Antitussive

- The only 12-hour liquid hydrocodone
- No middle-of-the-night or mid-day dosing
- Contains no iodinated glycerol
- One of the most economical prescription antitussives
- The most frequently prescribed liquid hydrocodone

Please see following page for Full Prescribing Information, including complete precautionary information.

TUSSIONEX is contraindicated in the presence of known allergy to hydrocodone or chlorpheniramine. The most common adverse reactions are sedation, drowsiness, and mental clouding, which may impair the mental and/or physical abilities required for potentially hazardous tasks, such as driving a car or operating machinery.

TUSSIONEX
HYDROCODONE BITARTRATE AND CHLORPHENIRAMINE POLISTIREX
EXTENDED-RELEASE SUSPENSION

Each teaspoonful (5 mL) provides the equivalent of 10 mg hydrocodone bitartrate and 8 mg chlorpheniramine maleate.
**TUSSIONEX® (hydrocodone polistirex) Extended-Release Suspension**

**Warnings:**

- Hypertrophy
- Headache
- Delirium
- Convulsions
- Seizures
- Opioid-induced respiratory depression

**Other Information:**

- **Pharmacology:**
  - Hydrocodone is a semisynthetic narcotic antitussive and analgesic with multiple actions qualitatively similar to those of codeine.
  - Its precise mechanism of action is unknown; however, hydrocodone is believed to act directly on the cough center.
  - In excessive doses, hydrocodone, like other opioid derivatives, will depress respiration.
  - The effects of hydrocodone in therapeutic doses on the cardiovascular system are insignificant.

**经济社会 Phase:**

- Hydrocodone sulfate syrup, with or without alcohol, is available as a semisynthetic hydrocodone derivative.
- Hydrocodone conveys a moderate risk of respiratory depression in the newborn, especially if higher doses are used.

**Pharmacokinetics:**

- Hydrocodone is rapidly absorbed after oral administration, with peak plasma concentrations occurring within 2-3 hours.
- The elimination half-life of hydrocodone is approximately 3-4 hours.

**INDICATIONS AND USAGE:**

- **Cough and Upper Respiratory Symptomatic Relief:**
  - TUSSIONEX® is indicated for the relief of cough and upper respiratory symptoms associated with a cold or allergy.

**CONTRAINDICATIONS:**

- Known allergy or sensitivity to hydrocodone or chlorpheniramine.

**WARNINGS:**

- Respiration Depression: As with all narcotics, TUSSIONEX® can produce profound respiratory depression which may be marked in patients with respiratory disease or when administered to patients with respiratory disease.

**Pediatric Use:**

- Use caution in children with respiratory disease, as respiratory depression may be marked in such patients.

**Adverse Reactions:**

- The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increased intracranial pressure.

**Adverse Effects:**

- CNS: Confusion, drowsiness, dizziness, hallucinations, anticholinergic effects (干眼), vertigo, ataxia, depression, sedation, psychomotor retardation, loss of coordination.

- GI: Constipation, nausea, vomiting, dry mouth, abdominal pain, cramps, diarrhea, flatulence.

- Other: Allergic reactions, rash, urticaria, angioedema, vasodilation, bronchospasm, wheezing.

**Drug Interactions:**

- Anticholinergic, antihistaminic, opioid, tricyclic antidepressant, CNS depressant drugs, or sedative hypnotics may be additive.

**OVERDOSAGE:**

- In patients with respiratory depression, supplemental oxygen and pressor agents should be given in addition to immediate efforts at intubation and establishment of an adequate airway.

**Precautions:**

- Use TUSSIONEX® with caution in the presence of head trauma, intracranial lesions, or other conditions that may lower the threshold to respiratory depression.

**Pregnancy:**

- Use during pregnancy only if the potential benefit justifies the potential risk.

**References:**

Make sure they’re covered.

Are all your patients adequately immunized? Be sure. Get the latest facts on immunization. Call 800 621-8335 for a free information packet from the American Medical Association and the Centers for Disease Control and Prevention. It covers everything from general information on vaccines and immunization schedules for children to facts on vaccines for older adults and immunocompromised patients. Call for your packet today, and ask for order number NC015895.

American Medical Association
Physicians dedicated to the health of America
BRIEF SUMMARY

INDICATIONS AND USAGE

Ambien® (zolpidem tartrate) is indicated for the short-term treatment of insomnia. Hypnics should generally be limited to 7 to 10 days of use, although treatment may be continued for up to 2 weeks if there is a continued need. Patients should be cautioned about the risk of oversleeping if the drug is taken for 7 to 10 days and then suddenly discontinued.

Contraindications

None known.

WARNINGS

Sexual side effects may be present in some patients. For some patients, sexual side effects may occur even if the drug is used for a short period of time. The drug should be used only by patients who do not have a history of sexual dysfunction.

The risk of sexual side effects may be increased in patients who have a history of sexual dysfunction or who are taking other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased in patients who are taking medications that may decrease sexual side effects.

In some patients, sexual side effects may be decreased if the drug is used in combination with other medications.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.

The risk of sexual side effects may be increased if the drug is used in combination with other medications that may cause sexual side effects.

The risk of sexual side effects may be decreased if the drug is used in combination with other medications that may decrease sexual side effects.
From a unique chemical class of non-benzodiazepine sleep agents

More sleep
Total sleep time is significantly increased compared with placebo. Patients fall asleep quickly; generally within 20 to 30 minutes.1-3

Better sleep
Awakenings were reduced, compared to placebo.

Through the night
No evidence of increased wakefulness during the last third of the night. Normal sleep stages are generally preserved1 (clinical significance unknown).

With no objective evidence of tolerance or rebound insomnia
In studies of up to 35 consecutive nights at recommended doses.1,2

Favorable safety and tolerability profile
Adverse events with dosages of ≤ 10 mg that were statistically significant vs placebo

<table>
<thead>
<tr>
<th></th>
<th>Short-term: ≤10 nights</th>
<th>Long-term: 28 to 35 nights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drowsiness</td>
<td>2%</td>
<td>dizziness 5%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1%</td>
<td>Drugged</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1%</td>
<td>Feelings 3%</td>
</tr>
</tbody>
</table>

Please see references and brief summary of prescribing information on the last page of this advertisement.
Some Musings on the Physician-God Syndrome
Arthur F. Schiff, MD

Rural Physician Retention and Workload: A Moving Target
Stephen H. Kriebel, MD
Marc Horowitz, MD
David A. Smith, MD

In Reply
Arch G. Mainous III, PhD;
Mary Ramsbottom-Lucier, MD, MPH;
Eugene C. Rich, MD
Donald Pathman, MD, MPH

Herpes Simplex Virus Infection in Family Practice: Epidemiology 101
Alfred O. Berg, MD, MPH

Mental Diagnoses in Primary Care: The Next Generation
Frank deGruy, MD, MSFM

Herpes Simplex Virus Infection in Family Practice: Epidemiology 101
Alfred O. Berg, MD, MPH

Mental Diagnoses in Primary Care: The Next Generation
Frank deGruy, MD, MSFM

Development and Validation of the SDDS-PC Screen for Multiple Mental Disorders in Primary Care
W. Eugene Broadhead, MD, PhD; Andrew C. Leon, PhD;
Myrna M. Weissman, PhD; James E. Barrett, MD;
Robert S. Blacklow, MD; Thomas T. Gilbert, MD, MPH;
Martin B. Keller, MD; Mark Olfson, MD;
Edmund S. Higgins, MD

Brief Diagnostic Interviews (SDDS-PC) for Multiple Mental Disorders in Primary Care: A Pilot Study
Myrna M. Weissman, PhD; Mark Olfson, MD;
Andrew C. Leon, PhD; W. Eugene Broadhead, MD, PhD;
Thomas T. Gilbert, MD, MPH; Edmund S. Higgins, MD;
James E. Barrett, MD; Robert S. Blacklow, MD;
Martin B. Keller, MD; Christina Hoven, DrPH
RELAFEN®
brand of nabumetone

Brief Summary: Consult full prescribing information before using.

