DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

TRANSMITTED BY FACSIMILE

Diane Mitrione
Assistant Vice President
Worldwide Regulatory Affairs
Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101

RE: NDA # 50-622
Suprax (cefixime) Oral
MACMIS ID # 11287

Dear Ms. Mitrione:

This letter objects to Wyeth-Ayerst Laboratories' (Wyeth) dissemination of promotional mailers[1] for Suprax (cefixime) that are in violation of the Federal Food, Drug, and Cosmetic Act (Act) and FDA's applicable implementing regulations. As a part of the Division of Drug Marketing, Advertising, and Communications' (DDMAC) routine surveillance, we have reviewed these promotional mailers for Suprax, submitted under form FDA 2253, and find them to be false, lacking in fair balance or otherwise misleading. Specifically, we object to the following:

Omission of Facts Material in Light of Representations/Minimization of Risk Information

Promotional materials are false or misleading if they fail to reveal facts material in light of representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials. Section 201(n) of the Act. Specifically, the promotional mailers present claims and representations concerning Suprax's effectiveness, including but not limited to "Potent. Proven. Practical.," "When bronchitis hits, help him get Suprax Strong," "Rediscover Suprax (cefixime) and reach for potency against acute otitis media," "When bronchitis has them feeling weak, Suprax (cefixime) comes on strong," and "Suprax is the choice you want for excellent efficacy." However, with the exception of disclosing that "GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT," you fail to present any risk information for Suprax, including the bolded Warning from the PI concerning serious acute hypersensitivity reactions that may occur in up to 10% of patients with a history of penicillin allergy. Moreover, although you disclose that "GI upset is the most frequently reported side effect," you fail to point out that patients have developed severe diarrhea and documented pseudomembranous colitis with some of these patients requiring hospitalization.

[1] Material ID Codes: 78205-00, 78206-00, 78207-00, and 78191-02

Requested Action

You should immediately cease dissemination of the violative promotional mailers and other promotional materials for Suprax that fail to present important risk information and make the same or similar claims or representations. Please submit a written response on or before November 19, 2002 describing your intent and plans to comply with the above. Your letter should include a list of materials discontinued and the date on which these materials were discontinued.

You should direct your response to the undersigned by facsimile at (301) 594-6771, or to the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm 8B-45, 5600 Fishers Lane, Rockville, MD 20857. We remind you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 11287 in addition to the NDA number.

