A Brief History of the Brief Summary

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FDA

DTC National, April 10, 2007

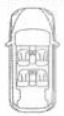
Overview

- Why don’t I see brief summaries in other types of ads?
- Quick & easy regulation primer
- The Whole Ad and Nothing but the Whole Ad
- What does the brief summary look like?
- What *can* the brief summary look like?

We believe your car should have more airbags than cup holders.

6 AIRBAGS

4 CUP HOLDERS



Every new Hyundai Santa Fe comes with six airbags. And four cup holders. In fact, the all-new Santa Fe is nicely equipped with two advanced front airbags, two front side-impact airbags, and two side curtain airbags–helping it earn the rare and heralded 5-star crash test rating. With Electronic Stability Control, standard, starting at $21,815*. Therefore, you can drive anywhere, feel safe, be secure, and relax with your soy decaf, double vanilla latte. Now, that's good thinking. Learn more at **HyundaiUSA.com**.

America's Best Warranty 10 years/100,000 miles

HYUNDAI

Government star ratings are part of the National Highway Traffic Safety Administration's (NHTSA's) New Car Assessment Program (www.safercar.gov). Model tested with standard side-impact airbags (SABs). Safety belts should always be worn. Limited model shown, $26,815. *MSRP for base model with manual transmission. MSRPs include freight; exclude taxes, title, license, and options. Dealer price may vary. Hyundai and Hyundai model names are registered trademarks of Hyundai Motor America. All rights reserved. ©2007 Hyundai Motor America.

WORKING MOTHER BEST SMALL COMPANIES • SIMPLE STRESS BUSTERS • AWESOME FAMILY ADVENTURES APRIL 2007

Here's an overactive-bladder treatment you can stick with

Dry can be good — and not so good. If your OAB medicine makes your mouth so dry you don't feel like taking it, maybe it's time to talk with your doctor about something different. And that would be the OXYTROL® Patch. All you do is apply it to your hip, abdomen, or buttock. The patch delivers the medicine in a low, steady dose, so you can get all the benefits. Not all the dry mouth.

You should not use OXYTROL if you have certain types of stomach, urinary, or glaucoma problems. OXYTROL is generally well tolerated. The most common side effects are application site reactions, dry mouth, constipation, diarrhea, painful or difficult urination, and abnormal vision.

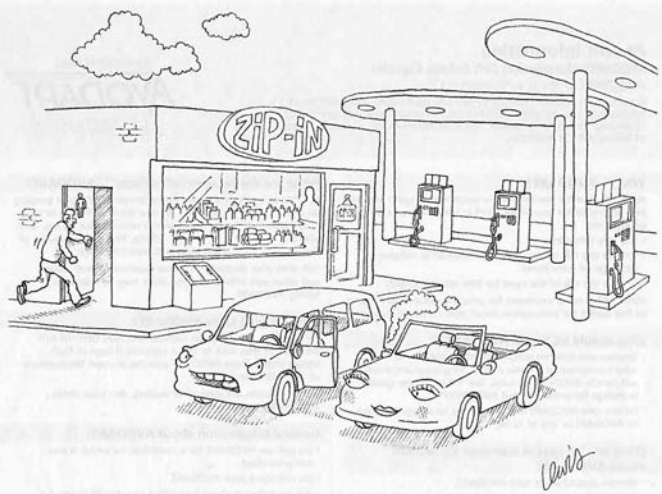
Ask your doctor about the only OAB treatment that comes in a patch.

See important patient information on the next page. Visit www.oxytrol.com or call 1.888.OXYTROL.

OXYTROL
Oxybutynin Transdermal System

THERE'S ANOTHER WAY

WATSON Pharma, Inc.



"One of these days, he'll actually come here to buy some gas."

You probably think you have a going problem. Instead, it might be a growing problem.

If you not only have to go to the bathroom often, but find it's hard to start once you get there. Or see that you're starting and stopping, or going often at night, you may have an enlarging prostate. And you don't have to put up with it. Ask your doctor if *Avodart* is right for you. Most medicines only treat urinary symptoms. *Avodart*, with time, actually shrinks the prostate and reduces symptoms. So it's an open road. Sit back and enjoy the ride.

Important Safety Information About Prescription AVODART® (dutasteride): *Avodart* is used to treat urinary symptoms of Enlarging Prostate. Only your doctor can tell if your symptoms are from an enlarged prostate and not a more serious condition, such as prostate cancer. See your doctor for regular exams. Women and children should not take *Avodart*. Women who are or could become pregnant should not handle *Avodart* due to the potential risk of a specific birth defect. Do not donate blood until at least six months after stopping *Avodart*. Tell your doctor if you have liver disease. *Avodart* may not be right for you. Possible side effects, including sexual side effects and swelling or tenderness of the breast, occur infrequently. ***See important information on next page.***

AVODART® (dutasteride)
Soft Gelatin Capsules 0.5 mg
FOR YOUR GROWING PROBLEM

Do you have an enlarging prostate?
If you have any of these urinary symptoms, talk to your doctor.

- Urination starts and stops.
- Frequent urge to urinate.
- Difficulty emptying your bladder.
- Symptoms get in the way of your life.
- Getting up to urinate 2 or more times a night.

GlaxoSmithKline

For more information, call 1-800-769-8402 or visit avodart.com. If you don't have prescription coverage, visit pparx.org, or call 1-888-4PPA-NOW (1-888-477-2669)

FTC vs FDA

- FTC regulates advertising (cars, home mortgages, mops, etc.)
- FDA regulates labeling (all legal drugs, medical devices, foods)
- *Memorandum of Understanding* - Ads
  - FTC regulates ads for foods, OTC drugs, non-restricted devices, cosmetics, dietary supplements
  - FDA regulates ads for prescription drugs and restricted medical devices

FDA Regulations

"All advertisements for any prescription drug…shall present a true statement of information in brief summary relating to side effects, contraindications…and effectiveness."

- 21 CFR § 202.1(e)

FDA Regulations

- "…side effects, contraindications" include side effects, warnings, precautions, and contraindications, and include any such information under such headings as cautions, special considerations, important notes, etc…"

- 21 CFR § 202.1(e)

FDA Regulations

- Translation:
  - The brief summary should be a comprehensive look at risk information related to a drug product

- Big Picture:
  - FDA is committed to ensuring access to accurate and useful information

The Whole Ad

- FDA considers the brief summary to be part of the ad
- Adding brief summary does not get you off the hook
- Recent enforcement letters for omission of risk, despite risk information pages:
  - Vitrase, November 2005
  - Infergen, March, 2006

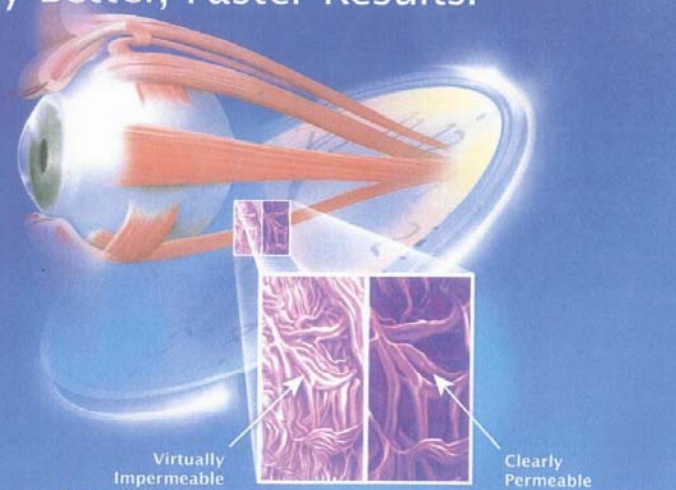
NEW Thimerosal-Free

Vitrase (hyaluronidase injection) Ovine, 200 USP Units/mL and
Vitrase (hyaluronidase for injection) Lyophilized, Ovine 6200 USP Units

A Pure Ovine Hyaluronidase Formulation.