CLINICAL PHARMACOLOGY: RELAFEN is a nonsteroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammation, analgesic and antipyretic properties in pharmacologic studies. As with other nonsteroidal anti-inflammatory agents, its mode of action is not known. However, the ability to inhibit prostaglandin synthesis may be involved in the anti-inflammatory effect.

The parent compound is a prodrug, which undergoes hepatic biotransformation to the active component, 6-methoxy-2-naphthylacetic acid (MNA), a potent inhibitor of prostaglandin synthesis.

INDICATIONS AND USAGE: Acute and chronic treatment of signs and symptoms of osteoarthritis and rheumatoid arthritis.

CONTRAINDICATIONS: Patients (1) who have exhibited hypersensitivity to it; (2) whom aspirin, aspirin or other NSAIDs induce asthma, urticaria or other allergic-type reactions.

WARNINGS: Renal failure after ulceration and bleeding in patients treated chronically, even in the absence of previous GI tract symptoms.

In controlled clinical trials involving 1,877 patients treated with RELAFEN (1,140 followed for one year and 927 for two years), the cumulative incidence of peptic ulcers was 0.3% (95% CI: 0.1%, 0.5%) in those less than ten months, 0.5% (95% CI: 0.1%, 0.9%) in one year, and 0.8% (95% CI: 0.5%, 1%) in two years. Informed patients of the signs and symptoms of serious GI toxicity and what steps to take if they occur. In patients with active peptic ulcer, weigh the benefits of RELAFEN therapy against possible hazards. Institute an appropriate ulcer treatment regimen and monitor the patient's progress carefully.

In considering the use of relatively large doses within the recommended dosage range, anticipate benefit to be sufficient to offset the potential increased risk of GI toxicity.

PRECAUTIONS: Because nabumetone undergoes extensive hepatic metabolism, no adjustment of RELAFEN dosage is generally necessary in patients with renal insufficiency. However, use all NSAIDs, monitor patients with impaired renal function more closely than patients with normal renal function.

Evaluate patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, for evidence of the development of a more severe hepatic reaction while on RELAFEN. If abnormal liver test results or jaundice develop, or if symptoms consistent with liver disease arise, or if jaundice manifests occur, e.g., pruritus, rash, etc., discontinue RELAFEN. Use RELAFEN cautiously in patients with severe hepatic impairment.

As with other NSAIDs, use RELAFEN cautiously in patients with a history of congestive heart failure, hypertension or other conditions predisposing to fluid retention.

Based on U.V. light photostability testing, RELAFEN may be associated with more reactions to sun exposure than might be expected based on skin tanning types.

Physicians may wish to discuss with their patients the potential risks (see WARNINGS, PRECAUTIONS and ADVERSE REACTIONS) and likely benefits of RELAFEN treatment, particularly when the drugs are used in the unusual conditions where treatment without NSAIDs may represent an acceptable alternative to form the patient and the physician. Exercise caution when administering RELAFEN with warfarin since interactions have been seen with other NSAIDs.

If severe studies conducted in mice and rats, nabumetone had no statistically significant teratogenic effect. Nabumetone did not show mutagenic potential in the Ames test and mouse micronucleus test in vivo. However, nabumetone and MNA-induced chromosomal aberrations in in vitro synchronized cultures at low concentrations (equal to the average human exposure to RELAFEN at the maximum recommended dose).

Nabumetone did not impair fertility of male or female rats treated orally at doses of 330 mg/kg body weight.

Pregnancy Category C: Nabumetone did not cause any teratogenic effect in rats given up to 400 mg/kg and in rabbits up to 300 mg/kg orally. However, increased post-implantation loss was observed in rats at 100 mg/kg orally and at higher doses (equal to the average human exposure to RELAFEN at the maximum recommended dose).

RELAFEN is not recommended for use in nursing mothers.

Safety and efficacy is children have not been established.

Of the 1,877 patients in U.S. clinical trials who were treated with RELAFEN, 411 patients (24%) were 65 years of age or older, 131 patients (7%) were 75 years of age or older. No overall differences in efficacy or safety were observed between these earlier patients and younger ones. Similar results were observed in a one-year, non-U.S. postmarketing surveillance study of 10,860 RELAFEN patients, of whom 6,578 patients (42%) were 65 years of age or older.

ADVERSE REACTIONS: Incidence: %—Probably Causally Related—Diabetes (14%), convulsions (13%), abdominal pain (12%), constipation, headache, nausea, vomiting, diarrhea, rash.

Incidence: %—Causal Relationship—Bilirubinuria, incidence, urticaria, headache, myalgia, arthralgia, anorexia, abdominal pain, anxiety, palpitations, insomnia, nervousness, somnolence, pruritus, rash, tremors, edema.

Incidence: %—Reactions occurring with less than 3% and 3% to 9%: headache, nasal congestion, nausea, epigastric pain, pyrexia, dyspepsia, diarrhea, arthralgia, myalgia, urticaria, nasal congestion, edema, rash, pruritus, headache, rash, urticaria, vomiting, nervousness, somnolence.

Injection site reactions occurring with less than 3% and 3% to 9%: pain, redness, induration, bruising, swelling.

OVERDOSAGE: If acute overdose occurs, empty the stomach by vomiting or lavage and institute general supportive measures. Activated charcoal, up to 88 gms, may effectively deplete nabumetone absorption. Co-administration of naxenotone with charcoal to man has resulted in a 30% decrease in maximum plasma concentrations of the active metabolite.

One overdose occurred in a 17-year-old female patient who had a history of abdominal pain and was hospitalised last for increased abdominal pain following ingestion of 36 RELAFEN tablets (1.1 gms total). Stools were negative for occult blood and haematochromatosis was not in serum hemoglobin concentration was low. The patient had no other symptoms. She was given an H2-receptor antagonist and discharged from the hospital without sequelae.

DOSAGE AND ADMINISTRATION: Recommended starting dose: 1,000 mg taken as a single dose or without food. In some cases, a single dose of 65 mg (equivalent to about 160 mg of nabumetone) was administered. This dose may be increased to 2,000 mg daily. If a single-dose regimen is used, the patient should be evaluated on a regular basis. The starting dose may be increased to 2,000 mg daily, but the upper limit of 4,000 mg daily has not been studied. Use the lowest effective dose for chronic treatment.

HOW SUPPLIED: Tablets: 50 mg—white, imprinted with the product name RELAFEN and 500, in bottles of 100 and 500, and in Single Unit Package of 100 (intended for institutional use only). 750 mg—beige, imprinted with the product name RELAFEN and 750, in bottles of 100 and 500, and in Single Unit Package of 100 (intended for institutional use only). Store at controlled room temperature (15° to 30°C) in well-closed container; dispense in light-resistant container.

Call toll-free 1-800-AMA-2350
Turn everyday challenges into everyday activities

*GI symptoms comparable to other NSAIDs, including diarrhea, dyspepsia, and abdominal pain. In patients treated chronically with NSAID therapy, serious GI toxicity such as perforation, ulceration, and bleeding can occur.

As with other NSAIDs, rare renal and hepatic reactions have been reported. Please see precautions section of prescribing information. Contraindicated in patients who are hypersensitive to aspirin or other NSAIDs.

Please see brief summary of prescribing information on adjacent page.

Effective relief with a low incidence of peptic ulcer*
Directory of Information Services

ONLINE SERVICES

CD Plus Technologies
333 Seventh Avenue
New York, NY 10001
Phone: 212-563-3006; Fax: 212-563-3784
Full-text articles from JAMA

Dialog Information Services, Inc.
3460 Hillview Avenue, PO Box 10101
Palo Alto, CA 94303
Phone: 800-3-DIALOG; Fax: 415-858-7099
Full-text articles from JAMA and the Archives journals

Information Access Company
562 Lakeside Drive
Foster City, CA 94404
Phone: 800-227-8431; Fax: 415-378-5369
Full-text articles from JAMA, the Archives journals and American Medical News

Note: AMA publications are no longer available through Nexis/Lexis Research Services.

