**SKELAXIN®** (metaxalone) Tablets

**DESCRIPTION**

SKELAXIN® (metaxalone) is available as an 800 mg oral, scored pink tablet. Chemically, metaxalone is 5-[[2,6-dimethylphenyl]methylene]methyl-2-oxazoline. The empirical formula is C13H18N2O, which corresponds to a molecular weight of 221.26. The structural formula is:

![Chemical Structure of Metaxalone](image)

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 other water or alcohol. Each tablet contains 400 mg metaxalone and the following inactive ingredients: aluminum oxide, amonium 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. Following a single oral dose, metaxalone is not absorbed by the rectum. After oral administration, metaxalone is absorbed by the small intestine and is rapidly distributed to all tissues and the cerebrospinal fluid. It is strongly bound to plasma proteins (80-95%). The absolute bioavailability of metaxalone is 40% to 60%.

**Distribution:** Metaxalone is extensively distributed in a volume of distribution (V/F) of about 800 L. The apparent volume of distribution of metaxalone is not significantly different between young and elderly subjects. The plasma protein binding of metaxalone is not known, but the fraction bound is not substantially different from that in plasma.

**Metabolism:** Metaxalone is metabolized by the liver and the urine. The principal metabolites of metaxalone are the glucuronide and sulfate conjugates of metaxalone and its O-demethylated and O-glucuronidated derivatives. Metaxalone has been shown to inhibit the activity of several human cytochrome P450 enzymes, including CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. Metaxalone does not significantly inhibit major CYP enzymes such as CYP1A2, CYP2A6, CYP2B6, to a lesser extent, CYP2C8, CYP2C9, and CYP2C19 appear to metabolize metaxalone.

**Excretion:** Although plasma protein binding and absolute bioavailability of metaxalone are not known, the apparent volume of distribution of metaxalone is about 800 L. Metaxalone is eliminated primarily in the urine and feces. The extent of excretion of metaxalone in the urine and feces is approximately 30% and 10%, respectively.

**Animal Pharmacology:** Metaxalone administration to rats and mice did not induce any liver tumors. The observed effects were considered to be of no toxicological significance.

**Human Pharmacology:** Postmarketing 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: dizziness, drowsiness, headache, and nervousness or "irritability";
- Gastrointestinal: nausea, vomiting, anorexia;
- Other adverse reactions are:
  - Immune System: hypersensitivity reactions, rash with or without pruritus;
  - Hematological: leukopenia, hemolytic anemia;
  - Hepatobiliary: jaundice.
- Though rare, anaphylactic 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, LD₅₀ (oral) could be determined as the higher doses produced an enemic 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 times a day.

**HOW SUPPLIED**

SKELAXIN® (metaxalone) is available as an 800 mg oral, scored pink tablet. Metaxalone tablets are supplied in bottles of 100 tablets (N 3000846-F).

Rx Only

Prescribing information as of April 2008.

**Table 1: Mean (CV%) Pharmacokinetic Parameters Following Single Administration of Two 400 mg SKELAXIN Tablets (800 mg) under Fasted and Fed Conditions**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Fasted (n=29)</th>
<th>Fed (n=29)</th>
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<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>1335 (93)</td>
<td>20683 (41)</td>
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<tr>
<td>Tmax (h)</td>
<td>3.0 (49)</td>
<td>4.9 (48)</td>
</tr>
<tr>
<td>t1/2 (h)</td>
<td>2.6 (67)</td>
<td>6.5 (67)</td>
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<tr>
<td>NURSING MOTHERS</td>
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