FDA APPROVED

Simply Better, Faster Results.[1]



Better, Faster Results vs Anesthetic Alone.

- At 10 minutes post-injection, hyaluronidase achieved over 3 times as many successful blocks as the anesthetic-only control group
- The first pure, preservative-free, ovine-based hyaluronidase
- Hyaluronidase increases hyaluronic acid permeability and porosity

Vitrase® (hyaluronidase for injection) Lyophilized, Ovine, is indicated as an adjuvant to increase the absorption and dispersion of other injected drugs, for hypodermoclysis, and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.

The most frequently reported adverse experiences have been local injection site reactions. Hyaluronidase has been reported to enhance the adverse events associated with co-administered drug products. Edema has been most frequently associated with hypodermoclysis. Allergic reactions (urticaria, angioedema) have been reported in less than 0.1% of patients receiving hyaluronidase.

Reference: 1. Nicoll JM, Theunen B, Acharya PA, Ahlen K, James M. Retrobulbar anesthesia: the role of hyaluronidase. Anesth Analg. 1966;65(12):1324-1328.

To Order, Call (866) 264-8568

NEW Thimerosal-Free

Vitrase
(hyaluronidase injection)
Ovine, 200 USP Units/mL

Vitrase
(hyaluronidase for injection)
Lyophilized, Ovine
6200 USP Units

Pure Science of Time

ISTA Pharmaceuticals®

www.istavision.com

Please see brief summary of prescribing information on next page.

VIT301-9/04

VITRASE® (hyaluronidase injection) Ovine, 200 USP Units/mL

Brief Summary of Prescribing Information

INDICATIONS AND USAGE

Vitrase (hyaluronidase injection) is indicated as an adjuvant to increase the absorption and dispersion of other injected drugs; for hypodermoclysis; and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.

CONTRAINDICATIONS

Hypersensitivity to hyaluronidase or any other ingredient in the formulation is a contraindication to the use of this product.

WARNINGS

Discontinue Vitrase (hyaluronidase injection) if cerebellazion occurs.

Hyaluronidase should not be used to enhance the absorption and dispersion of dopamine and/or alpha agonist drugs.

Hyaluronidase should not be injected into or around an infected or acutely inflamed area because of the danger of spreading a localized infection.

Hyaluronidase should not be used to reduce the swelling of lakes or stings.

Hyaluronidase should not be applied directly to the cornea.

Hyaluronidase should not be used for intravenous injections because the enzyme is rapidly inactivated.

PRECAUTIONS

General

Furosemide, the benzodiazepines and phenytoin have been found to be incompatible with hyaluronidase.

When considering the administration of any other drug with hyaluronidase, it is recommended that appropriate references first be consulted to determine the usual precautions for the use of the other drug; e.g., when epinephrine is injected along with hyaluronidase, the precautions for the use of epinephrine in cardiovascular disease, thyroid disease, diabetes, digital nerve block, ischemia of the fingers and toes, etc., should be observed.

Laboratory Tests

A preliminary skin test for hypersensitivity to Vitrase can be performed. The skin test is made by an intradermal injection of approximately 0.02 mL (3 Units) of a 150 Units/mL solution (see "Dosage and Administration" in full prescribing information). A positive reaction consists of a wheal with pseudopodia appearing within 5 minutes and persisting for 20 to 30 minutes and accompanied by localized itching. Transient vasodilation at the site of the test, i.e., erythema, is not a positive reaction.

Drug Interactions

When hyaluronidase is added to a local anesthetic agent, it hastens the onset of analgesia and tends to reduce the swelling caused by local infiltration, but the wider spread of the local anesthetic solution increases its absorption; this shortens its duration of action and tends to increase the incidence of systemic reaction. Patients receiving large doses of salicylates, corticoids, ACTH, estrogens, or antihistaminics may require larger amounts of hyaluronidase for equivalent dispersing effect, since these drugs apparently render tissues partly resistant to the action of hyaluronidase.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to assess the carcinogenic or mutagenic potential of hyaluronidase. Hyaluronidase is found in most tissues of the body.

Long-term animal studies have not been performed to assess whether hyaluronidase impaired fertility; however, it has been reported that testicular degeneration may occur with the production of organ-specific antibodies against this enzyme following repeated injections. Human studies on the effect of intravenous hyaluronidase in sterility due to oligospermia indicated that hyaluronidase may have aided conception. Thus, it appears that hyaluronidase may not adversely affect fertility in females.

Pregnancy

Teratogenic Effects—Pregnancy Category C

No adequate and well-controlled animal studies have been conducted with Vitrase to determine reproductive effects. No adequate and well-controlled studies have been conducted with Vitrase in pregnant women. Vitrase should be used during pregnancy only if clearly needed.

Labor and Delivery

Administration of hyaluronidase during labor was reported to cause no complications; no increase in blood loss or differences in cervical trauma were observed. It is not known whether hyaluronidase has an effect on the fetus if used during labor; the effect of hyaluronidase on the later growth, development, and functional maturation of the infant is unknown.

Nursing Mothers

It is not known whether hyaluronidase is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when hyaluronidase is administered to a nursing woman.

ADVERSE REACTIONS

The most frequently reported adverse experiences have been local injection site reactions. Hyaluronidase has been reported to enhance the adverse events associated with co-administered drug products. Edema has been most frequently associated with hypodermoclysis. Allergic reactions (urticaria, angioedema) have been reported in less than 0.1% of patients receiving hyaluronidase. Anaphylactoid-like reactions following retrobulbar block or intravenous injections have occurred, rarely.