DOCUMENT DELIVERY

Genuine Article/Institute for Scientific Information
3501 Market Street
Philadelphia, PA 19104
Phone: 215-386-0100, ext. 1140-1145; Fax: 215-386-4343
and 215-222-6840; Internet: TGA @ ISINET.COM
Copies of complete articles from JAMA and the Archives journals

Uncover Company
3801 E. Florida, Suite 200
Denver, CO 80210
Phone: 303-758-0330; Fax: 303-758-5946; Internet: database.carl.org
Copies of complete articles from JAMA and the Archives journals

CD-ROM

Appleton and Lange
25 Van Zant Avenue, PO Box 5630
Norwalk, CT 06856-5630
Phone: 203-838-4400; Fax: 203-857-4148
JAMA available from 1976 through 1993 on a single disc

Information Access Company
362 Lakeside Drive
Foster City, CA 94404
Phone: 800-227-8431; Fax: 415-378-5369
Full-text of JAMA and AMNews updated monthly in a rolling 3-year format

American Psychiatric Press
1400 K Street, NW
Washington, DC 20005
Phone: 202-682-6268; Fax: 202-789-2648
Full-text of Archives of General Psychiatry updated quarterly

Directory of Reader Services

SUBSCRIBER SERVICES

For information about subscribing to any of the AMA publications, change of address, missing issues, or purchasing back issues, please contact Subscriber Services Center, PO Box 10945, Chicago, IL 60610, at the numbers below. The center's hours are between 8:30 am and 4:30 pm CST.

JAMA BOUND VOLUMES

Preserve a complete year of JAMA with an archival, bound volume set. Issues are printed on acid-free paper and include full-color covers. Each compact volume holds six months of issues and is just 2 1/4 inches thick for easy handling. Bound volume sets are available beginning with 1994. See Information below to order. Please specify 1994 or 1995 subscription year when ordering.

SINGLE COPY SALES

Issues published in the last two years are available for purchase, subject to availability. Single-copy rates for delivery in the US are: $11 per copy of JAMA; $16 per copy of the Archives journals; and $8 per copy of AMNews. Prepayment is required. Issues can be ordered by phone, mail, or fax through Subscriber Services at the numbers below.

REPRINTS

Authorized reprints may be purchased in quantities of 300 or more. For smaller quantities, back issues may be purchased at the single-copy rate. For prices and ordering information, contact the Reprints Coordinator, PO Box 10945, Chicago, IL 60610. Phone: 312-464-2521.

CLASSIFIED ADVERTISING

JAMA classified rates are $4.25 per word, per issue (bold type is $4.65 per word, per issue), with a minimum of 20 words. Blind Box Service is available at an additional cost of $20 per issue. For further information and rates on classified display advertising and network buys for all AMA publications, contact an AMA Classified Representative at 312-464-2475 /2490 /2401/4485; Fax: 312-464-5909.

SUBSCRIBE TO AMA PUBLICATIONS

For information on any of these AMA publications, or to place an order, contact Subscriber Services at 800-AMA-2350 (Fax: 312-464-5831). A surcharge for expedited airmail delivery will be added for all orders outside the US. Mail your order to: Subscriber Services Center, PO Box 10945, Chicago, IL 60610.

1995 Subscription Rates

<table>
<thead>
<tr>
<th>Publication</th>
<th>Individual</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>JAMA: The Journal of the American Medical Association (48 issues)</td>
<td>$120 $140</td>
<td></td>
</tr>
<tr>
<td>Archives of Dermatology (12 issues)</td>
<td>$155 $150</td>
<td></td>
</tr>
<tr>
<td>Archives of Family Medicine (12 issues)</td>
<td>$5 $105</td>
<td></td>
</tr>
<tr>
<td>Archives of General Psychiatry (12 issues)</td>
<td>$5 $110</td>
<td></td>
</tr>
<tr>
<td>Archives of Internal Medicine (23 issues)</td>
<td>$115 $135</td>
<td></td>
</tr>
<tr>
<td>Archives of Neurology (12 issues)</td>
<td>$145 $175</td>
<td></td>
</tr>
<tr>
<td>Archives of Ophthalmology (12 issues)</td>
<td>$110 $125</td>
<td></td>
</tr>
<tr>
<td>Archives of Otolaryngology-Head &amp; Neck Surgery (12 issues)</td>
<td>$125 $145</td>
<td></td>
</tr>
<tr>
<td>Archives of Pediatrics &amp; Adolescent Medicine (12 issues)</td>
<td>$100 $125</td>
<td></td>
</tr>
<tr>
<td>Archives of Surgery (12 issues)</td>
<td>$100 $115</td>
<td></td>
</tr>
<tr>
<td>American Medical News (48 issues)</td>
<td>$59 $139</td>
<td></td>
</tr>
<tr>
<td>New! Archives Journal Club/ Women's Health (6 issues)</td>
<td>$69 $99</td>
<td></td>
</tr>
<tr>
<td>New! JAMA Bound Volumes (2 volumes)</td>
<td>Set $95 $95</td>
<td></td>
</tr>
</tbody>
</table>

PHONE: 312-670-SUBS (670-7827)
FAX: 312-464-5831
AUTHOR RESPONSIBILITY FORM

AUTHORSHIP RESPONSIBILITY, FINANCIAL DISCLOSURE, AND ASSIGNMENT OF COPYRIGHT

Each author must read and sign (1) the statement on authorship responsibility; (2) the statement on financial disclosure; and (3) either the statement on copyright transfer or the statement on federal employment. If necessary, photocopy this document to distribute to coauthors for their signatures. Please return all copies to the address below.

1. Authorship Responsibility

I certify that I have participated sufficiently in the conception and design of this work and the analysis of the data (where applicable), as well as the writing of the manuscript, to take public responsibility for it. I believe the manuscript represents valid work. I have reviewed the final version of the manuscript and approve it for publication.

Author(s) Signature(s)

Neither this manuscript nor one with substantially similar content under my (our) authorship has been published or is being considered for publication elsewhere, except as described in an attachment.

Furthermore, I attest that I shall produce the data upon which the manuscript is based for examination by the editors or their assignees should they request it.

Date Signed

script (eg, employment, consultancies, stock ownership, honoraria), except as disclosed in an attachment.

Any financial project support of this research is identified in an acknowledgment in the manuscript.

Date Signed

2. Financial Disclosure

I certify that I have no affiliation with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the manuscript.

Author(s) Signature(s)

signing, or otherwise conveying all copyright ownership, including any and all rights incidental thereto, exclusively to the AMA.

In consideration of the action of the AMA in reviewing and editing this submission, the author(s) undersigned hereby transfer(s), or otherwise convey(s) all copyright ownership to the AMA in the event that such work is published by the AMA.

Date Signed

US Federal Employees: If you are an employee of the US federal government, please sign the following statement: I was an employee of the US federal government when this work was conducted and prepared for publication; therefore, it is not protected by the Copyright Act and there is no copyright, thus ownership cannot be transferred.

Date Signed

3. Copyright

In compliance with the Copyright Revision Act of 1976, effective January 1, 1978, the American Medical Association (AMA), in consideration of taking further action in reviewing and editing your submission, requests that each author sign a copy of this form before manuscript review can proceed. Such signature shall evidence the mutual understanding between the AMA and the undersigned author(s) thereby transferring, as

Author(s) Signature(s)

Return the original signed form to Marjorie A. Bowman, MD, MPA, Editor, Archives of Family Medicine, Bowman Gray School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157-1084. Retain one copy for your files. (Photocopies may be made as needed.)
AQ Comfort
and QD Convenience...

Just One Nasal Steroid Has Both:
NEW
FLONASE™
(fluticasone propionate)

- A first-line therapy for management of seasonal and perennial allergic rhinitis in patients 12 years and older - not indicated for nonallergic rhinitis.
- Relief of nasal symptoms may begin within 12 hours.
- Maximum benefit may take several days. Onset of action and degree of relief may vary in individual patients.
- Effectiveness depends on regular use.
- Side effects occurring at >1% (causal relationship possible) included epistaxis and nasal burning (3% to 6%) and nasal irritation, headache, and pharyngitis (1% to 3%).