Sincerely,

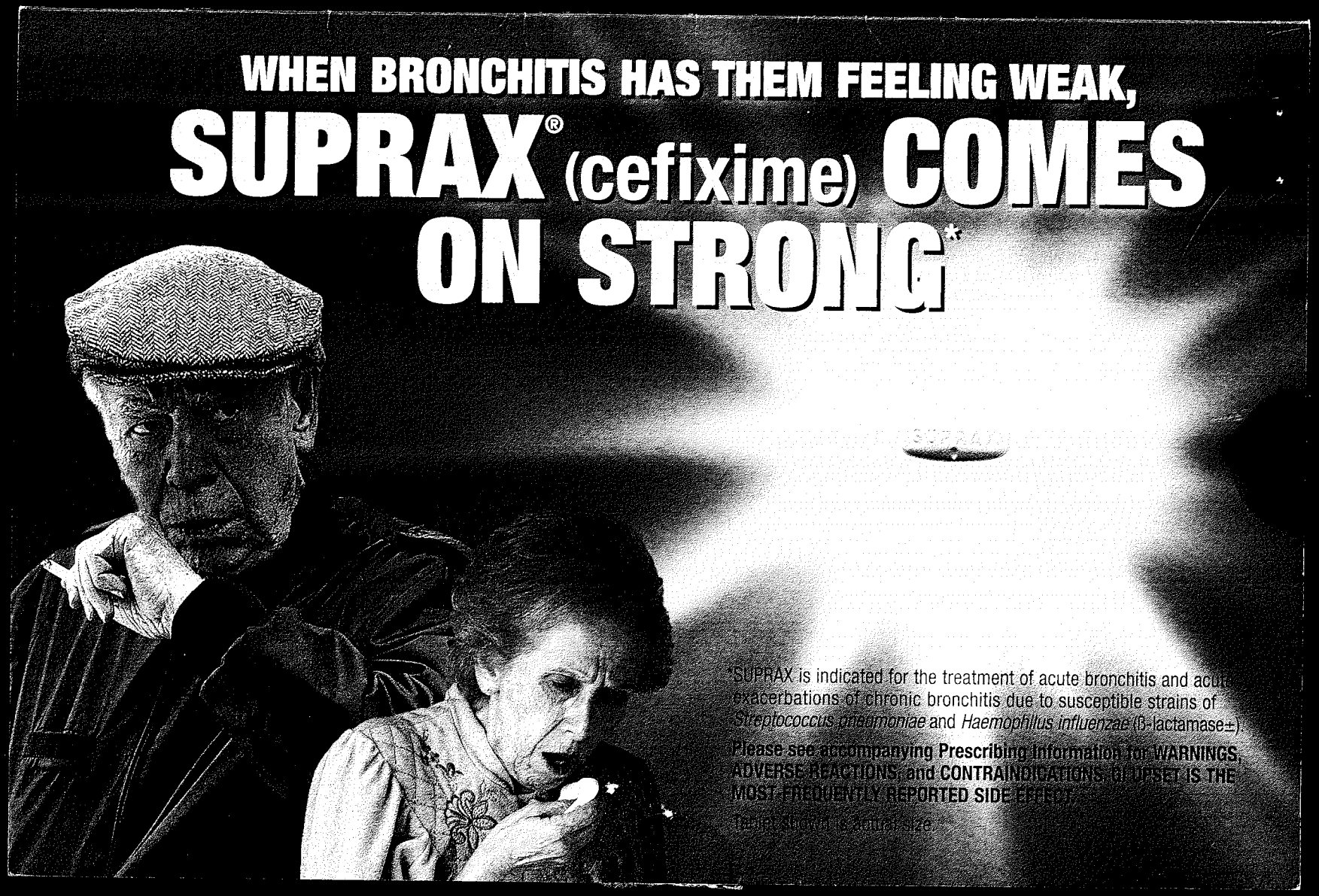
{See appended electronic signature page}

James R. Rogers, Pharm.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Rogers
11/5/02 02:32:21 PM


WHEN BRONCHITIS HAS THEM FEELING WEAK,
SUPRAX® (cefixime) COMES ON STRONG*
SUPRAX
*SUPRAX is indicated for the treatment of acute bronchitis and acute exacerbations of chronic bronchitis due to susceptible strains of *Streptococcus pneumoniae* and *Haemophilus influenzae* (β-lactamase±).
Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. (DIARRHEA IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.)
Tablet shown is actual size.

When patients over 60 have bronchitis[1]*

SUPRAX has the strength to help

SUPRAX is the choice you want for excellent efficacy

Clinical Response[1] (n=124)
Cured† (n=66) **53%** Improved† (n=47) **38%** **91%**

*Due to susceptible strains of *S. pneumoniae* and *H. influenzae* (ß-lactamase±) in acute bronchitis and acute exacerbations of chronic bronchitis.

†In this study, cured was defined as complete resolution of signs and symptoms of infection or a return to baseline level of functioning. Improved was defined as a significant improvement of symptoms without complete resolution.

Clinically proven benefits can help hit bronchitis hard

Fight against bronchitis with features that can beat pathogens* and aid compliance.

SUPRAX is highly effective against *H. influenzae*, one of the most prominent pathogens in bronchitis[2,3]

Once-daily dosing can help reinforce compliance[4]

Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

SUPRAX is administered as a single dose, once a day, or if preferred, in equally divided doses twice a day.

Tablets shown are actual size.