VITRASE® (hyaluronidase for injection) Lyophilized, Ovine 6200 USP Units

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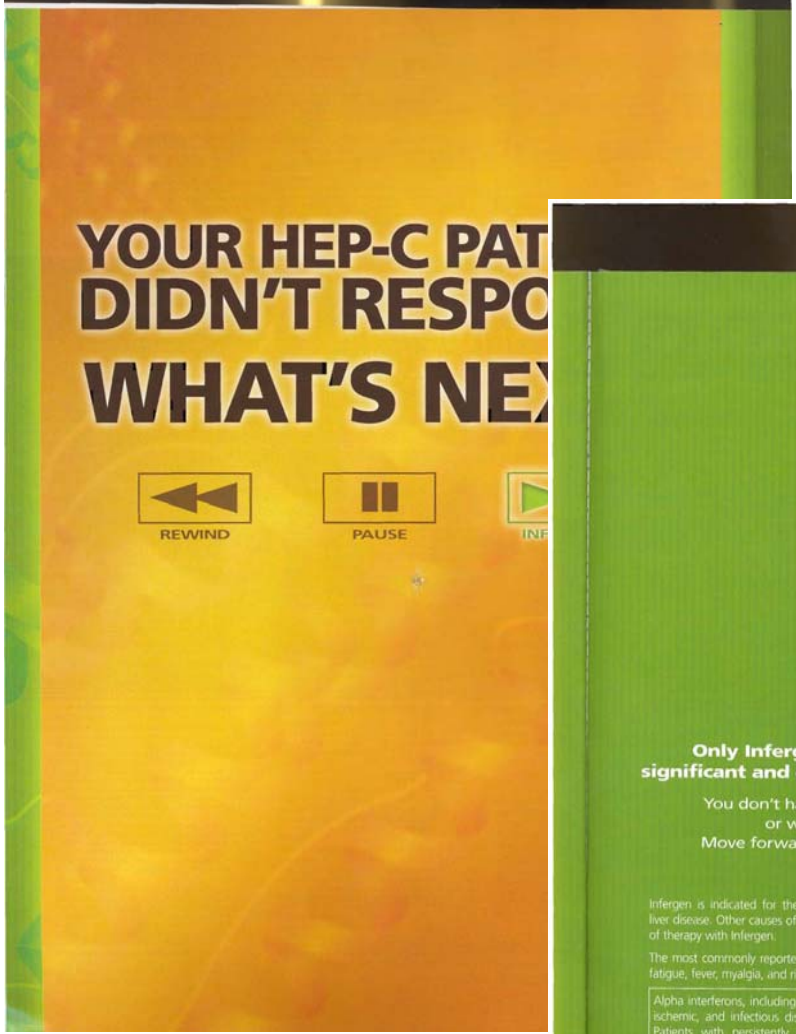
www.istavision.com | ISTA Pharmaceuticals ©2005 Allen Parkway Irvine, CA 92618 | ISTA Pharmaceuticals®



Only Infergen® offers a proven treatment option for the significant and growing number of nonresponders and relapsers.[1,2]

You don't have to rewind and retreat with another interferon alfa-2 or watch and wait for a new therapy. It's your move. Move forward with the unique interferon—bioengineered Infergen.

Infergen is indicated for the treatment of chronic HCV infection in patients 18 years of age or older with compensated liver disease. Other causes of hepatitis, such as viral hepatitis B or autoimmune hepatitis, should be ruled out prior to initiation of therapy with Infergen.

The most commonly reported adverse events during initial and subsequent treatment were flulike symptoms (eg, headache, fatigue, fever, myalgia, and rigors).

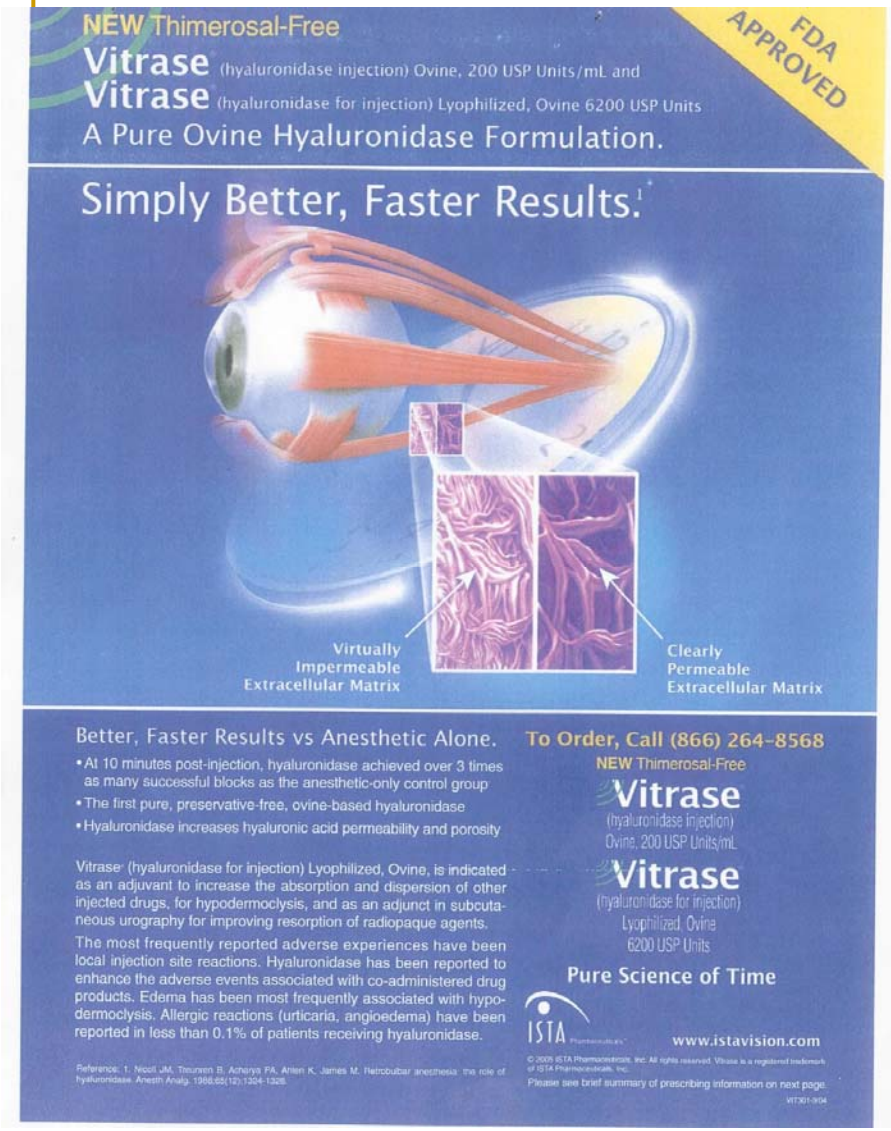
Alpha interferons, including Interferon alfacon-1, cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening symptoms of these conditions should be withdrawn from therapy. In many but not all cases, these disorders resolve after stopping Interferon alfacon-1 therapy. See WARNINGS and ADVERSE REACTIONS in full prescribing information.

Please see brief summary of prescribing information and references on following page.