Please consult Brief Summary of Prescribing Information on adjacent page.

Focused Relief for Allergic Rhinitis...
NEW
FLONASE™
(fluticasone propionate)

The Aqueous/Once-a-Day ANTI-RHINITIC™

NASAL SPRAY, 0.05%
QD
AQ
Flonase™
(fluтиcasonе propionate)
Nasal Spray, 0.05% w/w

For Intranasal Use Only.

The following is a brief summary only. Before prescribing, see complete prescribing information in Flonase™ Nasal Spray product labeling.

CONTRAINDICATIONS: Flonase™ Nasal Spray is contraindicated in patients with a hypersensitivity to any of its ingredients.

WARNINGS: The replacement of a systemic glucocorticoid with a topical glucocorticoid can be accompanied by signs of adrenal insufficiency, and in addition some patients may experience symptoms of withdrawal, e.g., joint and/or muscular pain, listlessness, and depression. Patients previously treated for prolonged periods with systemic glucocorticoids and transferred to topical glucocorticoids may be particularly prone to this problem. Systemic glucocorticoids should be carefully monitored for acute adrenal insufficiency in response to stress. In those patients who have asthma or other clinical conditions requiring long-term systemic glucocorticoid treatment, too rapid a decrease in systemic glucocorticoids may cause a severe exacerbation of their symptoms.

The use of Flonase™ Nasal Spray with a alternate-day systemic prednisone could increase the likelihood of hypothalamic-pituitary-adrenal (HPA) suppression compared with a therapeutic dose of either one alone. Therefore, Flonase Nasal Spray should be used with caution in patients already receiving alternate-day prednisone treatment for any disease. In addition, the concomitant use of Flonase Nasal Spray with other inhaled glucocorticoids could increase the risk of signs or symptoms of hypercorticism and/or suppression of the HPA axis.

Patients who are on immunosuppressant drugs are more susceptible to infections than healthy individuals. Discontinue and, for example, can have a more serious or more fatal course in patients on immunosuppressant doses of corticosteroids. In such patients who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella immunoglobulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intranasal immunoglobulin (GIN) may be indicated. (See the respective package inserts for complete VZIG and PIG prescribing information). If chickenpox develops, treatment with antiviral agents may be considered.

PRECAUTIONS: General: In patients with immediate hypersensitivity reactions or contact dermatitis may occur after the intranasal administration of Fluticasone propionate. Rare instances of wheezing, nasal septum perforation, cataracts, glaucoma, and increased intracranial pressure have been reported following the intranasal administration of glucocorticoids.

Use of excessive doses of glucocorticoids may lead to signs or symptoms of hypercorticism, suppression of HPA function, and suppression of growth of children and teenagers. Kneemetry studies in adolescent children on orally inhaled glucocorticoids showed inhibitory effects on short-term growth rate. The relationship between short-term changes in leg growth and long-term effects on growth is unclear at this time. Physicians should discontinue use of glucocorticoids, by any route, and weight the benefits of glucocorticoid therapy against the possibility of growth suppression if an adolescent's growth appears slowed.

Although systemic effects have been minimal with recommended doses of Flonase™ Nasal Spray, potential risk increases with larger doses. Therefore, larger than recommended doses of Flonase Nasal Spray should be avoided.

When used at larger doses, systemic glucocorticoid effects such as hypercorticism and adrenal suppression may appear. If such changes occur, the dosage of Flonase Nasal Spray should be discontinued slowly and consistently with accepted procedures for discontinuing oral glucocorticoid therapy.

In clinical studies with Fluticasone propionate administered intranasally, the development of localized infections of the nose and pharynx with Candida albicans has occurred only rarely. When such an infection develops, it may require therapy with appropriate local therapy and discontinuation of Flonase Nasal Spray. Patients using Flonase Nasal Spray over several months or longer should be examined periodically for evidence of Candida infection or other signs of adverse effects on the nasal mucosa.

Flonase Nasal Spray should be used with caution, if at all, in patients with active or quiescent tuberculous infections; untreated fungal, bacterial, or systemic viral infections; or ocular herpes simplex.

Because of the inhibitory effect of glucocorticoids on wound healing, patients who have experienced recent nasal surgery, ulcers, or nasal trauma should not use a nasal glucocorticoid until healing has occurred.

Information for Patients: Patients being treated with Flonase Nasal Spray should receive the following information and instructions. This information is intended to aid them in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Patients should be warned to avoid exposure to chickenpox or measles and, if exposed, to consult their physician without delay.

Patients should use Flonase Nasal Spray at regular intervals as directed since its effectiveness depends on its regular use. A decrease in nasal symptoms may occur as soon as 12 hours after starting therapy with Flonase Nasal Spray. Results in several clinical trials indicate statistically significant improvement within the first day or two of treatment; however, the full benefit of Flonase Nasal Spray may not be achieved until treatment has been administered for several days. The patient should not increase the prescribed dosage but should contact the physician if symptoms do not improve or if the condition worsens. For the proper use of the nasal spray and to obtain maximum improvement, the patient should read and follow carefully the patient's instructions accompanying the product.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Fluticasone propionate demonstrated no tumorogenic potential in a range of in vivo tests (up to 1.0 mg/kg (3 mg/m²) as calculated on a surface area basis) for 78 weeks in the mouse or inhalation of up to 57 mg/kg (336 mg/m³) for 104 weeks in the rat. Fluticasone propionate did not induce gene mutation in prokaryotic or eukaryotic cells in vitro. No significant diaphragmatic effect was seen in cultured human peripheral lymphocytes in vitro or in the mouse microsome test when administered at high doses by the oral or subcutaneous routes. Furthermore, the compound did not delay erythroblast division in bone marrow.

No evidence of impairment of fertility was observed in reproductive studies conducted in rats dosed subcutaneously with doses up to 50 mg/kg (95 mg/m²) in males and females. However, prostate weight was significantly reduced in rats.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Subcutaneous studies in the mouse and rat at 25 and 100 mg/kg, respectively (135 and 590 mg/m², respectively, as calculated on a surface area basis), revealed fetal toxicologically significant characteristics of corticosterone compounds, including endocrine growth retardation, omphalocoele, cleft palate, and retarded cranial ossification. In the rabbit, fetal weight reduction and cleft palate were observed following subcutaneous doses of 4 mg/kg (48 mg/m²). However, following oral administration of up to 300 mg/kg (3.6 mg/m²) of fluticasone propionate to the rabbit, there were no maternal effects nor increased incidence of external, visceral, or skeletal fetal defects. Fluticasone propionate was not seen in the rabbit in this study consistent with the established low bioavailability following oral administration (see CLINICAL PHARMACOLOGY section of the full prescribing information). Fewer than 0.008% of the dose crosses the placenta following oral administration to rats (100 mcg/kg, 590 mg/m²) or rabbits (300 mcg/kg, 3.6 mg/m²).

Nursing Mothers: It is not known whether fluticasone propionate is excreted in human breast milk. Subcutaneous administration of trilatid drug to lactating rats (10 mcg/kg, 59 mg/m³) resulted in measurable radioactivity in both plasma and milk. Because other glucocorticoids are excreted in human milk, caution should be exercised when Flonase Nasal Spray is administered to a nursing woman.

ADVERSE REACTIONS: In controlled US studies, 2,427 patients received treatment with intranasal fluticasone propionate In general, adverse reactions in clinical studies have been primarily associated with irritations of the nasal mucous membranes, and the adverse reactions were reported with approximately the same frequency by patients treated with the vehicle itself. The comparators did not usually interfere with treatment. Less than 2% of patients in clinical trials discontinued because of adverse events; this rate was similar for vehicle and active comparators.

Systemic glucocorticoid side effects were not reported during controlled clinical studies up to 6 months duration with Flonase™ Nasal Spray. If recommended doses are exceeded, however, or if individuals are particularly sensitive or if in conjunction with systemically administered glucocorticoids, symptoms of hypoglycemia, e.g., urination, could occur. The following incidence of common adverse reactions is based upon seven controlled clinical trials in which Flonase Nasal Spray was administered to 2,427 patients (57 girls and 108 boys aged 1 year to 11 years, 219 females and 234 males). All patients and adults) were treated with Flonase Nasal Spray 200 mcg once daily over 3 to 4 weeks and two controlled clinical trials in which 246 patients (119 female and 107 males adolescents and adults) were treated with Flonase Nasal Spray 200 mcg once daily over 12 weeks.