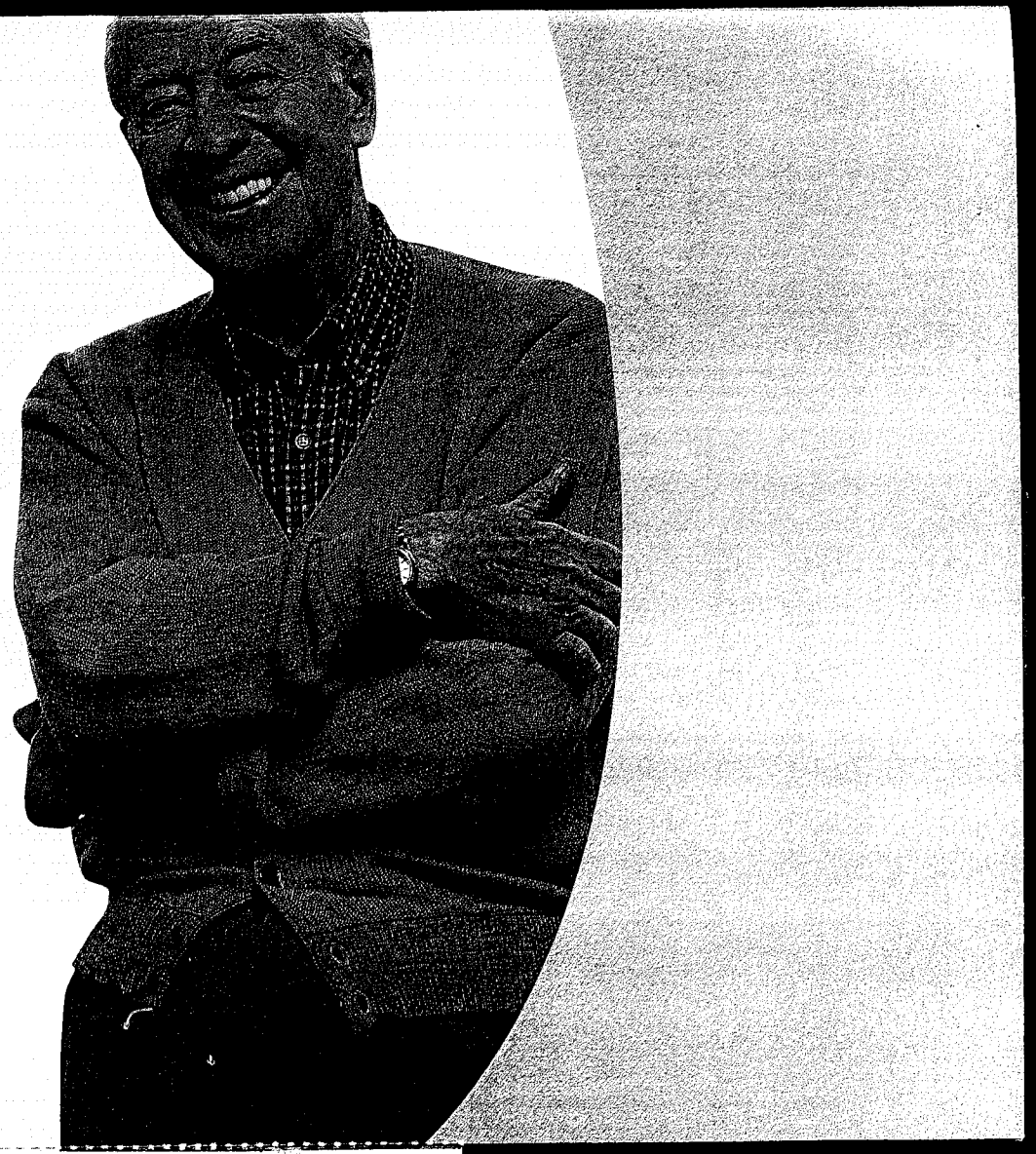
References:

1. Quintiliani R. Cefixime in the treatment of patients with lower respiratory tract infections: results of US clinical trials. *Clin Ther.* 1996;18:373-390. 2. Arthur M, McAdoo M, Guerra J, et al. Clinical comparison of cefuroxime axetil with cefixime in the treatment of acute bronchitis. *Am J Ther.* 1996;3:622-629. 3. Drehobl M, Sahn S, Puopolo A, et al. A multicenter trial of cefixime and cefuroxime axetil in the treatment of acute LRTI. *Infect Med.* 1993;10(suppl):22-28. 4. Cockburn J, Gibberd RW, Reid AL, et al. Determinants of non-compliance with short term antibiotic regimens. *Br Med J.* 1987;295:814-818.

ONCE-A-DAY SUPRAX®

(cefixime) Tablets 400 mg

Potent. Proven. Practical.