The Consensus Interferon
INFERGEN™
Interferon alfacon-1

A First Choice for a Second Chance

For more information visit www.infergen.com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Vitrase (hyaluronidase injection) Ovine, 200 USP Units/mL and
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A Pure Ovine Hyaluronidase Formulation.
FDA APPROVED
Simply Better, Faster Results.[1]
Virtually Impermeable Extracellular Matrix
Clearly Permeable Extracellular Matrix
Better, Faster Results vs Anesthetic Alone.
• At 10 minutes post-injection, hyaluronidase achieved over 3 times as many successful blocks as the anesthetic-only control group
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Pure Science of Time
ISTA Pharmaceuticals
www.istavision.com
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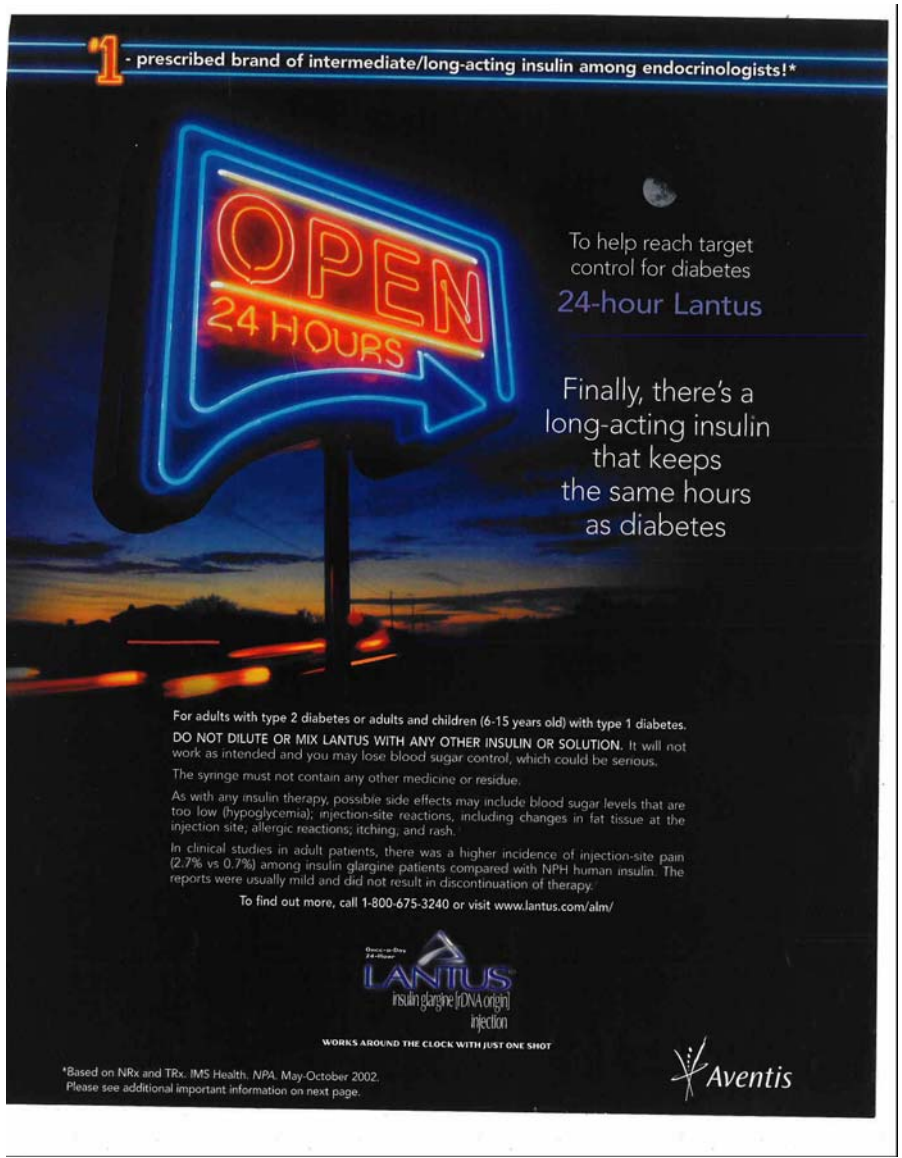
Please see brief summary of prescribing information on next page.
VIT301-9/04


#1 - prescribed brand of intermediate/long-acting insulin among endocrinologists!*
OPEN 24 HOURS
To help reach target control for diabetes
24-hour Lantus
Finally, there's a long-acting insulin that keeps the same hours as diabetes
For adults with type 2 diabetes or adults and children (6-15 years old) with type 1 diabetes.
DO NOT DILUTE OR MIX LANTUS WITH ANY OTHER INSULIN OR SOLUTION. It will not work as intended and you may lose blood sugar control, which could be serious.
The syringe must not contain any other medicine or residue.
As with any insulin therapy, possible side effects may include blood sugar levels that are too low (hypoglycemia); injection-site reactions, including changes in fat tissue at the injection site; allergic reactions; itching, and rash.
In clinical studies in adult patients, there was a higher incidence of injection-site pain (2.7% vs 0.7%) among insulin glargine patients compared with NPH human insulin. The reports were usually mild and did not result in discontinuation of therapy.
To find out more, call 1-800-675-3240 or visit www.lantus.com/alm/
LANTUS
insulin glargine [rDNA origin] injection
WORKS AROUND THE CLOCK WITH JUST ONE SHOT
*Based on NRx and TRx. IMS Health, NPA. May-October 2002.
Please see additional important information on next page.
Aventis

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The Consensus Interferon
INFERGEN™
Interferon alfacon-1

A First Choice for a Second Chance

For more information visit www.infergen.com

Does your family's allergy medicine treat both indoor and outdoor allergies?

If not, ask your doctor about switching to Zyrtec.

To learn more, visit www.zyrtec.com or call 1-800-ZYRTEC-2.

Allergies tend to run in families. Unlike some allergy medicines, prescription Zyrtec® is approved to treat all your family's indoor and outdoor allergies. Like grass. Ragweed. Dust. Mold. And even pet dander.

In fact, no other antihistamine is approved to treat more allergies than Zyrtec. Ask your doctor for free samples of Zyrtec pills or syrup.

In adults, the most common side effect was feeling drowsy. Some of the others were feeling tired and dry mouth. In children, 2 to 11 years old, some of the side effects were headache and stomach pain. Others were feeling drowsy and sore throat. Most were mild to moderate.

ZYRTEC®
cetirizine HCl

Lots of allergies. Just one Zyrtec.™

(Zur'-tek)

Please see important information about Zyrtec 5-mg and 10-mg tablets and 1-mg/mL syrup on the next page.

Professional vs. DTC

- Regulations do not distinguish
- Historically, approved physician labeling was reprinted as brief summary

Exhibit F

ZYRTEC® cetirizine HCl

For Seasonal and Year-round Allergies and Chronic Idiopathic Urticaria. Due caution should be exercised when driving a car or operating potentially dangerous machinery.

BRIEF SUMMARY ZYRTEC® (CETIRIZINE HYDROCHLORIDE) TABLETS AND SYRUP FOR ORAL USE
(FOR FULL PRESCRIBING INFORMATION, CONSULT PACKAGE INSERT)