Incidence Greater than 1% (Causal Relationship Possible): Respiratory: Epistaxis, nasal burning (incidence 3% to 6%), blood in nasal mucosa, pharyngitis, nasal infection (incidence 1% to 3%).

Neurological: Dizziness (incidence 1% to 3%)

Incidence Less than 1% (Causal Relationship Possible): Respiratory: Sneezing, runny nose, nasal dryness, serous, nasal congestion, bronchitis, nasal ulcer, nasal septum exorption.

Skin and Appendages: Urticaria

OVERDOSAGE: There are no data available on the effects of acute or chronic overdose with Flonase™ Nasal Spray. Intranasal administration of 2 mg (10 times the recommended dose) of fluticasone propionate twice daily for 7 days to healthy human volunteers was well tolerated. Single oral doses up to 16 mg have been studied in human volunteers with no acute toxic effects reported. Repeat oral doses up to 80 mg daily for 10 days in volunteers and repeat oral doses up to 10 mg daily for 14 days in patients were well tolerated. Adverse reactions were of mild or moderate severity. Palpitations were similar in active and placebo treatment groups. Acute overdose with this dosage form is unlikely since one bottle of Flonase Nasal Spray contains approximately 8 mg of fluticasone propionate. Chronic overdose may result in signs/syptoms of hypercorticism (see PRECAUTIONS).

Allen & Hanbursys
Research Triangle Park, NC 27709

Recommended Adult Dosage

FLONASE
(Rx)

Rx

Flonase Nasal Spray
Sig: 1 spray per nostril OD

October 1994

OM BS A

Printed in USA
January 1995

RECYCLED
50% Pre-Consumer Content
20% Post-Consumer Content
The New Face of Family Medicine


Family medicine has a new face and the clinical journal the specialty demands — Archives of Family Medicine. Peer reviewed, cutting-edge, primary source material. Easily read. Immediately applicable to daily practice.

For subscriber information, call toll free: 800-AMA-2350.

American Medical Association
Physicians dedicated to the health of America

American Medical Association
Physicians dedicated to the health of America
Now you have instant access to full text parameters

New Practice Parameters on CD-ROM 1995 Edition gives you the convenience of having full text practice parameters at your fingertips. And you get free updates in 1995 so you have the most current information on recently completed or withdrawn texts.

Practice Parameters on CD-ROM includes:

- Full text parameters from more than 25 organizations.
- Directory of Practice Parameters, 1995 Edition, a listing of 1,800 parameters
- Practice Parameter Resources, contact information for practice parameters sponsors
- Practice Parameters Perspective, an update on organizational activities.

Practice Parameters on CD-ROM is simple to use with easy-to-follow menus and commands. System requirements: 386-486 IBM PC or compatible running Windows 3.1; 8 MB of RAM and 1.5 MB free space on hard drive; CD-ROM unit and interface card. Compatible with most Postscript printers. CD license remains in effect through December, 1995.

To order, call toll free 800 621-8335 and order your Practice Parameters on CD-ROM today.

Practice Parameters on CD-ROM 1995 Edition

Single User Order #: OP270495LS
Price: $995.
ISBN: 0-89970-689-4

Network Version Order #: OP270695LS
Price: $1,495.
ISBN: 0-89970-690-8

American Medical Association
Physicians dedicated to the health of America
Keep your professional career on the right track . . .

The Future of Medical Practice
This major new study from the AMA Council on Long Range Planning and Development analyzes 32 potential trends that are likely to occur during the next 10 to 15 years. Provides solid, reliable information about the future of medicine to use to develop effective strategies for dealing with the fast-changing health care system. An indispensable guide to ensuring the future success of any medical practice.


Whether you're starting a new practice or moving an established one, this new edition will save you time and aggravation. It's the only reference that gives statistics and licensure information for every state in the US in a single source.


The most up-to-date, practical guide for students, residents, graduates of foreign medical schools, and physicians contemplating a move.


Guide to Locum Tenens Recruitment
Recruiting locum tenens physicians? This resource describes how to create and manage an effective recruitment program for physicians who will take temporary assignments in a practice. Includes how to find qualified candidates, design a compensation package, and write an employment contract as well as details on practice and professional liability.


Leaving the Bedside: The Search for a Non-clinical Medical Career
Physicians in the process of considering a career change need information about themselves and their options in order to make informed decisions. Leaving the Bedside offers physicians guidance in assessing professional and personal strengths, developing self-marketing strategies, and identifying and evaluating career options for the future.


To order, call toll free 800 621-8335

American Medical Association
Physicians dedicated to the health of America
Give allergic noses relief for itchy eyes due to seasonal allergic conjunctivitis.

When seasonal allergies strike, it's not just the nose they ambush. The eyes are fair game, too. In fact, 8 out of 10 patients with allergic noses also suffer from itchy eyes due to seasonal allergic conjunctivitis. Stop the itch with ACULAR Solution.

In a recent survey (n=272), the vast majority of responding patients confirmed that ACULAR stopped their ocular itching quickly and effectively. Plus, ACULAR has a favorable safety profile. There are no steroid-like side effects that can alter intraocular pressure, and no decongestant-like side effects, i.e., no risk to patients with narrow chamber angles.

So help rescue eyes from itching with ACULAR, the #1 prescribed ophthalmic preparation for the #1 patient complaint of seasonal allergic conjunctivitis — ocular itch. Because annoying antigens prey on more than just the nose.

The most frequently reported adverse events have been transient stinging and burning on instillation (approximately 40%). Not for use while wearing soft contact lenses.

ACULAR
(ketorolac tromethamine) 0.5%
Sterile Ophthalmic Solution

Please see adjacent page for prescribing information.
ACULAR®
(ketorolac tromethamine) 0.5% Sterile Ophthalmic Solution

INDICATIONS AND USAGE
ACULAR® ophthalmic solution is indicated for the relief of ocular itching due to seasonal allergic conjunctivitis.

CONTRAINDICATIONS
ACULAR® ophthalmic solution is contraindicated in patients while wearing soft contact lenses and in patients with previously demonstrated hypersensitivity to any of the ingredients in the formulation.

WARNINGS
There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other nonsteroidal anti-inflammatory agents. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

With some nonsteroidal anti-inflammatory drugs, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied nonsteroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

PRECAUTIONS
General: It is recommended that ACULAR® ophthalmic solution be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Carcinogenesis, Mutagenesis, and Impairment of Fertility: An 18-month study in mice at oral doses of ketorolac tromethamine equal to the parenteral MRHD (Maximum Recommended Human Dose) and a 24-month study in rats at oral doses 2.5 times the parenteral MRHD, showed no evidence of tumorigenicity. Ketorolac tromethamine was not mutagenic in Ames test, unscheduled DNA synthesis and repair, and in forward mutation assays. Ketorolac did not cause chromosome breakage in the in vivo mouse micro-nucleus assay. At 1500 µg/mL (approximately 1000 times the average human plasma levels) and at higher concentrations ketorolac tromethamine increased the incidence of chromosomal aberrations in Chinese hamster ovarian cells. Impairment of fertility did not occur in male or female rats at oral doses of 9 mg/kg (53.1 mg/m²) and 16 mg/kg (94.4 mg/m²) respectively.

Pregnancy: Pregnancy Category C. Reproduction studies have been performed in rabbits, using daily oral doses at 3.6 mg/kg (42.35 mg/m²) and in rats at 10 mg/kg (59 mg/m²) during organogenesis. Results of these studies did not reveal evidence of teratogenicity to the fetus. Oral doses of ketorolac tromethamine at 1.5 mg/kg (8.6 mg/m²), which was half of the human oral exposure, administered after gestation day 17 caused dystocia and higher pup mortality in rats. There are no adequate and well-controlled studies in pregnant women. Ketorolac tromethamine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Caution should be exercised when ACULAR® is administered to a nursing woman.

