FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE
Carisoprodol Tablets USP are indicated for the relief of discomfort associated with acute, painful musculoskeletal conditions in adults. (1)

WARNINGS AND PRECAUTIONS
• Sedation
• Abuse, Dependence, and Withdrawal
• Seizures
• Hypersensitivity reactions to a carbamazepine such as rash or urticaria (4)

Dosage and Administration
The recommended dose of carisoprodol is 250 mg to 350 mg three times a day and at bedtime. (2)

DOSE FORMS AND STRENGTHS
Tablets: 350 mg (5)

CONTRAINDICATIONS
• Acute intermittent porphyria (4)

FULL PRESCRIBING INFORMATION

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HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Carisoprodol Tablets, USP safely and effectively. See full prescribing information for Carisoprodol Tablets, USP.

CARISOPRODO Tablets USP for Oral use
Initial U.S. Approval: 1959

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Tablets: 350 mg (5)

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Adverse Reactions

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Carisoprodol 250 mg</th>
<th>Carisoprodol 350 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>43 (12)</td>
<td>42 (13)</td>
</tr>
<tr>
<td>Headache</td>
<td>11 (3)</td>
<td>28 (41)</td>
</tr>
</tbody>
</table>

Other reports of adverse reactions have included reports with frequencies greater than 2% and more frequently than placebo. 5

To report suspected adverse reactions, contact Qualitest Pharmaceuticals at 1-800-444-4051 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Drug Interactions
• CNS depressants, e.g., alcohol, benzodiazepines, opioids, tricyclic antidepressants - additive sedative effects (5.1, 21)

Adverse reactions reported with frequencies of at least 2% and more frequently than placebo are:

• Headache

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Drug Interactions
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See 17 for patient counseling information

Revised: 2/2013

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9.2 Abuse

Abuse of carisoprodol poses a risk of overdose which may lead to death, CNS and respiratory depression, hypotension, seizures and other disorders (see Warnings and Precautions (5.1) and Clinical Pharmacology (12)). Abuse at high risk of carisoprodol abuse may include those with previous history of carisoprodol, with a history of drug abuse, or those who use carisoprodol in combination with other abused drugs.

Prescription drug abuse is the intentional non-therapeutic use of a drug, even once, for its rewarding psychological effects. Drug abuse, which develops after repeated drug use, is characterized by a strong desire to take a drug despite harmful consequences, difficulty in controlling its use, giving a higher priority to drug use than to obligations, increased tolerance, and sometimes withdrawal symptoms when the drug is discontinued. Drug dependence is separate and distinct from physical dependence and tolerance (for example, abuse or addiction may not be accompanied by tolerance or physical dependence) (see Drug Abuse and Dependence (3.3)).

9.3 Tolerance

Tolerance is a decrease in a patient’s response to a drug, requiring an increase in the dosage to maintain the same physical. Physical dependence is characterized by withdrawal symptoms after abrupt discontinuation or a significant decrease in a drug. Both tolerance and physical dependence have been reported with the prilosec use of carisoprodol. Reported withdrawal symptoms with carisoprodol include insomnia, sweating, abdominal cramps, headache, tremors, muscle twitching, anxiety, anxiety, hallucinations, and seizures. Institutional patients taking large doses of carisoprodol or those taking the drug for a prolonged time to not abruptly stop (see Warnings and Precautions (5.2)).

10. OVERDOSAGE

Overdose of carisoprodol commonly produces CNS depression. Death, coma, respiratory depression, hypotension, seizures, tachycardia, hallucinations, dystonic reactions, ophthalmic, urinary, gastrointestinal and respiratory failures, rigidity, and/or seizures have been reported with carisoprodol overdose. Seizures should be treated with intravenous benzodiazapines and the meperidine or meperidine may be treated with phenobarbital. In cases of severe CNS depression with an airway protective reflexes may be compromised and tracheal intubation should be considered for airway protection and respiratory support. For decontamination in cases of acute toxicity, activated charcoal should be considered in a hospital setting with patients with large overdose of carisoprodol who present early and in the absence of CNS depression and can protect their airway. For more information on the management of an overdose of carisoprodol, contact a Poison Control Center.

11 DESCRIPTION

Carisoprodol Tablets USP are available as 350 mg round, white tablets for oral administration. Carisoprodol is a white, crystalline powder, having a mild, characteristic odor and a bitter taste. It is practically independent of pH. Carisoprodol is present as a racemic mixture. Chemically, carisoprodol is known as cis-2-carboxy-1,3-propanediol dihydrochloride and the molecular formula is C_{9}H_{14}Cl_{2}NO_{3}, with a molecular weight of 260.33. The structural formula is:

\[\text{C}_{9}\text{H}_{14}\text{Cl}_{2}\text{NO}_{3}\]

Other ingredients in Carisoprodol Tablets, USP include croscarmellose sodium, hydrogenated vegetable oil, hypromellose, magnesium stearate and microcrystalline cellulose.