CONTRAINDICATIONS ZYRTEC is contraindicated in those 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 some patients taking ZYRTEC; due caution should therefore be exercised when driving a car or operating potentially dangerous machinery. Concurrent use of ZYRTEC with alcohol or other CNS depressants should be avoided because additional reductions in alertness and additional impairment of CNS performance may occur. **Drug-Drug Interactions:** No clinically significant drug interactions have been found with theophylline at a low dose, azithromycin, pseudoephedrine, ketoconazole, or erythromycin. There was a small decrease in the clearance of cetirizine caused by a 400-mg dose of theophylline; it is possible that larger theophylline doses could have a greater effect. **Carcinogenesis, Mutagenesis and Impairment of Fertility:** In a 2-year carcinogenicity study in rats, cetirizine was not carcinogenic at dietary doses up to 20 mg/kg (approximately 15 times the maximum recommended daily oral dose in adults on a mg/m² basis, or approximately 10 times the maximum recommended daily oral dose in children on a mg/m² basis). In a 2-year carcinogenicity study in mice, cetirizine caused an increased incidence of benign liver tumors in males at a dietary dose of 16 mg/kg (approximately 6 times the maximum recommended daily oral dose in adults on a mg/m² basis, or approximately 4 times the maximum recommended daily oral dose in children on a mg/m² basis). No increase in the incidence of liver tumors was observed in mice at a dietary dose of 4 mg/kg (approximately 2 times the maximum recommended daily oral dose in adults on a mg/m² basis, or approximately equal to the maximum recommended daily oral dose in children on a mg/m² basis). The clinical significance of these findings during 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 in vivo micronucleus test in rats. In a fertility and general reproductive performance study in mice, cetirizine did not impair fertility at an oral dose of 64 mg/kg (approximately 25 times the maximum recommended daily oral dose in adults on a mg/m² basis). **Pregnancy Category B:** In mice, rats, and rabbits, cetirizine was not teratogenic at oral doses up to 96, 225, and 135 mg/kg, respectively (approximately 40, 100 and 220 times the maximum recommended daily oral dose in adults on a mg/m² 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:** 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 was excreted in milk. Cetirizine has been reported to be excreted in human breast milk. Because many drugs are excreted in human milk, use of ZYRTEC in nursing mothers is not recommended. **Geriatric Use:** In placebo-controlled trials, 186 patients aged 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. Subset analysis of efficacy in this group was not done. **Pediatric Use:** The safety of ZYRTEC at daily doses of 5 or 10 mg, has been demonstrated in 376 pediatric patients aged 6 to 11 years in placebo-controlled trials lasting up to four weeks and in 254 patients in a non-placebo-controlled 12-week trial. The safety of cetirizine has been demonstrated in 168 patients aged 2 to 5 years in placebo-controlled trials of up to 4 weeks duration. On a mg/kg basis, most of the 168 patients received between 0.2 and 0.4 mg/kg of cetirizine HCl. The effectiveness of ZYRTEC for the treatment of seasonal and perennial allergic rhinitis and chronic idiopathic urticaria in pediatric patients aged 2 to 11 years is based on an extrapolation of the demonstrated efficacy of ZYRTEC in adults in these conditions and the likelihood that the disease course, pathophysiology and the drug's effect are substantially similar between these two populations. The recommended doses for the pediatric population are based on cross-study comparisons of the pharmacokinetics and pharmacodynamics of cetirizine in adult and pediatric subjects and on the safety profile of cetirizine in both adult and pediatric patients at doses equal to or higher than the recommended doses. The cetirizine AUC and C_{max} in pediatric subjects aged 2 to 5 years who received a single dose of 5 mg of cetirizine syrup and in pediatric subjects aged 6 to 11 years who received a single dose of 10 mg of cetirizine syrup were estimated to be intermediate between that observed in adults who received a single dose of 10 mg of cetirizine tablets and those who received a single dose of 20 mg of cetirizine tablets. The safety and effectiveness of cetirizine in pediatric patients under the age of 2 years have not yet been established. **ADVERSE REACTIONS** Controlled and uncontrolled clinical trials conducted in the United States and Canada included more than 6000 patients aged 12 years and older, with more than 3900 receiving ZYRTEC at doses of 5 to 20 mg per day. 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 or 10 mg was not significantly different from placebo (2.9% vs. 2.4%, respectively). The most common adverse reaction in patients aged 12 years and older that occurred more frequently on ZYRTEC than placebo was somnolence. The incidence of somnolence associated with ZYRTEC was dose related, 6% in placebo, 11% at 5 mg and 14% 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 the incidence of adverse reactions. Table 1 lists adverse experiences in patients aged 12 years and older which were reported for ZYRTEC 5 and 10 mg in controlled clinical trials in the United States and that were more common with ZYRTEC than placebo. **Table 1. Adverse Experiences Reported in Patients Aged 12 Years and Older in Placebo-Controlled United States ZYRTEC Trials (Maximum Dose of 10 mg) at Rates of 2% or Greater (Percent Incidence) ZYRTEC (N=2034) Placebo (N=1612) respectively:** Somnolence (13.7 vs 6.3) Fatigue (5.9 vs 2.6) Dry Mouth (5.0 vs 2.3) Pharyngitis (2.0 vs 1.9) Dizziness (2.0 vs 1.2) In addition, headache and nausea occurred in more than 2% of the patients, but were more common in placebo patients. Pediatric studies were also conducted with ZYRTEC. More than 1300 pediatric patients aged 6 to 11 years with more than 900 treated with ZYRTEC at doses of 1.25 to 10 mg per day were included in controlled and uncontrolled clinical trials conducted in the United States. The duration of treatment ranged from 2 to 12 weeks. Placebo-controlled trials up to 4 weeks duration included 168 pediatric patients aged 2 to 5 years who received cetirizine, the majority of whom received single daily doses of 5 mg. The majority of adverse reactions reported in pediatric patients aged 2 to 11 years with ZYRTEC were mild or moderate. In placebo-controlled trials, the incidence of discontinuations due to adverse reactions in pediatric patients receiving up to 10 mg of ZYRTEC was uncommon (0.4% on ZYRTEC vs. 1.0% on placebo). Table 2 lists adverse experiences which were reported for ZYRTEC 5 and 10 mg in pediatric patients aged 6 to 11 years in placebo-controlled clinical trials in the United States and were more common with ZYRTEC than placebo. Of these, abdominal pain was considered treatment-related and somnolence appeared to be dose-related. 1.3% in placebo, 1.9% at 5 mg and 4.2% at 10 mg. The adverse experiences reported in pediatric patients aged 2 to 5 years in placebo-controlled trials were qualitatively similar in nature and generally similar in frequency to those reported in trials with children aged 6 to 11 years. **Table 2. Adverse Experiences Reported in Pediatric Patients Aged 6 to 11 Years in Placebo-Controlled United States ZYRTEC Trials (5 or 10 mg Dose) Which Occurred at a Frequency of ≥ 2% in Either the 5-mg or the 10-mg ZYRTEC Group, and More Frequently Than in the Placebo Group. ZYRTEC 5 mg (N=161), 10 mg (N=215) vs placebo (N=309):** Headache (11.0%, 5 mg; 14.0%, 10 mg; 12.3%, placebo); Pharyngitis (6.2%, 5 mg; 2.8%, 10 mg; 2.9%, placebo); Abdominal pain (4.4%, 5 mg; 5.6%, 10 mg; 1.9%, placebo); Coughing (4.4%, 5 mg; 2.8%, 10 mg; 3.9%, placebo); Somnolence (1.9%, 5 mg; 4.2%, 10 mg; 1.3%, placebo); Diarrhea (3.1%, 5 mg; 1.9%, 10 mg; 1.3%, placebo); Epistaxis (3.7%, 5 mg; 1.9%, 10 mg; 2.9%, placebo); Bronchospasm (3.1%, 5 mg; 1.9%, 10 mg; 1.9%, placebo); Nausea (1.9%, 5 mg; 2.8%, 10 mg; 1.9%, placebo); Vomiting (2.5%, 5 mg; 2.3%, 10 mg; 1.0%, placebo). The following events were observed infrequently (less than 2%), in either 3982 adults and children 12 years and older or in 659 pediatric patients aged 6 to 11 years who received ZYRTEC in U.S. trials, including an open adult study of six months' duration. A causal relationship of these infrequent events with ZYRTEC administration has not been established. **Autonomic Nervous System:** anorexia, flushing, increased salivation, urinary retention. **Cardiovascular:** cardiac failure, hypertension, palpitation, tachycardia. **Central and Peripheral Nervous Systems:** abnormal coordination, ataxia, confusion, dysphonia, hyperesthesia, hyperkinesia, hypertonia, hypoesthesia, leg cramps, migraine, myelitis, paralysis, paresthesia, ptosis, syncope, tremor, twitching, vertigo, visual field defect. **Gastrointestinal:** abnormal hepatic function, aggravated tooth caries, constipation, dyspepsia, eructation, flatulence, gastritis, hemorrhoids, increased appetite, melena, rectal hemorrhage, stomatitis including ulcerative stomatitis, tongue discoloration, tongue edema. **Genitourinary:** cystitis, dysuria, hematuria, micturition frequency, polyuria, urinary incontinence, urinary tract infection. **Hearing and Vestibular:** deafness, earache, ototoxicity, tinnitus. **Metabolic/Nutritional:** dehydration, diabetes mellitus, thirst. **Musculoskeletal:** arthralgia, arthritis, arthrosis, muscle weakness, myalgia. **Psychiatric:** abnormal thinking, agitation, amnesia, anxiety, decreased libido, depersonalization, depression, emotional lability, euphoria, impaired concentration, insomnia, nervousness, paroniria, sleep disorder. **Respiratory System:** bronchitis, dyspnea, hyperventilation, increased sputum, pneumonia, respiratory disorder, rhinitis, sinusitis, upper respiratory tract infection. **Reproductive:** dysmenorrhea, female breast pain, intermenstrual bleeding, leukorrhea, menorrhagia, vaginitis. **Reticuloendothelial:** lymphadenopathy. **Skin:** acne, alopecia, angioedema, bullous eruption, dermatitis, dry skin, eczema, erythematous rash, furunculosis, hyperkeratosis, hypertrichosis, increased sweating, maculopapular rash, photosensitivity reaction, photosensitivity toxic reaction, pruritus, purpura, rash, seborrhea, skin disorder, skin nodule, urticaria. **Special Senses:** parosmia, taste loss, taste perversion. **Vision:** blindness, conjunctivitis, eye pain, glaucoma, loss of accommodation, ocular hemorrhage, xerophthalmia. **Body as a Whole:** accidental injury, asthenia, back pain, chest pain, enlarged abdomen, face edema, fever, generalized edema, hot flashes, increased weight, leg edema, malaise, nasal polyp, pain, pallor, periorbital edema, peripheral edema, rigors. Occasional instances of transient, reversible hepatic transaminase elevations have occurred during cetirizine therapy. Hepatitis with significant transaminase elevation and elevated bilirubin in association with the use of ZYRTEC has been reported. In foreign marketing experience the following additional rare, but potentially severe adverse events have been reported: anaphylaxis, cholestasis, glomerulonephritis, hemolytic anemia, hepatitis, orofacial dyskinesia, severe hypotension, stillbirth, and thrombocytopenia. **DRUG ABUSE AND DEPENDENCE** There is no information to indicate that abuse or dependency occurs with ZYRTEC. **OVERDOSAGE** Overdosage has been reported with ZYRTEC. In one adult 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. In an 18-month-old pediatric patient who took an overdose of ZYRTEC (approximately 180 mg), restlessness and irritability were observed initially; this was followed by drowsiness. Should overdose occur, treatment should be symptomatic or supportive, taking into account any concomitantly ingested medications. There is no known specific antidote to ZYRTEC. ZYRTEC is not effectively removed by dialysis, and dialysis will be ineffective unless a dialysable agent has been concomitantly ingested. The acute minimal lethal oral doses were 237 mg/kg in mice (approximately 95 times the maximum recommended daily oral dose in adults on a mg/m² basis, or approximately 55 times the maximum recommended daily oral dose in children on a mg/m² basis) and 562 mg/kg in rats (approximately 400 times the maximum recommended daily oral dose in adults on a mg/m² basis, or approximately 270 times the maximum recommended daily oral dose in children on a mg/m² basis). In rodents, the target of acute toxicity was the central nervous system, and the target of multiple-dose toxicity was the liver.