Pediatric Use: Safety and efficacy in children have not been established.

ADVERSE REACTIONS
In patients with allergic conjunctivitis, the most frequent adverse events reported with the use of ACULAR® ophthalmic solution have been transient stinging and burning on instillation. These events were reported by approximately 40% of patients treated with ACULAR® ophthalmic solution. In all development studies conducted, other adverse events reported during treatment with ACULAR® include ocular irritation (3%), allergic reactions (3%), superficial ocular infections (0.5%) and superficial keratitis (1%).

ACULAR®, a registered trademark of Syntex (U.S.A.) Inc, is manufactured and distributed by Allergan, Inc. under license from its developer, Syntex (U.S.A.) Inc., Palo Alto, California, U.S.A.


©1996 Allergan, Inc.
Irvine, CA 92615

Fisons Pharmaceuticals
Fisons Corporation
Rochester, N.Y. 14623 U.S.A.
Through time and experience knowledge is collected.

With trusted experience it is delivered.

Where it all begins.

JAMA
The Journal of the American Medical Association

American Medical Association
Physicians dedicated to the health of America
Notice To Our Readers

If you are unable to access AMA publications through Lexis/Nexis Research Services you may find these publications on the following online services:

- **Dialog Information Services, Inc**
  3460 Hillview Avenue
  PO Box 10010
  Palo Alto, CA 94303-0993
  800-3-DIALOG
  FAX 415-858-7069
  *(JAMA, Archives series)*

- **Information Access Company**
  362 Lakeside Drive
  Foster City, CA 94404
  800-227-8431
  FAX 415-378-5369
  *(JAMA, Archives series, AMNews)*

- **CD Plus Technologies** (formerly BRS-Colleague)
  333 Seventh Avenue
  New York, NY 10001
  212-563-3006
  FAX 212-563-3784
  *(JAMA only)*
AQ Comfort and QD Convenience...

Just One Nasal Steroid Has Both:

NEW FLONASE™
(fluticasone propionate)

- A first-line therapy for management of seasonal and perennial allergic rhinitis in patients 12 years and older – not indicated for nonallergic rhinitis.
- Relief of nasal symptoms may begin within 12 hours.
- Maximum benefit may take several days. Onset of action and degree of relief may vary in individual patients.
- Effectiveness depends on regular use.
- Side effects occurring at >1% (causal relationship possible) included epistaxis and nasal burning (3% to 6%) and nasal irritation, headache, and pharyngitis (1% to 3%).

Please consult Brief Summary of Prescribing Information on adjacent page.

Focused Relief for Allergic Rhinitis...
NEW FLONASE™
(fluticasone propionate)
The Aqueous/Once-a-Day ANTI-RHINITIC™
NASAL SPRAY, 0.05% QD AQ
Flonase™ (fluticasone propionate)
Nasal Spray, 0.05% w/w

For Intranasal Use Only.

The following is a brief summary only. Before prescribing, see complete prescribing information in Flonase™ Nasal Spray product labeling.

CONTRAINDICATIONS: Flonase™ Nasal Spray is contraindicated in patients with a hypersensitivity to any of its ingredients.

WARNINGS: The replacement of a systemic glucocorticoid with a topical glucocorticoid can be accompa-
nied by signs of adrenal insufficiency, and in addition some patients may experience symptoms of with-
drawal, e.g., joint and/or muscular pain, fatigue, and depression. Patients previously treated for prolonged periods with systemic glucocorticoids and transferred to topical glucocorticoids should be carefully moni-
tored for acute adrenal insufficiency in response to stress. In those patients who have asthma or other clin-
cical indications requiring long-term systemic glucocorticoid treatment, too rapid a decrease in systemic glu-
cocorticoids may cause a severe exacerbation of their symptoms.

The use of Flonase™ Nasal Spray with alternate-day systemic prednisone could increase the likelihood of hypothalamic–pituitary–adrenal (HPA) axis suppression compared with a therapeutic dose of either one alone. Therefore, Flonase Nasal Spray should be used with caution in patients already receiving alternate-day prednisone treatment for any disease. In addition, the concomitant use of Flonase Nasal Spray with other inhaled glucocorticoids could increase the risk of signs or symptoms of hypercorticism and/or suppression of the HPA axis.

Patients who are on immunosuppressant drugs are more susceptible to infections than healthy individu-
als. Chickenpox and measles, for example, can have a more severe or even fatal course in patients on immunosuppressant doses of corticosteroids. In such patients who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying dis-
ease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophyl-
axis with varicella-zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IMIG) may be indicated. (See the respective package inserts for com-
plete VZIG and IMIG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.

PRECAUTIONS:

General: Rarely, immediate hypersensitivity reactions or contact dermatitis may occur after the intranasal administration of fluticasone propionate. Rare instances of wheezing, nasal septum perforation, calcaracts, glaucoma, and increased intrathoracic pressure have been reported following the intranasal application of glucocorticoids.

Use of excessive doses of glucocorticoids may lead to signs or symptoms of hypercorticism, suppression of HPA function, and/or suppression of growth in children or teenagers. Kinemometry studies in asthmatic children on orally inhaled glucocorticoids showed inhibitory effects on short-term growth rate. The relation-
ship between short-term changes in leg growth and long-term effects on growth is unclear at this time. Physicians should closely monitor the growth of adolescents taking glucocorticoids, by any route, and weigh the benefits of glucocorticoid therapy against the possibility of growth suppression if an adolescent’s growth appears slowed.

Although systemic effects have been minimal with recommended doses of Flonase™ Nasal Spray, potential risk increases with larger doses. Therefore, larger than recommended doses of Flonase Nasal Spray should be avoided.

When used at larger doses, systemic glucocorticoid effects such as hypercorticism and adrenal suppres-
sion may appear. If such changes occur, the dosage of Flonase Nasal Spray should be discontinued slowly consistent with accepted procedures for discontinuing oral glucocorticoid therapy.

In clinical studies with fluticasone propionate administered intranasally, the development of localized infections of the nose and pharynx with Candida albicans has occurred only rarely. When such an infection develops, it may require treatment with an antifungal agent and discontinuation of local and/or intranasal glucocorticoid therapy. Patients using Flonase Nasal Spray over several months or longer should be exam-
ined periodically for the possibility of Candida infection or other signs of adverse effects on the nasal mucosa. Flonase Nasal Spray should be avoided with caution if, at all, in patients with active or quiescent tuberculous infections, untreated fungal, bacterial, or systemic viral infections, or ocular herpes simplex.

Because of the inhibitory effect of glucocorticoids on wound healing, patients who have experienced recent nasal septal ulcers, nasal surgery, or nasal trauma should not use a nasal glucocorticoid until heal-
ing has occurred.

Information for Patients: Patients being treated with Flonase Nasal Spray should receive the following information and instructions. This information is intended to aid them in the safe and effective use of this medication. It is not a disclosure of all possible adverse or intended effects.

Patients should be warned to avoid exposure to chickenpox or measles and, if exposed, to consult their physician without delay.

Patients should use Flonase Nasal Spray at regular intervals as directed since its effectiveness depends on its regular use. A decrease in nasal symptoms may occur as soon as 12 hours after starting therapy with Flonase Nasal Spray. Results in several clinical trials indicate statistically significant improvement within the first day or two of treatment; however, the full benefit of Flonase Nasal Spray may not be achieved until treatment has been administered for several days. The patient should not increase the pres-
scribed dosage but should consult the physician if symptoms do not improve or if the condition worsens.

For the proper use of the nasal spray and to obtain maximum improvement, the patient should read and fol-
low carefully the patient’s instructions accompanying the product.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Fluticasone propionate demonstrated no tumor-
igenic potential and there was no evidence of genetic potential in allotransplanted or intralaboratory passages in mice or rats in the mouse micronucleus test when administered at high doses by the oral or subcutaneous routes. Furthermore, the compound did not delay erythroblast division in bone marrow.

