

Senate Bill Would Encourage Switch to Geriatrics

BY JANE ANDERSON
Contributing Writer

Sen. Barbara Boxer (D-Calif.) introduced legislation in March aimed at addressing the potential crisis in providing care for elderly Americans. The bill offers a combination of educational-loan forgiveness and career-advancement opportunities for health care professionals choosing practice in nursing homes.

The Caring for an Aging America Act,

S. 2708, would have the federal government provide \$130 million over 5 years to benefit physicians, physician assistants, advance practice nurses, psychologists, and social workers choosing geriatrics and gerontology. Aid would come primarily through educational loan repayments for these professionals in. The bill already has been endorsed by the American Geriatrics Society, the National Council on Aging, the National Association of Geriatric Education, the

Alzheimer's Association, and the National Association of Social Workers.

The American Medical Directors Association (AMDA), which represents nursing facility practitioners, has approved the bill's concepts in principle. "I'm very positive on the bill," said Dr. Paul Katz, AMDA vice president and chief of geriatrics at the University of Rochester (N.Y.). "I think overall, this really is a big step forward."

To benefit from the loan repayment

provisions, health care professionals would not only need to complete specialty training in geriatrics or gerontology but also agree to provide full-time clinical practice and service to older adults for a minimum of 2 years. In addition, the bill would expand eligibility for the Nursing Education Loan Repayment Program to include registered nurses who complete specialty training and provide nursing services to older adults in long-term care settings. The proposed law also would expand midcareer specialty training in long-term care services through an existing training-grant program.

Sen. Boxer also proposes creation of a Health and Long-Term Care Workforce Advisory Panel for an Aging America, which would advise federal policy makers

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on workforce issues related to long-term care for the country's aging population.

"The medical and health community is already struggling to meet the demand for geriatric health care and support services, and the need

for trained professionals is only growing," Sen. Boxer said in a statement. "This legislation will provide incentives to help encourage qualified practitioners to join the geriatrics and gerontology fields."

Kathleen M. Wilson, AMDA's director of government affairs, said that the association supports the concepts included in the legislation, based on a draft that Sen. Boxer's staff provided last year. At press time, AMDA's public policy committee was reviewing the actual legislation, which Wilson said is made up of initiatives closely similar to the concepts endorsed last year.

The loan guarantees in the legislation could be worth up to \$150,000 for a professional who provides full-time health care to older adults for 4 years. "That's fairly substantial, and it has to be substantial to get peoples' attention," said Dr. Katz. "That's something I've been preaching for awhile."

However, Dr. Katz also warned that the bill needs to better define "geriatric providers" for the purposes of the legislation's financial aid, especially nonphysician providers.

"Right now, for physicians there's a formal process of being trained in geriatrics, so it's not an issue. But for social workers and therapists, there aren't always specialty courses." And, he added, the bill needs to specify what kinds of courses would qualify.

Dr. Katz also noted that the bill isn't specific to long-term care. "It's focusing on geriatricians," he said. "What about people who want to practice in long-term care?"

Overall, though, Dr. Katz said he supports S. 2708. ■

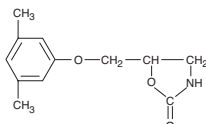
SKELAXIN®

(Metaxalone) Tablets

DESCRIPTION

SKELAXIN® (metaxalone) is available as an 800 mg oval, scored pink tablet.

Chemically, metaxalone is 5-[[3,5-dimethylphenoxy]methyl]-2-oxazolidinone. The empirical formula is C₁₇H₂₁NO₃, which corresponds to a molecular weight of 271.36. The structural formula is:



Metaxalone is a white to almost white, odorless crystalline powder freely soluble in chloroform, soluble in methanol and in 96% ethanol, but practically insoluble in ether or water.

Each tablet contains 800 mg metaxalone and the following inactive ingredients: alginate acid, ammonium calcium alginate, B-Rose Liquid, corn starch and magnesium stearate.

CLINICAL PHARMACOLOGY

Mechanism of Action: The mechanism of action of metaxalone in humans has not been established, but may be due to general central nervous system depression. Metaxalone has no direct action on the contractile mechanism of striated muscle, the motor end plate or the nerve fiber.

Pharmacokinetics:

The pharmacokinetics of metaxalone have been evaluated in healthy adult volunteers after single dose administration of SKELAXIN under fasted and fed conditions at doses ranging from 400 mg to 800 mg.

Absorption

Peak plasma concentrations of metaxalone occur approximately 3 hours after a 400 mg oral dose under fasted conditions. Thereafter, metaxalone concentrations decline log-linearly with a terminal half-life of 9.0 ± 4.8 hours. Doubling the dose of SKELAXIN from 400 mg to 800 mg results in a roughly proportional increase in metaxalone exposure as indicated by peak plasma concentrations (C_{max}) and area under the curve (AUC). Dose proportionality at doses above 800 mg has not been studied. The absolute bioavailability of metaxalone is not known.