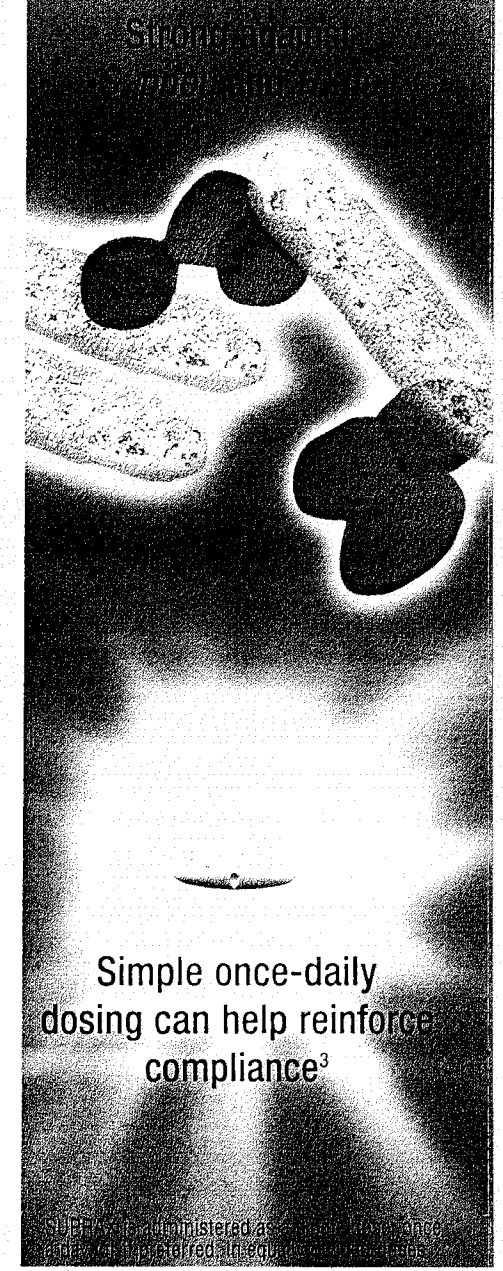
Marketed by:
WYETH LEDERLE VACCINES
Wyeth-Ayerst Pharmaceuticals, Philadelphia, PA 19101

Under License of
Fujisawa Pharmaceutical Co., Ltd.
Osaka, Japan

December 2001

78191-02

Clinically proven features can help beat bronchitis*

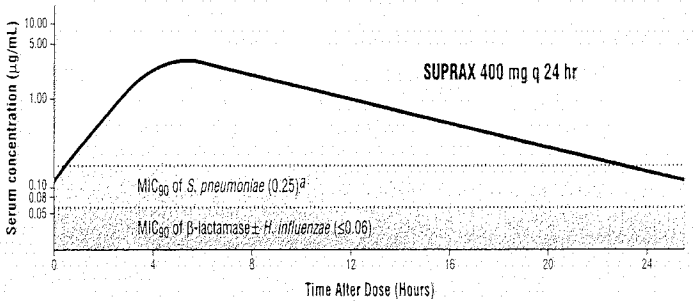


Simple once-daily dosing can help reinforce compliance[3]

SUPRAX is administered as [illegible] once a day. It is preferred in equal [illegible]

SUPRAX Strong! Lasts Long!

SUPRAX aggressively maintains inhibitory concentrations above MIC_{90} for virtually 24 hours[1,2†]