No evidence of impairment of fertility was observed in reproductive studies conducted in rats dosed subcutaneously with doses up to 50 mg/kg (305 mg/m²) in males and females. However, prostate weight was significantly reduced in rats.

Pregnancy: Teratogenic Effects: Pregnancy Category C: Subcutaneous studies in the mouse and rat at 45 and 100 mcg/kg, respectively (135 and 590 mcg/m²), respectively, as calculated on a surface area basis, revealed no fetal toxicity characteristics of potent glucocorticoid compounds, including embryonic growth retardation, omphalocoe, cleft palate, and retarded cranial ossification.

In the rabbit, fetal weight reduction and cleft palate were observed following subcutaneous doses of 4 mcg/kg (16 mcg/m²).

However, following oral administration of up to 300 mcg/kg (3.6 mcg/m²) of fluticasone propionate to the rabbit, there were no maternal effects nor increased incidence of delayed implantation, visceral, or skeletal fetal defects. No fluticasone propionate was detected in the plasma in this study, consistent with the established low bioavailability following oral administration (see CLINICAL PHARMACOLOGY section of the full prescrib-
ing information).

Less than 0.006% of the dose crosses the placenta following oral administration to rats (100 mcg/kg, 590 mcg/m²) or rabbits (300 mcg/kg, 3.6 mg/m²).

Flonase™ (fluticasone propionate) Nasal Spray, 0.05% w/w

There are no adequate and well-controlled studies in pregnant women. Fluticasone propionate should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus. There are no data on fluticasone glucocorticoids since their introduction in pharmacology, as opposed to physiologic, doses suggests that rodents are more prone to teratogenic effects from glucocorticoids than humans. In addition, because there is a natural increase in glucocorticoid production during pregnancy, most women will require a lower exogenous glucocorticoid dose and many will not need glucocorticoid treatment during pregnancy.

Nursing Mothers: It is not known whether fluticasone propionate is excreted in human breast milk. Subcutaneous administration of inhaled drug to lactating rats (10 mcg/kg, 59 mcg/m²) resulted in measure-
able radioactivity in both plasma and milk. Because other glucocorticoids are excreted in human milk, cau-
tion should be exercised when Flonase Nasal Spray is administered to a nursing woman.

Pediatric Use: The safety and effectiveness of Flonase Nasal Spray in children below 12 years of age have not been established. Oral glucocorticoids have been shown to cause growth suppression in children and teenagers with extended use. If a child or teenager on any glucocorticoid appears to have growth suppres-
sion, the possibility that they are particularly sensitive to this effect of glucocorticoids should be considered (see PRECAUTIONS).

Geriatric Use: A limited number of patients above 60 years of age (n=132) have been treated with Flonase Nasal Spray in US and non-US clinical trials. While the number of patients is too small to permit separate analysis of efficacy and safety, the adverse reactions reported in this population were similar to those reported by younger patients.

ADVERSE REACTIONS: In controlled US studies, 2,427 patients received treatment with intranasal flutica-
sone propionate. In general, adverse reactions in clinical studies have been primarily associated with irrita-
tion of the nasal mucous membranes, and the adverse reactions were reported with approximately the same frequency by patients treated with the vehicle itself. The complaints did not usually interfere with treatment. Less than 2% of patients in clinical trials discontinued because of adverse events; this rate was similar for vehicle and active comparators.

Systemic glucocorticoid side effects were not reported during controlled clinical studies up to 6 months duration with Flonase™ Nasal Spray. If recommended doses are exceeded, however, or if individuals are particularly sensitive or if in conjunction with systemically administered glucocorticoids, symptoms of hypercorticism, e.g., Cushings’ syndrome, could occur.

The following incidence of common adverse reactions is based upon seven controlled clinical trials in which 536 patients were treated with Flonase Nasal Spray 200 mcg once daily over 4 weeks (see Table 1). The incidences in the 1% to 20% category may not be unexpected.

Incidence Greater than 1% (Causal Relationship Possible): Respiratory: Epistaxis, nasal burning (inci-
dence 3% to 6%); blood in nasal mucus, pharyngitis, nasal irritation (incidence 1% to 3%); Neurological: Headache (incidence 1% to 3%).

Incidence Less than 1% (Causal Relationship Possible): Respiratory: Sneezing, runny nose, nasal dry-
ness, epistaxis, hemicrania, congestion, bronchitis, nasal ulcer, nasal septum excoriation.

OVERDOSAGE: There are no data available on the effects of acute or chronic overdose with Flonase™ Nasal Spray. Intranasal administration of 2 mg (10 times the recommended dose) of fluticasone propionate twice daily for 7 days to healthy human volunteers was well tolerated. Single oral doses up to 16 mg have been studied in human volunteers with no acute toxic effects reported. Repeat oral doses up to 50 mcg daily for 10 days in volunteers and repeat oral doses up to 10 mg daily for 14 days in patients were well tolerated. Adverse reactions were of mild or moderate severity, and incidences were similar in active and placebo treatment groups. Acute overdose with this dosage form is unlikely since one bottle of Flonase Nasal Spray contains approximately 8 mg of fluticasone propionate. Chronic overdose may result in signs/symptoms of hypercorticism (see PRECAUTIONS).
The Osler Institute 1995
Family Practice Boards Review Course
March 12-18 – San Francisco  April 23-29 – Cincinnati
May 21-27 – Los Angeles  June 11-17 – Baltimore  July 6-12 – Chicago
Plus optional day of psychiatry just before and optional day of obstetrics just after

OBJECTIVES
• Improve basic and clinical knowledge in family practice
• Prepare candidates to take Family Practice board exams
• Provide family practitioners with a review and update

METHODS
• SELF-DIRECTED STUDY questions, answers, and assignments
• SEMINAR with projection slides and lecture-note syllabus
• PRACTICE EXAMS with written questions and answers

OPTIONAL DAY BEFORE CORE
Psychiatry
Depression and Mania
Schizophrenia
Anxiety and Neurosis
Personality Disorders
Psychosexual
Alcohol & Drug Abuse
Obesity/Eating Disorders
Sleep Disorders
Geriatric Psychiatry
Psychotherapeutic Drugs

SEVEN DAY CORE COURSE
Medicine and Gerontology
Pulmonology
Asthma and COPD
Pneumonia & Bronchitis
Diffuse Lung Diseases
Pulmonary Emboli
Respiratory Failure
Cardiology
EKG’s & Arrhythmias
Preventive Cardiology
Hypertension
Myocardial Infarction
Valvular Disease
Congestive Failure
Gastroenterology
Oral Diseases
Esophageal Problems
Peptic Ulcers
Hepatitis and Cirrhosis
Gallbladder & Pancreas
Chronic Bowel Disease
Anorectal Problems
Nephrology
Acid-Base and 'lytes
Urinary Infections
Renal Failure

Endocrinology
Diabetes Mellitus
Thyroid Diseases
Parathyroid & Adrenal Osteoporosis
Heme. & Oncology
Anemia
Abnormal White Counts
Bleeding Disorders
Cancer Detection
Cancer Prevention
Primary Care Oncology
Rheum. & Sports
Rheumatic Syndromes
Inflammatory Arthritis
Overuse Injuries
Acute Knee Injuries
Neurology
Headache & Back Pain
Dizziness & Tinnitus
Delirium and Stroke
Dementia & Parkinson’s
Epilepsy & Head Injury
Derm. and Pharm.
Common Dermatosis
Systemic Disease Signs
Geriatric Pharmacology
Antibiotic Choices
Potpourri
AIDS and Other STDs
Common Infections
Pain Management
Chest X-ray Review
Abdominal X-rays
Gynecology
Gynecologic Infections
Menstrual Disorders
Pelvic Pain Evaluation
Contraception
Infertility Options
Sexual Assault
Abnormal Pap Smears
Cancer in Women
Menopause Management

Community Med.
Preventive Health Care
Occupational Medicine
Environmental Medicine
Ethical & Legal Issues

Pediatrics
Care of the Newborn
Growth & Development
Vaccinations
Behavior Problems
Learning Disorders
Fever and Infections
Vomiting and Diarrhea
Seizures and Epilepsy
Allergy & Immunology
Common Exanthesms
Child Abuse
Adolescent Medicine