Cetirizine is licensed from UCB Pharma, Inc.

Printed in U.S.A. 70-4573-00-3 Revised May 1998

CX056A00-B

Manufactured/Marketed by Pfizer U.S. Pharmaceuticals

Distributed by UCB Pharma


hydroxyzine. **PRECAUTIONS Activities Requi**
reported in some patients taking ZYRTEC; due ca
dangerous machinery. Concurrent use of ZYRTE
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significant drug interactions have been found wit
erythromycin. There was a small decrease in the c
larger theophylline doses could have a greater effe
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recommended daily oral dose in adults on a mg/m
children on a mg/m² basis). In a 2-year carcinoger
in males at a dietary dose of 16 mg/kg (approximat
or approximately 4 times the maximum recommen
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controlled trials, 186 patients aged 65 to 94 years r
group to patients under age 65. Subset analysis of
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0.6% on placebo). Fatigue and dry mouth also ap

Professional vs. DTC

- Regulations do not distinguish
- Historically, approved physician labeling was reprinted as brief summary
- When broadcast started, brief summary also used as part of adequate provision in 1997

Brief summary draft guidance

- Published February 2004

- Main points:
  - Using physician labeling is OK, but not preferable
  - Most serious and most common risks are essential
  - Request for comment and research
  - Format options

Format Options

- Approved Patient Package Insert
  - Often, but not always, in Q & A format

Patient Information 9094220

SINGULAIR® (SING-u-lair) Tablets, Chewable Tablets, and Oral Granules

Generic name: montelukast (mon-te-LOO-kast) sodium

Read this information before you start taking SINGULAIR®. Also, read the leaflet you get each time you refill SINGULAIR, since there may be new information in the leaflet since the last time you saw it. This leaflet does not take the place of talking with your doctor about your medical condition and/or your treatment.

What is SINGULAIR®?

- SINGULAIR is a medicine called a leukotriene receptor antagonist. It works by blocking substances in the body called leukotrienes. Blocking leukotrienes improves asthma and allergic rhinitis. SINGULAIR is not a steroid. Studies have shown that SINGULAIR does not affect the growth rate of children. (See the end of this leaflet for more information about asthma and allergic rhinitis.)

SINGULAIR is prescribed for the treatment of asthma and allergic rhinitis:

1. **Asthma.**
   SINGULAIR should be used for the long-term management of asthma in adults and children ages 12 months and older.

   Do not take SINGULAIR for the immediate relief of an asthma attack. If you get an asthma attack, you should follow the instructions your doctor gave you for treating asthma attacks.

2. **Allergic Rhinitis.**
   SINGULAIR is used to help control the symptoms of allergic rhinitis (sneezing, stuffy nose, runny nose, itching of the nose). SINGULAIR is used to treat seasonal allergic rhinitis (outdoor allergies that happen part of the year) in adults and children ages 2 years and older, and perennial allergic rhinitis (indoor allergies that happen all year) in adults and children ages 6 months and older.

Who should not take SINGULAIR?

Do not take SINGULAIR if you are allergic to SINGULAIR or any of its ingredients.

The active ingredient in SINGULAIR is montelukast sodium.

See the end of this leaflet for a list of all the ingredients in SINGULAIR.

What should I tell my doctor before I start taking SINGULAIR?

Tell your doctor about:

- **Pregnancy:** If you are pregnant or plan to become pregnant, SINGULAIR may not be right for you.
- **Breast-feeding:** If you are breast-feeding, SINGULAIR may be passed in your milk to your baby. You should consult your doctor before taking SINGULAIR if you are breast-feeding or intend to breast-feed.
- **Medical Problems or Allergies:** Talk about any medical problems or allergies you have now or had in the past.
- **Other Medicines:** Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, and herbal supplements. Some medicines may affect how SINGULAIR works, or SINGULAIR may affect how your other medicines work.

How should I take SINGULAIR?

