increased incidence of renal tumors found in the original studies did not occur. Acarbose was also given in food and by postnatal gavage in two separate studies in Wistar rats. No increased incidence of renal tumors was found in either of these Wistar rat studies. In two feeding studies of hamsters, with and without glucose supplementation, there was also no evidence of carcinogenicity.

Acarbose showed no mutagenic activity when tested in six in vitro and three in vivo assays.

Fertility studies conducted in rats after oral administration produced no untoward effect on fertility or on the overall capability to reproduce.

Pregnancy: Teratogenic Effects: Pregnancy Category B. The safety of PRECOSE® in pregnant women has not been established. Reproduction studies have been performed in rats at doses up to 480 mg/kg (corresponding to 30 times the expected human dose at a weight of 70 kg) and have revealed no evidence of impaired fertility or harm to the fetus due to acarbose. In rabbits, reduced maternal body weight gain, probably the result of the pharmacodynamic activity of high doses of acarbose in the intestines, may have been responsible for a slight increase in the number of embryonic losses. However, rabbits given 160 mg/kg acarbose (corresponding to 70 times the dose in man, based on body surface area) showed no effect on body weight or body weight gain. At this dose, 480 mg/kg acarbose, the teratogenic effect of acarbose on the fetal rat was shown. However, there was no evidence of teratogenicity at a dose 32 times the dose in man (based on body surface area). There are, however, no adequate and well-controlled studies of PRECOSE® in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Because current information strongly suggests that abnormal blood glucose levels during pregnancy are associated with a high percentage of congenital anomalies, most experts recommend that insulin be used during pregnancy to maintain blood glucose levels as close to normal as possible.

Nursing Mothers: A small amount of radioactivity has been found in the milk of lactating rats after administration of radiolabeled acarbose. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, PRECOSE® should not be administered to a nursing woman.

Pediatric Use: Safety and effectiveness of PRECOSE® in pediatric patients have not been established.

ADVERSE REACTIONS

Esophageal Obstruction: When given to patients with strictures, esophageal obstruction, or other conditions that may cause esophageal obstruction during swallowing.

Dehydration: Patients with renal impairment or cardiac failure may be more susceptible to the effects of dehydration. Special precautions should be provided.

Caution: Federal law prohibits dispensing without a prescription.

REFERENCES

1. PRECOSE® (carbozyme tablets) Package Insert.
3. PRECOSE® 2009/2010 USA/1A
4. CAL 5421
5. 6160
6. Printed in U.S.A.

Pharmaceutical Division

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Unique, Nonsystemic Mode of Action

Lowers blood glucose as an adjunct to diet — alone or with a sulfonylurea 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.

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.

Please see brief summary of Prescribing Information on adjacent page.