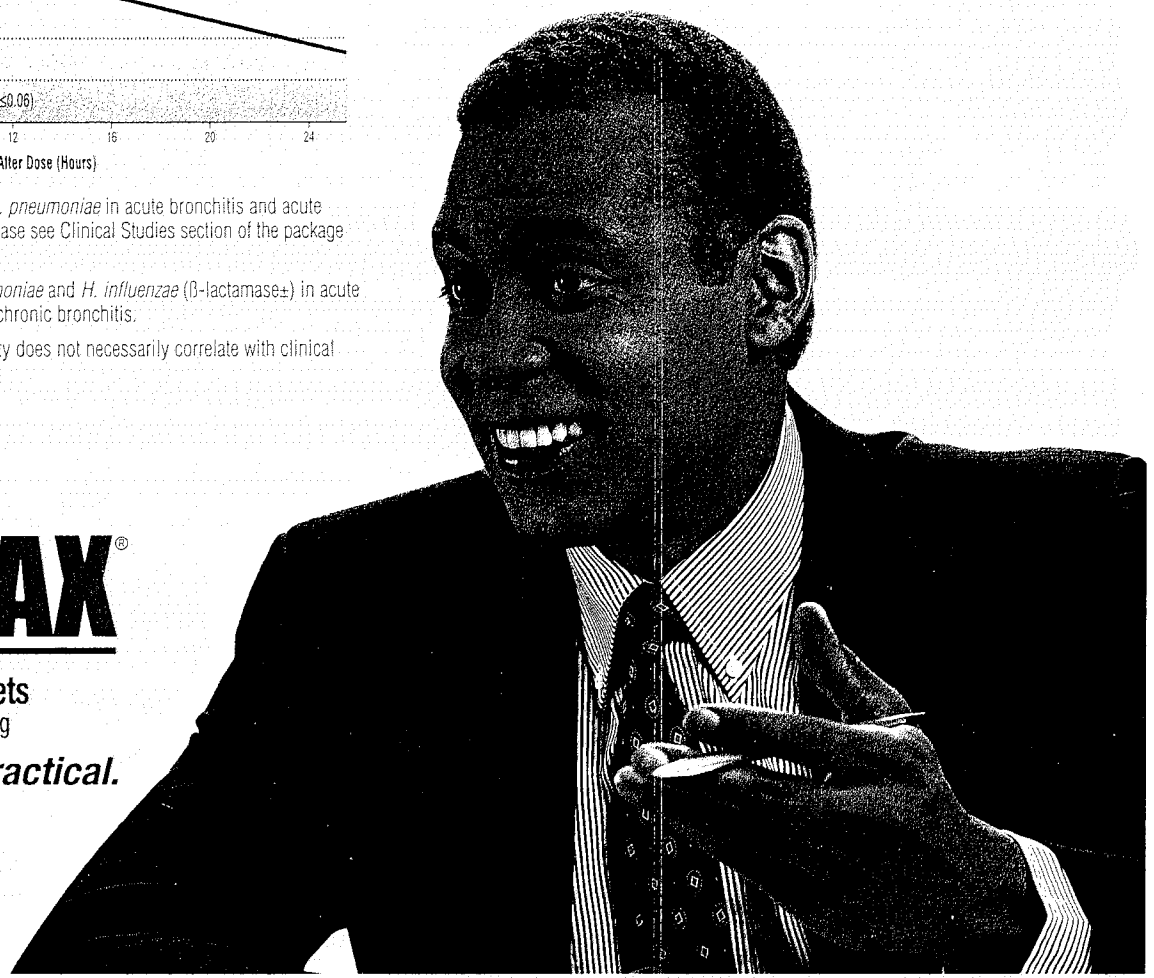
[d] SUPRAX is specifically indicated for *S. pneumoniae* in acute bronchitis and acute exacerbations of chronic bronchitis. Please see Clinical Studies section of the package insert for additional information.

* Due to susceptible strains of *S. pneumoniae* and *H. influenzae* (β-lactamase±) in acute bronchitis and acute exacerbations of chronic bronchitis.

† Although a useful guide, *in vitro* activity does not necessarily correlate with clinical response.

ONCE-A-DAY
SUPRAX®
(cefixime) Tablets 400 mg

Potent. Proven. Practical.



Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

References:

1. Schentag JJ. Pharmacokinetic profiles as predictors of therapeutic success. In: *Respiratory Tract Infections: Therapeutic Considerations in a Dynamic Environment.* Pearl River, NY: Lederle Laboratories;1990:14-17. **2.** Jones RN, Barry AL. Antimicrobial activity, spectrum, and recommendations for disk diffusion susceptibility testing of ceftibuten (7432-S; SCH 39720), a new orally administered cephalosporin. *Antimicrob Agents Chemother.* 1988;32:1576-1582. **3.** Cockburn J, Gibberd RW, Reid AL, et al. Determinants of non-compliance with short-term antibiotic regimens. *Br Med J.* 1987; 295:814-818.