For adults and children 12 months of age and older with asthma:

- Take SINGULAIR once a day in the evening.
- Take SINGULAIR every day for as long as your doctor prescribes it, even if you have no asthma symptoms.
- You may take SINGULAIR with food or without food.
- If your asthma symptoms get worse, or if you need to increase the use of your inhaled rescue medicine for asthma attacks, call your doctor right away.
- **Do not take SINGULAIR for the immediate relief of an asthma attack.** If you get an asthma attack, you should follow the instructions your doctor gave you for treating asthma attacks.
- Always have your inhaled rescue medicine for asthma attacks with you.
- Do not stop taking or lower the dose of your other asthma medicines unless your doctor tells you to.
- If your doctor has prescribed a medicine for you to use before exercise, keep using that medicine unless your doctor tells you not to.

For adults and children 2 years of age and older with seasonal allergic rhinitis, or for adults and children 6 months of age and older with perennial allergic rhinitis:

- Take SINGULAIR once a day, at about the same time each day.
- Take SINGULAIR every day for as long as your doctor prescribes it.
- You may take SINGULAIR with food or without food.

How should I give SINGULAIR oral granules to my child?

Do not open the packet until ready to use.

SINGULAIR 4-mg oral granules can be given:

- directly in the mouth;
- dissolved in 1 teaspoonful (5 mL) of cold or room temperature baby formula or breast milk;
- mixed with a spoonful of one of the following soft foods at cold or room temperature: applesauce, mashed carrots, rice, or ice cream.

Be sure that the entire dose is mixed with the food, baby formula, or breast milk and that the child is given the entire spoonful of the food, baby formula, or breast milk mixture right away (within 15 minutes).

IMPORTANT: Never store any oral granules mixed with food, baby formula, or breast milk for use at a later time. Throw away any unused portion.

Do not put SINGULAIR oral granules in any liquid drink other than baby formula or breast milk. However, your child may drink liquids after swallowing the SINGULAIR oral granules.

What is the daily dose of SINGULAIR for asthma or allergic rhinitis?

For Asthma (Take in the evening):

- One 10-mg tablet for adults and adolescents 15 years of age and older,
- One 5-mg chewable tablet for children 6 to 14 years of age,
- One 4-mg chewable tablet or one packet of 4-mg oral granules for children 2 to 5 years of age, or
- One packet of 4-mg oral granules for children 12 to 23 months of age.

For Allergic Rhinitis (Take at about the same time each day):

- One 10-mg tablet for adults and adolescents 15 years of age and older,
- One 5-mg chewable tablet for children 6 to 14 years of age,
- One 4-mg chewable tablet for children 2 to 5 years of age, or
- One packet of 4-mg oral granules for children 2 to 5 years of age with seasonal allergic rhinitis, or for children 6 months to 5 years of age with perennial allergic rhinitis.

What should I avoid while taking SINGULAIR?

If you have asthma and if your asthma is made worse by aspirin, continue to avoid aspirin or other medicines called non-steroidal anti-inflammatory drugs while taking SINGULAIR.

What are the possible side effects of SINGULAIR?

The side effects of SINGULAIR are usually mild, and generally did not cause patients to stop taking their medicine. The side effects in patients treated with SINGULAIR were similar in type and frequency to side effects in patients who were given a placebo (a pill containing no medicine).

The most common side effects with SINGULAIR include:

- stomach pain
- stomach or intestinal upset
- heartburn
- tiredness
- fever
- stuffy nose
- cough
- flu
- upper respiratory infection
- dizziness
- headache
- rash

Less common side effects that have happened with SINGULAIR include (listed alphabetically):
agitation including aggressive behavior, allergic reactions (including swelling of the face, lips, tongue, and/or throat, which may cause trouble breathing or swallowing), hives, and itching, bad/vivid dreams, increased bleeding tendency, bruising, diarrhea, drowsiness, hallucinations (seeing things that are not there), hepatitis, indigestion, inflammation of the pancreas, irritability, joint pain, muscle aches and muscle cramps, nausea, palpitations, pins and needles/numbness, restlessness, seizures (convulsions or fits), swelling, trouble sleeping, and vomiting.

Rarely, asthmatic patients taking SINGULAIR have experienced a condition that includes certain symptoms that do not go away or that get worse. These occur usually, but not always, in patients who were taking steroid pills by mouth for asthma and those steroids were being slowly lowered or stopped. Although SINGULAIR has not been shown to cause this condition, **you must tell your doctor right away if you get one or more of these symptoms:**

- a feeling of pins and needles or numbness of arms or legs
- a flu-like illness
- rash
- severe inflammation (pain and swelling) of the sinuses (sinusitis)

These are not all the possible side effects of SINGULAIR. For more information ask your doctor or pharmacist.

Talk to your doctor if you think you have side effects from taking SINGULAIR.

General Information about the safe and effective use of SINGULAIR

Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use SINGULAIR for a condition for which it was not prescribed. Do not give SINGULAIR to other people even if they have the same symptoms you have. It may harm them. **Keep SINGULAIR and all medicines out of the reach of children.**

Store SINGULAIR at 25°C (77°F). Protect from moisture and light. Store in original package.

This leaflet summarizes information about SINGULAIR. If you would like more information, talk to your doctor. You can ask your pharmacist or doctor for information about SINGULAIR that is written for health professionals.

What are the ingredients in SINGULAIR?

Active ingredient: montelukast sodium

SINGULAIR chewable tablets contain aspartame, a source of phenylalanine.
Phenylketonurics: SINGULAIR 4-mg and 5-mg chewable tablets contain 0.674 and 0.842 mg phenylalanine, respectively.

Inactive ingredients:

- 4-mg oral granules: mannitol, hydroxypropyl cellulose, and magnesium stearate.
- 4-mg and 5-mg chewable tablets: mannitol, microcrystalline cellulose, hydroxypropyl cellulose, red ferric oxide, croscarmellose sodium, cherry flavor, aspartame, and magnesium stearate.
- 10-mg tablet: microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, hydroxypropyl cellulose, magnesium stearate, hydroxypropyl methylcellulose, titanium dioxide, red ferric oxide, yellow ferric oxide, and carnauba wax.

What is asthma?

Asthma is a continuing (chronic) inflammation of the bronchial passageways which are the tubes that carry air from outside the body to the lungs.

Symptoms of asthma include:

- coughing
- wheezing
- chest tightness
- shortness of breath

What is allergic rhinitis?

- Seasonal allergic rhinitis, also known as hay fever, is triggered by outdoor allergens such as pollens from trees, grasses, and weeds.
- Perennial allergic rhinitis may occur year-round and is generally triggered by indoor allergens such as dust mites, animal dander, and/or mold spores.
- Symptoms of allergic rhinitis may include:
  - stuffy, runny, and/or itchy nose
  - sneezing

Rx only
US Patent No.: 5,565,473

Issued September 2006

Distributed by:
MERCK & CO., INC.
Whitehouse Station, NJ 08889, USA
20652988(1)(220)-SNG-CON

Patient Information

AVODART® (dutasteride) Soft Gelatin Capsules

AVODART is for use by men only.

Read this information carefully before you start taking AVODART. Read the information you get with AVODART each time you refill your prescription. There may be new information. This information does not take the place of talking with your doctor.

0.5 mg/Once Daily

AVODART® (dutasteride)

What is **AVODART**?

AVODART is a medication for the treatment of symptoms of benign prostatic hyperplasia (BPH) in men with an enlarged prostate to:

- Improve symptoms
- Reduce the risk of acute urinary retention (a complete blockage of urine flow)
- Reduce the risk of the need for BPH-related surgery

AVODART is not a treatment for prostate cancer. See the end of this leaflet for information about how AVODART works.

Who should NOT take **AVODART**?