The single-dose pharmacokinetic parameters of metaxalone in two groups of healthy volunteers are shown in Table 1.

| Dose (mg) | C _{max} (ng/mL) | T _{max} (h) | AUC ₀₋₁₂ (ng·h/mL) | t _{1/2} (h) | CL/F (L/h) |
|------------------|--------------------------|----------------------|-------------------------------|----------------------|------------|
| 400 ¹ | 983 (53) | 3.3 (35) | 7479 (51) | 9.0 (53) | 68 (50) |
| 800 ² | 1816 (43) | 3.0 (39) | 15044 (46) | 8.0 (58) | 66 (51) |

¹Subjects received 1x400 mg tablet under fasted conditions (N=42)

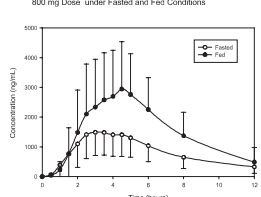
²Subjects received 2x400 mg tablets under fasted conditions (N=59)

Food Effects

A randomized, two-way, crossover study was conducted in 42 healthy volunteers (31 males, 11 females) administered one 400 mg SKELAXIN tablet under fasted conditions and following a standard high-fat breakfast. Subjects ranged in age from 18 to 48 years (mean age = 23.5 ± 5.7 years). Compared to fasted conditions, the presence of a high fat meal at the time of drug administration increased C_{max} by 177.5% and increased AUC (AUC₀₋₁₂, AUC_∞) by 123.5% and 115.4%, respectively. Time-to-peak concentration (T_{max}) was also delayed (4.3 h versus 3.3 h) and terminal half-life was decreased (2.4 h versus 9.0 h) under fed conditions compared to fasted.

In a second food effect study of similar design, two 400 mg SKELAXIN tablets (800 mg) were administered to healthy volunteers (N=59, 37 males, 22 females), ranging in age from 18-50 years (mean age = 25.6 ± 8.7 years). Compared to fasted conditions, the presence of a high fat meal at the time of drug administration increased C_{max} by 193.6% and increased AUC (AUC₀₋₁₂, AUC_∞) by 146.4% and 142.2%, respectively. Time-to-peak concentration (T_{max}) was also delayed (4.9 h versus 3.0 h) and terminal half-life was decreased (4.2 h versus 8.0 h) under fed conditions compared to fasted conditions. Similar food effect results were observed in the above study when one SKELAXIN 800 mg tablet was administered in place of two SKELAXIN 400 mg tablets. The increase in metaxalone exposure coinciding with a reduction in half-life may be attributed to more complete absorption of metaxalone in the presence of a high fat meal (Figure 1).

Figure 1. Mean (SD) Concentrations of Metaxalone following an 800 mg Dose under Fasted and Fed Conditions



Distribution, Metabolism, and Excretion

Although plasma protein binding and absolute bioavailability of metaxalone are not known, the apparent volume of distribution (V/F ~ 800 L) and lipophilicity (log P = 2.42) of metaxalone suggest that the drug is extensively distributed in the tissues. Metaxalone is metabolized by the liver and excreted in the urine as unidentified metabolites.

Pharmacokinetics in Special Populations

Age: The effects of age on the pharmacokinetics of metaxalone were determined following single administration of two 400 mg tablets (800 mg) under fasted and fed conditions. The results were analyzed separately, as well as in combination with the results from three other studies. Using the combined data, the results indicate that the pharmacokinetics of metaxalone are significantly more affected by age under fasted conditions than under fed conditions, with bioavailability under fasted conditions increasing with age.

The bioavailability of metaxalone under fasted and fed conditions in three groups of healthy volunteers of varying age is shown in Table 2.

| Age (years) | Younger Volunteers | | Older Volunteers | |
|--------------------------|--------------------|------------|------------------|-----------|
| | Fasted | Fed | Fasted | Fed |
| 25.6 ± 8.7 | 39.3 ± 10.8 | 71.5 ± 5.0 | | |
| N | 59 | 21 | 23 | |
| Food | Fasted | Fed | Fasted | Fed |
| | 1816 (43) | 3510 (41) | 2719 (46) | 2915 (55) |
| C _{max} (ng/mL) | | | 3168 (43) | 3680 (59) |

| T _{max} (h) | 3.0 | 4.9 | 3.0 | 8.7 | 2.6 | 6.5 |
|-------------------------------|------------|------------|------------|------------|------------|------------|
| (n) | (39) | (48) | (40) | (91) | (30) | (67) |
| AUC ₀₋₁₂ (ng·h/mL) | 14531 (47) | 20683 (41) | 19836 (40) | 20482 (37) | 23797 (45) | 24340 (48) |
| AUC _∞ (ng·h/mL) | 15045 (46) | 20833 (41) | 20490 (39) | 20815 (37) | 24194 (44) | 24704 (47) |

