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Dear Colleague,

We received feedback on our educational letter of November 2009 about the use of low-dose quetiapine (Seroquel) for unlabeled uses, including insomnia. This letter responds to requests for additional information and suggestions on alternative medications for treatment of insomnia, a sleep disturbance that affects approximately one-third of the adult US population.<sup>1,2</sup>

Effective January 1, 2010, MassHealth will no longer require prior authorization for zolpidem (generic Ambien) for prescriptions up to 30 tablets per month for the 10 mg dose and 45 tablets per month for the 5 mg dose. Zolpidem is now a generic product and is reasonable for many patients with chronic insomnia. Prescriptions for quantities that exceed these limits will require prior authorization.

Despite a relatively small evidence base, trazodone (Desyrel and others) is the most commonly prescribed medication for the treatment of insomnia in the US, according to a 2005 NIH State-of-the-Science Conference report.<sup>3</sup> There are small randomized placebo-controlled trials (RCTs) showing efficacy and safety of trazodone for diverse problems, including deep sleep induction,<sup>4</sup> SSRI-induced insomnia,<sup>5</sup> and alcohol post-withdrawal insomnia,<sup>6</sup> as well as several reports of effectiveness in post-traumatic stress disorder (PTSD).<sup>7</sup> Stephen Stahl has written a recent article<sup>8</sup> asserting that trazodone works on sleep by three mechanisms and may be "the ideal hypnotic." Other centrally acting antihistaminic agents have also been reported to be useful. For example, hydroxyzine (generic Vistaril and others), doxepin (generic Sinequan and others), and other low-dose tricyclic antidepressants are all potent histamine-1 antagonists in the central nervous system (CNS). These agents differ slightly in their effects on serotonergic neurotransmission, but will still produce sedation.

People with PTSD require individualized treatment depending on the targeted symptom(s). When treating patients for disturbed sleep and nightmares, prazosin (Minipress and others) is well-evidenced with 2 placebo-controlled RCTs in combat veterans<sup>9,10</sup> and one RCT in civilians, mostly sexual trauma in women.<sup>11</sup> Hypotension is a concern but was seen infrequently in these studies.

Please review the differential diagnosis of insomnia and identify the various contributing factors. These factors are diverse and range from primary psychiatric disorders (depression, anxiety), to poor sleep hygiene, sleep apnea and restless leg syndrome, as well as the use of prescribed and nonprescribed stimulating drugs (e.g., SSRIs/SNRIs, caffeinated beverages), and conditioned insomnia (residual fear that one will not be able to sleep when the original cause is no longer present). The latter is best treated with cognitive therapy techniques. Manage these problems as appropriate. Please refer to Dr. Winkelman's "10 Tips for a Good Night's Sleep" published on the MassHealth Web site at [www.mass.gov/druglist](http://www.mass.gov/druglist).

The effects of quetiapine on weight gain and metabolism are not dose related<sup>12</sup> and can occur even at low doses. The knowledge base available regarding quetiapine-related weight gain is limited to the published studies. However, recent newspaper articles reveal that there are unpublished quetiapine trials, conducted in the 1990s, that found much higher rates of significant weight gain<sup>13</sup> compared to those that are in the literature. For hypnotics, please consider the suggestions above before turning to quetiapine.

Sincerely,

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