

# OREGON DUR BOARD NEWSLETTER<sup>©</sup>

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## Carisoprodol (Soma<sup>®</sup>) and Sedative Quantities to be Restricted on November 15, 2002

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The Oregon Office of Medical Assistance Programs (OMAP) will prior authorize sedatives for quantities greater than 15 doses in 30 days and carisoprodol (Soma<sup>®</sup>) and carisoprodol combinations for quantities greater than 56 tablets in 90 days. This policy begins on November 15, 2002 and affects only "open-card" patients. The Oregon Drug Use Review (DUR) Board recommended prior authorization for these drug products because there was evidence of continued long-term use in the Oregon Health Plan (OHP) open-card population in spite of RetroDUR educational efforts regarding literature recommendations for short-term use only.

### CARISOPRODOL

Carisoprodol has limited efficacy for short-term treatment of acute musculoskeletal conditions and is generally ineffective for the treatment of chronic pain. No evidence exists for a clinically significant effect other than sedation.<sup>1</sup> In addition, carisoprodol is associated with dependence when used on a long-term basis. This lack of efficacy and potential for abuse led the Portland VA Medical Center Formulary Committee to completely remove carisoprodol from its formulary in 1997.

The exact mechanism of action of carisoprodol is unknown. It does have an effect on the reticular system, but its effects are believed to be due to sedation rather than any direct effect on the muscle. Some of the effects of carisoprodol may be due to its major metabolite, meprobamate (Miltown<sup>®</sup>, Equanil<sup>®</sup>), a Schedule IV drug pharmacologically similar to barbiturates.<sup>2</sup>

Cases of carisoprodol dependence have been reported to the FDA's Adverse Event Reporting System and in the medical literature.<sup>2,3,4,5</sup> Non-medical use of carisoprodol is an increasing problem. Carisoprodol is used frequently by poly-drug abusers, particularly those dependent on opioids. It may be used as a substitute when narcotics are not available in order to combat opioid withdrawal. It may also be used to prolong the effects of a narcotic or alcohol, to enhance the effect of a primary drug of abuse, to "take the edge off the jittery feeling of cocaine", and to terminate a "cocaine binge."<sup>5,6,7</sup> A 1997 FDA review showed 72,000 carisoprodol tablets were seized by law enforcement personnel between 1980 and 1996 in 224 seizures. Carisoprodol was frequently encountered in cases where other controlled substances were being trafficked.

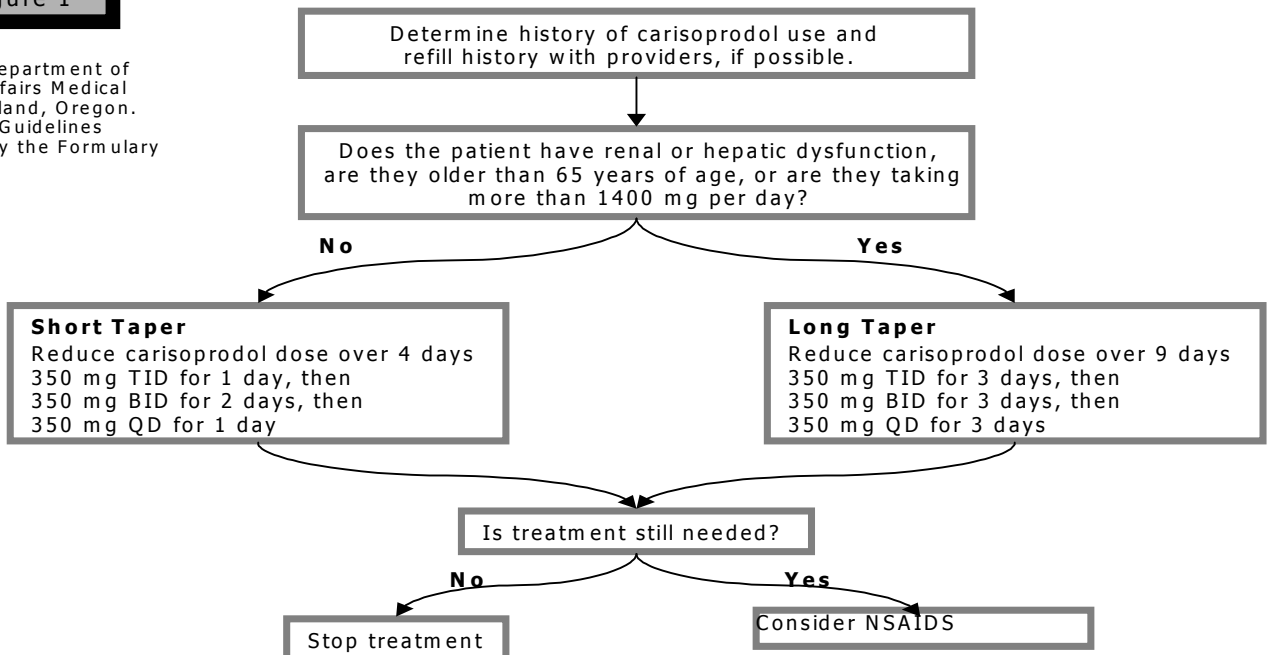
Carisoprodol alone is rarely fatal in overdose, but when taken with other CNS depressants, respiratory depression and death can result. Ethanol is reported to be a frequent co-intoxicant with carisoprodol, as are diazepam, propoxyphene, hydrocodone and alprazolam.<sup>8</sup> An Alabama investigation into 24 carisoprodol-related deaths showed that carisoprodol was never detected alone, but with various co-intoxicants.