Gender: The effect of gender on the pharmacokinetics of metaxalone was assessed in an open label study, in which 48 healthy adult volunteers (24 males, 24 females) were administered two SKELAXIN 400 mg tablets (800 mg) under fasted conditions. The bioavailability of metaxalone was significantly higher in females compared to males as evidenced by C_{max} (2115 ng/mL versus 1335 ng/mL) and AUC_∞ (17884 ng·h/mL versus 10328 ng·h/mL). The mean half-life was 11.1 hours in females and 7.6 hours in males. The apparent volume of distribution of metaxalone was approximately 22% higher in males than in females, but not significantly different when adjusted for body weight. Similar findings were also seen when the previously described combined dataset was used in the analysis.

Hepatic/Renal Insufficiency: The impact of hepatic and renal disease on the pharmacokinetics of metaxalone has not been determined. In the absence of such information, SKELAXIN should be used with caution in patients with hepatic and/or renal impairment.

INDICATIONS AND USAGE

SKELAXIN (metaxalone) is indicated as an adjunct to rest, physical therapy, and other measures for the relief of discomforts associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Metaxalone does not directly relax tense skeletal muscles in man.

CONTRAINDICATIONS

Known hypersensitivity to any components of this product. Known tendency to drug induced, hemolytic, or other anemias. Significantly impaired renal or hepatic function.

WARNINGS

SKELAXIN may enhance the effects of alcohol and other CNS depressants.

PRECAUTIONS

Metaxalone should be administered with great care to patients with pre-existing liver damage. Serial liver function studies should be performed in these patients.

False-positive Benedict's tests, due to an unknown reducing substance, have been noted. A glucose-specific test will differentiate findings.

Taking SKELAXIN with food may enhance general CNS depression; elderly patients may be especially susceptible to this CNS effect. (See CLINICAL PHARMACOLOGY: Pharmacokinetics and PRECAUTIONS: Information for Patients section).

Information for Patients

SKELAXIN may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle, especially when used with alcohol or other CNS depressants.

Drug Interactions

SKELAXIN may enhance the effects of alcohol, barbiturates and other CNS depressants.

Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential of metaxalone has not been determined.

Pregnancy

Reproduction studies in rats have not revealed evidence of impaired fertility or harm to the fetus due to metaxalone. Post marketing experience has not revealed evidence of fetal injury, but such experience cannot exclude the possibility of infrequent or subtle damage to the human fetus. Safe use of metaxalone has not been established with regard to possible adverse effects upon fetal development. Therefore, metaxalone tablets should not be used in women who are or may become pregnant and particularly during early pregnancy unless in the judgement of the physician the potential benefits outweigh the possible hazards.

Nursing Mothers

It is not known whether this drug is secreted in human milk. As a general rule, nursing should not be undertaken while a patient is on a drug since many drugs are excreted in human milk.

Pediatric Use

Safety and effectiveness in children 12 years of age and below have not been established.

ADVERSE REACTIONS

The most frequent reactions to metaxalone include: CNS: drowsiness, dizziness, headache, and nervousness or "irritability";

Digestive: nausea, vomiting, gastrointestinal upset.

Other adverse reactions are:

Immune System: hypersensitivity reaction, rash with or without pruritus;

Hematologic: leukopenia; hemolytic anemia;

Hepatobiliary: jaundice.

Though rare, anaphylactoid reactions have been reported with metaxalone.

OVERDOSAGE

Deaths by deliberate or accidental overdose have occurred with metaxalone, particularly in combination with antidepressants, and have been reported with this class of drug in combination with alcohol.

When determining the LD₅₀ in rats and mice, progressive sedation, hypnosis and finally respiratory failure were noted as the dosage increased. In dogs, no LD₅₀ could be determined as the higher doses produced an emetic action in 15 to 30 minutes.

Treatment - Gastric lavage and supportive therapy. Consultation with a regional poison control center is recommended.

DOSAGE AND ADMINISTRATION

The recommended dose for adults and children over 12 years of age is one 800 mg tablet three to four times a day.

HOW SUPPLIED

SKELAXIN (metaxalone) is available as an 800 mg oval, scored pink tablet inscribed with 8667 on the scored side and "S" on the other. Available in bottles of 100 (NDC 60793-136-01) and in bottles of 500 (NDC 60793-136-05).

Store at Controlled Room Temperature, between 15°C and 30°C (59°F and 86°F).

Rx Only

Prescribing Information as of April 2007.



King Pharmaceuticals

Distributed by: King Pharmaceuticals, Inc., Bristol, TN 37620
Manufactured by: Mallinckrodt Inc., Hobart, NY 13788



www.kingpharm.com www.skexalin.com

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