Marketed by:
WYETH LEDERLE™ VACCINES
Wyeth-Ayerst Pharmaceuticals, Philadelphia, PA 19101

Under License of
Fujisawa Pharmaceutical Co., Ltd.
Osaka, Japan

February 2002 78207-00

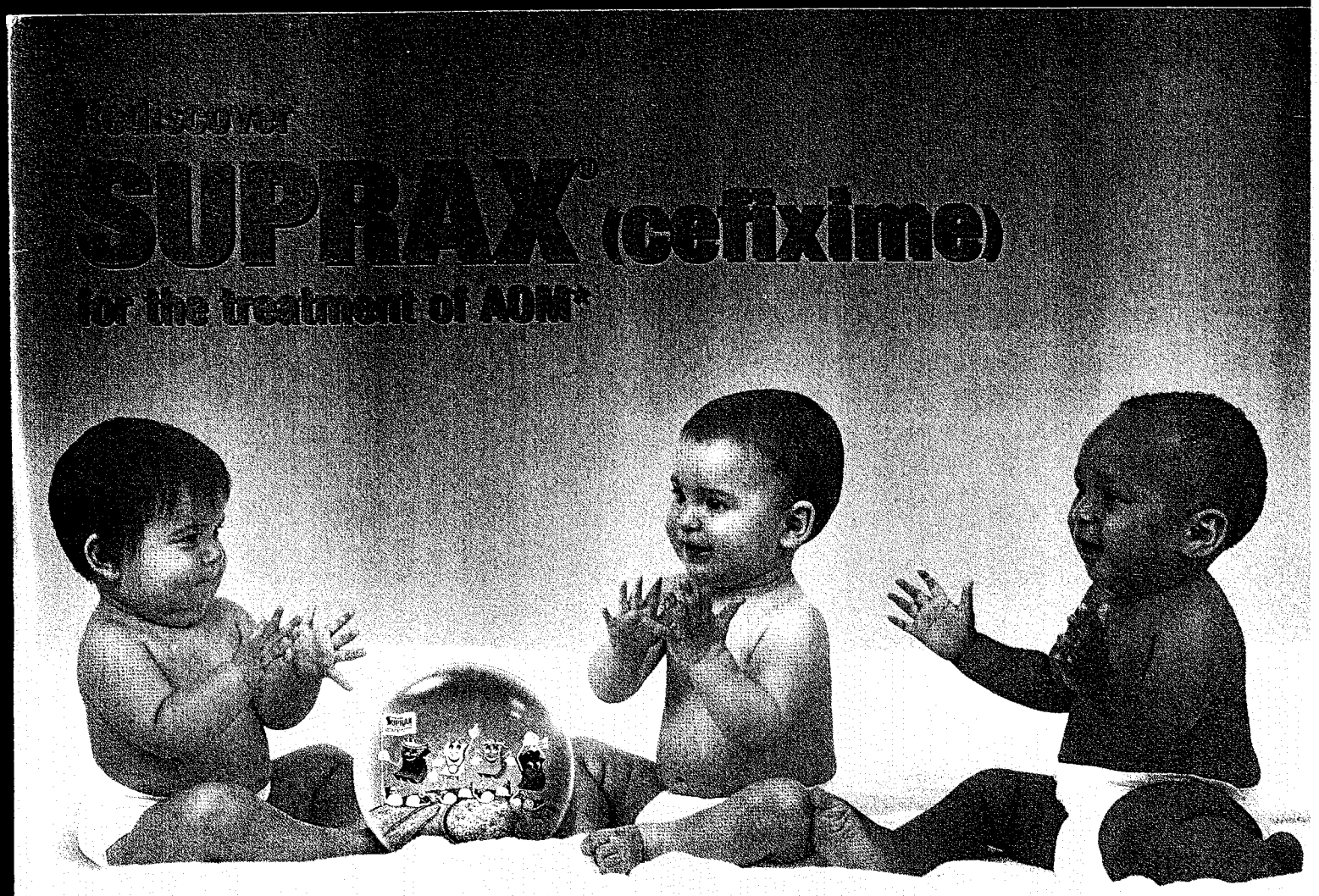
When bronchitis* hits, help him get

SUPRAX® STRONG
(cefixime)

*SUPRAX is indicated for the treatment of acute bronchitis and acute exacerbations of chronic bronchitis due to susceptible strains of *Streptococcus pneumoniae* and *Haemophilus influenzae* (ß-lactamase±).

Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

Tablet shown is actual size.