As previously reported in the Oregon DUR Newsletter<sup>9</sup>, carisoprodol drug abuse is a public health problem nationwide. Many cases of overdose are reported to poison control centers. The DUR Board has noted continued use of carisoprodol outside recommended guidelines. A review of OMAP

## Tapering carisoprodol

Figure 1

From the Department of Veterans Affairs Medical Center Portland, Oregon. Medication Guidelines Approved by the Formulary Committee



fee-for-service ("open-card") patients during the third quarter of 2001 showed that 11% of the 1507 patients on carisoprodol averaged over 1400mg (> 3 tablets) per day. Sixty-five percent of patients were dispensed quantities exceeding 60 tablets, with over 30% of patients receiving more than 270 tablets, indicating greater than three tablets per day for the entire 90-day period. Results of a previous DUR Board review indicated two areas of inappropriate use: patients taking high doses of carisoprodol who have chronic pain problems and patients with multiple prescriptions whose prescription history is suggestive of drug seeking behavior.

There is no justification for long-term use of carisoprodol. Prescribers should evaluate patients for discontinuation of carisoprodol. If relief of pain or associated symptoms is indicated, an alternative agent such as an anti-inflammatory drug or long-acting opioid, may be introduced while carisoprodol therapy is tapered. This allows carisoprodol to be discontinued without causing any unnecessary discomfort to the patient. Many patients with chronic pain may not be getting pain relief from the drug but may still be reluctant to discontinue it because of its effects on associated problems such as depression, anxiety and sleeping difficulties. These problems should be evaluated and addressed with appropriate therapies.

To assist in the carisoprodol tapering process, the algorithm in Figure 1 was produced at the Portland VA Medical Center. Upon the discontinuation of high doses of carisoprodol, patients may suffer withdrawal symptoms such as body aches, increased perspiration, palpitations and psychological symptoms such as sadness, restlessness, anxiety and insomnia.<sup>5</sup> A withdrawal program similar to one used for alcohol withdrawal may be required for these patients. A suggested tapering schedule for such patients is to reduce the dose daily by 25% of the previous day's dose. The advice of an addiction specialist may be necessary.

## SEDATIVES

As reported previously in the Oregon DUR Board Newsletter<sup>10</sup>, OMAP conducted an internal review of hypnotic prescribing patterns. Despite the fact that insomnia guidelines,<sup>11,12,13</sup> recommend only short-term (7-10 days) hypnotic drug therapy, the average duration of sedative use in the year 2000 was 3 to 6 months. Results showed 81 patients over the age of 64 (over 50% of this group) received higher than recommended doses.

These findings and placement of insomnia below the OHP treatment line on the list of prioritized services, prompted the DUR Board to recommend prior authorization of continuous use (more than 15 doses in 30 days) of zolpidem, zaleplon, temazepam, triazolam, quazepam, flurazepam and estazolam. Authorization will require an above the line diagnosis.

Drug therapy for the treatment of insomnia should be considered second-line to nonpharmacologic approaches. Effective non-drug strategies include sleep hygiene, cognitive behavioral therapy, and the elimination of possible causative factors. Utilization of pharmacologic therapy should be reserved for those patients who do not receive benefit from nonpharmacologic treatment and should be limited to a short course of treatment.

Benzodiazepines are frequently used in the treatment of insomnia. These agents should be dosed intermittently, for a limited duration and at the lowest dose possible due to their propensity to cause adverse effects, medication tolerance and dependence.<sup>11</sup> Tolerance and dependence may occur after only 1 to 2 weeks with short and intermediate-acting agents.<sup>14</sup> Benzodiazepines should be withdrawn gradually (e.g., 25% per week) to avoid withdrawal reactions (including seizures) and rebound insomnia.

Patients who have been on benzodiazepines long-term will require a slower, more individualized taper.

Two newer nonbenzodiazepines, zolpidem (Ambien) and zaleplon (Sonata), are strictly indicated for the short-term treatment (7-10 days) of insomnia.<sup>15,16</sup> There are no published data available that support the use of either agent long-term. In fact, in two unpublished controlled trials, it was determined that the beneficial effects of zolpidem are only short term, with tolerance developing by the fifth week of use. Chronic standard zolpidem therapy (5-10 mg qhs) is considered to be no better than placebo.<sup>15</sup> An advantage of these agents over some benzodiazepines is their rapid onset of action and short elimination half-life. Zaleplon, with an average onset of activity of 15 to 20 minutes, however, is comparable to triazolam with an onset of 15 to 30 minutes. Drawbacks to the nonbenzodiazepine hypnotics include impaired memory and concentration, headache, GI upset, drug tolerance, cost and lack of efficacy in some patients.

Chronic insomnia is rarely a primary disorder. More commonly, it is a symptom of an underlying medical or psychiatric illness. A thorough evaluation of the patient is warranted prior to the diagnosis of chronic idiopathic insomnia. Nonpharmacologic therapy is considered first-line in all patients. Short-term sedative-hypnotics may be required in certain patients in whom the insomnia does not resolve. If these agents are used longer-term, they should be prescribed intermittently. Chronic use of sedative-hypnotics is strongly discouraged.

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