- Women and children should not take AVODART. A woman who is pregnant or capable of becoming pregnant should not handle AVODART capsules. See **"What are the special warnings for women about AVODART?"**
- Do not take AVODART if you have had an allergic reaction to AVODART or any of its ingredients.

What are the special warnings for women about **AVODART**?

- Women should never take AVODART.
- Women who are pregnant or may become pregnant should not handle AVODART Capsules. If a woman who is pregnant with a male baby gets enough AVODART into her body after swallowing it or through her skin after handling it, the male baby may be born with abnormal sex organs.

What are the special precautions about **AVODART**?

- Men treated with AVODART should not donate blood until at least 6 months after their final dose to prevent giving AVODART to a pregnant female through a blood transfusion.
- Tell your doctor if you have liver problems. AVODART may not be right for you.

How should I take **AVODART**?

- Take 1 AVODART capsule once a day.
- Swallow the capsule whole.
- You can take AVODART with or without food.
- If you miss a dose, you may take it later that day. Do not make up the missed dose by taking 2 doses the next day.
- You may find it helpful to take AVODART at the same time every day to help you remember to take your dose.

What are the possible side effects of **AVODART**?

Possible side effects are impotence (trouble getting or keeping an erection), a decrease in libido (sex drive), enlarged breasts, a decrease in the amount of semen released during sex, and allergic reactions such as rash, itching, hives, and swelling of the lips or face. These events occurred infrequently.

Talk with your doctor if you have questions about these and other side effects that you think may be related to taking AVODART.

How should I store **AVODART**?

AVODART is a soft gelatin capsule that may become soft and leak or may stick to other capsules if kept at high temperatures. Store AVODART capsules at room temperature of 77°F (25°C) or lower.

If your capsules are cracked or leaking, don't use them, and contact your pharmacist.

General information about **AVODART**.

- Do not use AVODART for a condition for which it was not prescribed.
- Do not share your AVODART.
- Ask your doctor about how often you should return for a visit to check your BPH.
- A blood test called PSA (prostate-specific antigen) is sometimes used to detect prostate cancer. AVODART will reduce the amount of PSA measured in your blood. Your doctor is aware of this effect and can still use PSA to detect prostate cancer in you.

If you have questions about AVODART, ask your doctor or pharmacist. They can show you detailed information about AVODART that was written for healthcare professionals.

How does **AVODART** work?

Prostate growth is caused by a hormone in the blood called dihydrotestosterone (DHT). AVODART lowers DHT production in the body, leading to shrinkage of the enlarged prostate in most men. Just as your prostate became large over a long period of time, reducing the size of your prostate and improving your symptoms will take time. While some men have fewer problems and symptoms after 3 months of treatment with AVODART, a treatment period of at least 6 months is usually necessary to see if AVODART will work for you. Studies have shown that treatment with AVODART for 2 years reduces the risk of complete blockage of urine flow (acute urinary retention) and/or the need for surgery for benign prostatic hyperplasia.

GlaxoSmithKline

Manufactured by Cardinal Health
Beinheim, France for GlaxoSmithKline
Research Triangle Park, NC 27709

Money April 2007

Format Options

- Approved Patient Package Insert
  - Often, but not always, in Q & A format
- Consumer-friendly highlights
  - Content and Format Rule, January 2006

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fantom safely and effectively. See full prescribing information for Fantom.

FANTOM (motnaf) INJECTION

Initial U.S. Approval: 2003

WARNING: ANAPHYLAXIS

See full prescribing information for complete boxed warning

- **Anaphylaxis and severe hypersensitivity reactions, some of which were fatal, occurred in 2-4% of patients (5.1).**
- **Premedicate patients with a corticosteroid, diphenhydramine, and an H^2 antagonist (2.4, 5.1)**
- **Fatal reactions have occurred despite premedication (5.1)**

----------INDICATIONS AND USAGE----------

Fantom is an antineoplastic indicated for:

Advanced Carcinoma of the Ovary (1.1)

- First-line, in combination with cisplatin, and as subsequent therapy for the treatment of advanced carcinoma of the ovary.

Breast Cancer (1.2)

- After failure of combination chemotherapy for metastatic disease or after relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated. Fantom has not been shown to be beneficial in patients with estrogen and progesterone-receptor-positive tumors.
- Adjuvant treatment of node-positive breast cancer following doxorubicin-containing combination chemotherapy.

----------DOSAGE AND ADMINISTRATION----------

Fantom should not be prepared or administered using PVC containers and administration sets.

Advanced Carcinoma of the Ovary (2.1)

Previously untreated:

- 135 mg/m^2 over 24 hours or 175 mg/m^2 over 3 hours followed by cisplatin 75 mg/m^2 every 3 weeks

Prior chemotherapy:

- 135 mg/m^2 or 175 mg/m^2 over 3 hours every 3 weeks

Breast Cancer (2.2)

After failure of combination chemotherapy for metastatic disease or after relapse within 6 months of adjuvant chemotherapy:

- 175 mg/m^2 over 3 hours every 3 weeks

Adjuvant treatment of node-positive breast cancer:

- 175 mg/m^2 over 3 hours every 3 weeks for 4 courses, given after doxorubicin-containing combination chemotherapy.

Premedication (2.4)

- Dexamethasone 20 mg PO 12 hours pretreatment
- Diphenhydramine 50 mg IV 30 minutes pretreatment
- Cimetidine 300 mg IV or Ranitidine 50 mg IV 30 minutes pretreatment

See full prescribing information for subsequent courses (2.3) and IV administration instructions (2.5).

----------DOSAGE FORMS AND STRENGTHS----------

- 50 mg/5 ml multidose vial (3)
- 100 mg/10 ml multidose vial (3)

----------CONTRAINDICATIONS----------

History of hypersensitivity to Fantom or other drugs formulated with Xenophor XL (polyoxymethylated sunflower oil). (4)

----------WARNINGS AND PRECAUTIONS----------

- Anaphylaxis and hypersensitivity reactions (5.1)
- Bone marrow suppression, primarily neutropenia (5.2)
- Severe conduction abnormalities in < 1% of patients (5.4)
- Hypotension, bradycardia, and hypertension (5.4)
- Peripheral neuropathy, in some cases severe (5.6)
- Injection site reactions, including delayed and recall reactions (5.7)

----------ADVERSE REACTIONS----------

Most common adverse reactions (>50%) are neutropenia, alopecia, anemia, peripheral neuropathy, myalgia/arthralgia, and nausea and vomiting (6).

To report SUSPECTED ADVERSE REACTIONS, contact (manufacturer) at (phone # and Web address) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

----------DRUG INTERACTIONS----------

- Cisplatin may decrease clearance of Fantom, which can result in severe myelosuppression (5.3, 7.1)
- Drugs metabolized by cytochrome P450 isoenzymes CYP2C8 and CYP3A4 may decrease clearance of Fantom (7.2)
- Doxorubicin levels may be increased (7.3)

----------USE IN SPECIFIC POPULATIONS----------

- Fantom can cause fetal harm when used during pregnancy (5.8, 8.1)
- The concentration of dehydrated alcohol in the Fantom vehicle may cause CNS toxicity in pediatric patients when Fantom is administered over a short period of time (5.5, 8.4)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 5/200X

FULL PRESCRIBING INFORMATION: CONTENTS*

Other formats?

- FDA recognizes other ways to present information may be appropriate
- Currently conducting research
- Happy to review new brief summary formats

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