Surgery
Acute Abdomen
Breast Diseases
Trauma Assessment
Vascular Problems
Common Eye Problems
Hand Injuries
Office Orthopedics
Ortis and Sinusitis
Head and Neck Masses
Prostate Problems
Urinary Incontinence

OPTIONAL DAY AFTER CORE
Obstetrics
Prenatal Care
Fetal Testing
Diabetes in Pregnancy
Hypertension
Spontaneous Abortion
Premature and Post Dates
Preterm Labor
Induction of Labor
Labor Complications
Obstetric Anesthesia
Perinatal Infections
Medical Genetics

Faculty
Thomas Amidon, M.D.
Daniel Arkfeld, M.D.
Benjamin Banahan, M.D.
Robert Baumann, M.D.
Jon Bowersox, M.D.
Elllyn Bush, M.D.
Rodney Camp, M.D.
P. K. Chaudhuri, M.D.
Stuart Cohen, M.D.
Kevin Coulier, M.D.
Ralph Cutler, M.D.
Lloyd Damon, M.D.
Robert Dinneff, M.D.
L. Dungy-Poythress, M.D.
David Frankel, M.D.
Mitchell Geffner, M.D.
Charles Goldman, M.D.
Rhoda Hahn, M.D.
Theodore Hall, M.D.
Jorge Herrera, M.D.
Jerry Hickson, M.D.
Peter Katsufrakis, M.D.
John Lake, M.D.
Jay Lieberman, M.D.
Glen Lillington, M.D.
Jay Mininove, M.D.
Laura Mosqueda, M.D.
Lamont Murdoch, M.D.
Adena Nelson, M.D.
Gibbe Parsons, M.D.
Edward Philpot, M.D.
Michael Policar, M.D.
John Pottage, M.D.
James Recabaren, M.D.
Theodore Rose, M.D.
Sharon Schnare, R.N.
George Shacklel, M.D.
Kirk Shepard, M.D.
Lee Shulman, M.D.
Susan Smiga, M.D.
Randy Stevens, M.D.

...remarkably complete and pleasant.

Course Description
Course enrollment is limited to 120 to give personal attention to your questions. Self-directed study questions will be sent before the courses which will include case reviews and lectures with slides and syllabus and question sessions each evening.

Accommodations were comfortable....

Locations and Travel
Hyatt Regency at Orlando Airport; Crowne Sterling Suites San Francisco Airport; Regal Hotel Cincinnati; Radisson Plaza, Manhattan Beach, near Los Angeles Airport; Baltimore Washington Airport (BWI) Marriott; and Radisson Lisle/Naperville – 2 miles southwest of Chicago’s O’Hare Airport. For personal service with travel reservations, please call 800-356-7537 ext. 218.

...the most education for the money.

Fees and Course Hours
• 7 Day Core Course $870 $580 70
• Optional Day Before $150 $100 10
• Optional Day After $150 $100 10
• 9 Day Board Review $1080 $720 90
• 10% within 1 days of the course.
• Not in course hotel package add $30 per day.
• A $100 deposit will reserve your position.
• Subject to $100 fee, refunds will be made until the seminar begins.

...home study...was extremely helpful.

AAPF Prescribed Credit
This program has been reviewed and is acceptable up to 88 Prescribed hours by the AAPF. AAPF prescribed credit is accepted by the AMA as equivalent to AMA PRA Category 1 for the AMA Physicians Recognition Award. When applying for the AMA PRA, prescribed hours earned must be reported as prescribed hours, not as Category 1.

I feel [the course] helped me pass....

Information
Call Today for information and registration, hotel and travel reservations:
(800) 356-7537 or (812) 299-5658
FAX (812) 299-2775

Limited Enrollment: Family Practice Review Registration
Name ____________________________
Address ____________________________
City/State/Zip _________________________
Mail Today to:
1094 East Dawn Drive, Dept. 305
P.O. Box 2218
Terre Haute, IN 47802-0218

☐ March 12-18 – San Francisco
☐ April 23-29 – Cincinnati
☐ May 21-27 – Los Angeles
☐ June 11-17 – Baltimore
☐ July 6-12, 1995 – Chicago
☐ Please send FREE SAMPLE

Comments by Osler participants: ____________________________
ONCE-A-DAY CARIDZEM CD
(diltiazem HCl)
Capsules

CONTRAINDICATIONS:
CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, (3) patients with hypotension (less than 90 mm Hg systolic), (4) patients who have demonstrated hypersensitivity to the drug, and (5) patients with acute myocardial infarction and pulmonary congestion documented by x-ray on admission.

WARNINGS:
1. Cardiogenic Shock. CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may result in an abnormally slow heart rate (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (13 of 3200 patients or 0.4%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed episodes of asystole (2 to 5 seconds) 3 days after initiating concomitant diltiazem and digitalis therapy.

2. Congestive Heart Failure. Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic effects of diltiazem have not been consistently observed in clinical studies. Such elevations were transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, and others have been reported in patients with congestive heart failure. Therapy with diltiazem should be discontinued if there is worsening of congestive heart failure.

3. Hypotension. Dilation of blood vessels associated with CARIDZEM therapy may occasionally result in symptomatic hypotension.

4. Acute Hepatic Injury. Mild elevations of transaminases concomitant with cholestasis and/or bile ductular injury have been observed in clinical studies. Such elevations were transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, SGOT, SGPT, and other coagulation enzymes have been reported in patients with acute hepatic injury. Therapy with diltiazem should be discontinued if there is worsening of any of these abnormalities.

5. Diabetic Neutropenia. Neutropenia has been reported in patients with diabetes mellitus who are also taking diltiazem. Therapy with diltiazem should be discontinued if there is a significant decrease in neutrophil counts.

PRECAUTIONS:
General:
CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and bile. As with any drug given over prolonged periods, laboratory parameters of renal and hepatic function should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In animals and in one 3-day rat study designed to produce toxicity, high doses of diltiazem were associated with hepatic damage in some animals. In subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued therapy.

Drug Interactions:
Due to the potential for additive effects, caution and careful titration are warranted in patients receiving CARIDZEM concomitantly with other agents known to affect cardiac conduction and/or metabolism (See WARNINGS). Pharmacokinetic studies indicate that there may be additive effects in prolonging AV conduction when beta-blockers or digitalis are concomitantly used with CARDIZEM. (See WARNINGS.)

As with all drugs, care should be exercised when treating patients with multiple medications. CARDIZEM and other drugs known to affect cardiac conduction or metabolism may share similar pharmacokinetic properties. Close monitoring of patients receiving concomitant medications or who are known to have altered drug metabolism is necessary.

Concomitant use of drugs known to affect cardiac conduction or metabolism may result in additive effects on cardiac conduction. In patients with concomitant use of drugs that affect cardiac conduction or metabolism, the following should be considered:

Dilantin:
Patients on concomitant use of CARIDZEM and dilantin may experience additive effects on cardiac conduction. Therapy with diltiazem and dilantin should be adjusted to a minimum dose that maintains the desired therapeutic effect.

Carbamazepine:
Concomitant administration of diltiazem with carbamazepine has been reported to result in elevated serum levels of carbamazepine (40% to 72% increase), possibly due to a decrease in the metabolism of carbamazepine. Therapy with carbamazepine and diltiazem should be adjusted to maintain the desired therapeutic effect.

IN HYPERTENSION OR ANGINA

CARDIZEM® CD
(diltiazem HCl) 120-, 180-, 240-, 300-mg Capsules

FOR EFFECTIVE
24-HOUR CONTROL

ONCE A DAY

A unique hemodynamic and safety profile
for hypertension or angina

- A side-effect discontinuation rate comparable to placebo in both hypertension and angina trials
- Most commonly reported side effects are headache (5.4%), bradycardia (3.3%), first-degree AV block (3.3%), dizziness (3.0%), edema (2.6%), ECG abnormality (1.6%), and asthenia (1.8%)

Please see brief summary of prescribing information on adjacent page.