1.2 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The mechanism of action of carisoprodol in relieving discomfort associated with acute painful musculoskeletal conditions has not been clearly identified. In animal studies, muscle relaxation induced by carisoprodol is associated with altered interneuronal activity in the spinal cord and in the descending reticular formation of the brain. In vitro, carisoprodol induces prolonged acetylcholine release and a depression of the firing rates of single neurons. A metabolite of carisoprodol, meprobamate, has anxiolytic and sedative properties. The degree to which these properties of meprobamate contribute to the safety and efficacy of carisoprodol is unknown.

12.2 Pharmacodynamics

Carisoprodol has a central acting skeletal muscle relaxant that does not directly relax skeletal muscles. The mechanism of carisoprodol, mebeverine, has anesthetic and radiative properties. The degree to which these properties of mebeverine contribute to the safety and efficacy of carisoprodol is unknown.

12.3 Pharmacokinetics

The pharmacokinetics of carisoprodol and its metabolite mebeverine were studied in a crossover study of 24 healthy subjects (12 male and 12 female) who received single doses of 250 mg and 50 mg of carisoprodol and mebeverine was dose proportional between the 250 mg and 50 mg doses. The C_{max} of mebeverine was 2.5 ± 0.5 µg/mL (mean ± SD) after administration of 250 mg carisoprodol, which is approximately 80% of the C_{max} of mebeverine (approximately 8 µg/mL) after administration of a single 400 mg dose of mebeverine. The C_{max} of 2-carboxy-1,3-propanediol dihydrochloride and the molecular formula was C_{9}H_{14}Cl_{2}NO_{3}, with a molecular weight of 260.33. The structural formula is:

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The results for the primary efficacy evaluations in the acute, low back pain studies are presented in Table 2. The proportion of patients who used concomitant acetaminophen, NSAID and tramadol, opioid agonists, other muscle relaxants, benzodiazepines, tricyclic antidepressants, and anti-epileptic drugs was similar in the treatment groups. The results for the primary statistical comparison between the carisoprodol 250 mg and placebo groups in both studies. The primary statistical comparison was between the carisoprodol 250 mg and placebo groups in both studies. The proportions of patients who used concomitant anticholinergics, antidepressants, opioid agonists, other muscle relaxants, benzodiazepines and tricyclic antidepressants was similar in the treatment groups.

The results for the primary efficacy evaluations in the acute, low back pain studies are presented in Table 3. The primary efficacy endpoints (Effect of Starting Backache and Global Impression of Change) were assessed by the patients on Study Day 3. These endpoints were scored on a 5-point rating scale from 4 (worst outcome) to 2 (best outcome). The results for the primary statistical comparison between the carisoprodol 250 mg and placebo groups is shown in Table 3. The patients treated with carisoprodol experienced improvement in function as measured by the Roland-Morris Disability Questionnaire (RMDQ) scores on Days 3 and 7.

16 HOW SUPPLIED/STORAGE AND HANDLING

Carisoprodol Tablets USP: 350 mg, white, round, unscored tablets debossed “2410” on one side and plain on the reverse side; available as follows:

- Bottles of 100: NDC 0033-2583-21
- Bottles of 500: NDC 0033-2583-28
- Bottles of 1000: NDC 0033-2583-20

Storage: Shown to be 20° to 25°C (68° to 77°F) (see USP Controlled Room Temperature).

17 PATIENT COUNSELLING INFORMATION

Patients should be advised to contact their physician if they experience any adverse reactions to carisoprodol tablets. 13.1 CONTRAINDICATIONS

Patients should be advised that carisoprodol tablets may cause drowsiness and/or dizziness, and has been associated with motor vehicle accidents. Patients should be advised to avoid taking carisoprodol before engaging in potentially hazardous activities such as driving a motor vehicle or operating machinery (see Warnings and Precautions (5.1)).

17.2 Avoidance of Alcohol and Other CNS Depressants

Patients should be advised to avoid alcohol beverages while taking carisoprodol tablets and to check with their doctor before taking any other CNS depressants such as benzodiazepines, opioids, tricyclic antidepressants, sedating antihistamines, or other sedatives (see Warnings and Precautions (5.1)).

17.3 Carisoprodol Tablets Should Only Be Used for Short-Term Treatment

Patients should be advised that treatment with carisoprodol tablets should be limited to acute use (up to two or three weeks) for the relief of acute, musculoskeletal pain. In the setting of chronic, musculoskeletal pain, treatment with carisoprodol tablets, cases of dependence, withdrawal, and abuse have been reported with prolonged use. If the musculoskeletal condition still persists, patients should contact their healthcare provider for further evaluation.

To report SUSPECTED ADVERSE REACTIONS, contact Qualitac Pharmaceuticals at 1-800-441-0191 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.