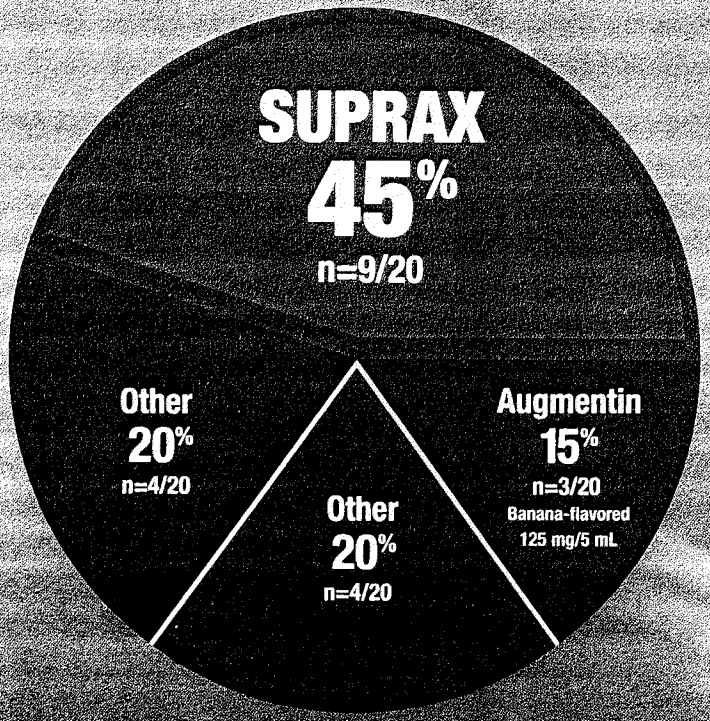
FREE SAMPLE OFFER INSIDE!

* SUPRAX suspension is indicated for the treatment of acute otitis media due to susceptible strains of *Haemophilus influenzae* (ß-lactamase±), *Moraxella (Branhamella) catarrhalis* (most of which are ß-lactamase+), and *Streptococcus pyogenes.*

Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

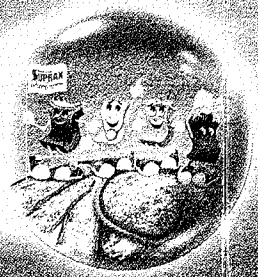
We're happy to compare SUPRAX® with Augmentin®

And kids know SUPRAX beats Augmentin in taste!



Over twice as many children preferred SUPRAX†

†Taste study results are based on pediatric data in children who expressed a preference, n=20.



If You're

If you're happ
Clap your har
If you're happ
Clap your har
If you're happ
Then you real
If you're happ
Clap your har

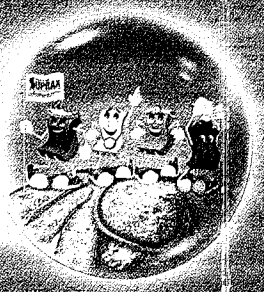
If you're happ
Stamp your fe
If you're happ
Stamp your fe
If you're happ
Then you real
If you're happ
Stamp your fe

If you're happ
Nod your hea
If you're happ
Nod your hea
If you're happ
Then you reall
If you're happ
Nod your hea

SUPRAX®

s many children
PRAX[1]

ased on pediatric data
ed a preference, n=20



If You're Happy

If you're happy and you know it,
Clap your hands.
If you're happy and you know it,
Clap your hands.
If you're happy and you know it,
Then you really ought to show it.
If you're happy and you know it,
Clap your hands.

If you're happy and you know it,
Stamp your feet.
If you're happy and you know it,
Stamp your feet.
If you're happy and you know it,
Then you really ought to show it.
If you're happy and you know it,
Stamp your feet.

If you're happy and you know it,
Nod your head.
If you're happy and you know it,
Nod your head.
If you're happy and you know it,
Then you really ought to show it.
If you're happy and you know it,
Nod your head.

Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

SUPRAX is administered as a single dose, once a day, or if preferred, in equally divided doses twice a day.

Augmentin (amoxicillin/clavulanate) is a registered trademark of SmithKline Beecham Pharmaceuticals.

Reference:

1. Angelilli ML, Toscani M, Matsui DM, et al. Palatability of oral antibiotics among children in an urban primary care center. *Arch Pediatr Adolesc Med.* 2000;154:267-270.

ONCE-A-DAY
SUPRAX®
(cefixime) Oral suspension 100 mg/5 mL

Potent. Proven. Practical.

Wyeth®

Fujisawa Pharmaceutical Co., Ltd. Osaka, Japan

SUPRAX is marketed by Wyeth-Pharmaceuticals and under license of Fujisawa Pharmaceutical Co., Ltd.

April 2002 7520C-10

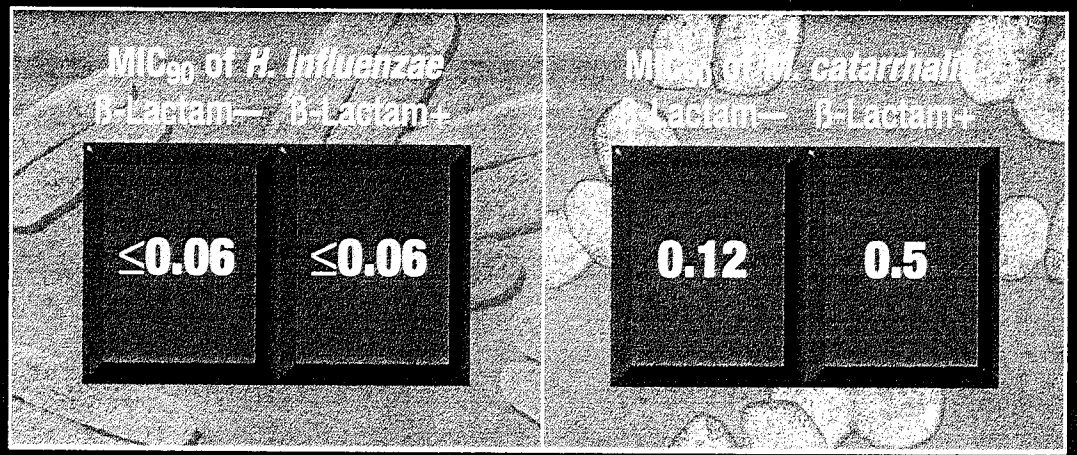
FREE SAMPLE OFFER INSIDE!

*SUPRAX suspension is indicated for the treatment of acute otitis media due to susceptible strains of *Haemophilus influenzae* (ß-lactamase±), *Moraxella (Branhamella) catarrhalis* (most of which are ß-lactamase+), and *Streptococcus pyogenes.*

Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

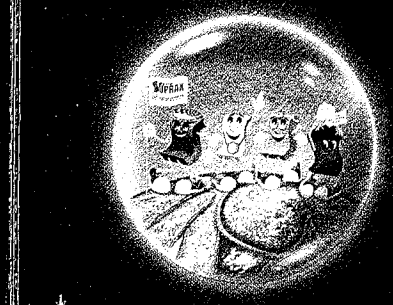
SUPRAX® hits the right notes against AOM*

SUPRAX is potent against beta-lactamase± strains of *H. influenzae* and *M. catarrhalis*[1†]



*SUPRAX suspension is indicated for the treatment of acute otitis media due to susceptible strains of *H. influenzae* (β-lactamase±), *M. catarrhalis* (most of which are β-lactamase+), and *S. pyogenes*.

† Although a useful guide, *in vitro* activity does not necessarily correlate with clinical response.



ONCE-A-DAY

SUPRAX®

(cefixime) Oral suspension 100 mg/5 mL

Potent. Proven. Practical.

Please see accompanying Prescribing Information for WARNINGS, ADVERSE REACTIONS, and CONTRAINDICATIONS. GI UPSET IS THE MOST FREQUENTLY REPORTED SIDE EFFECT.

SUPRAX is administered as a single dose, once a day or, if preferred, in equally divided doses twice a day.

Reference:

1. Barry AL, Pfaller MA, Fuchs PC, et al. In vitro activities of 12 orally administered antimicrobial agents against four species of bacterial respiratory pathogens from U.S. medical centers in 1992 and 1993. *Antimicrob Agents Chemother.* 1994;38:2419-2425.

Wyeth®

Fujisawa Pharmaceutical Co., Ltd.
Osaka, Japan

Suprax is marketed by Wyeth Pharmaceuticals and under license of Fujisawa Pharmaceutical Co., Ltd.

April 2002 78205-00