

## Over-the-Counter Purchase and Off-Label Use of Modafinil



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To the Editor;

Modafinil is a psychostimulant agent which is approved for the treatment of shift work disorder (SWD), narcolepsy and excessive daytime sleepiness in adults<sup>1</sup>. In vitro studies prove that modafinil can be attached directly to the dopamine and norepinephrine transporters, resulting in a moderate inhibition of transporter function<sup>2</sup>.

In Turkey, medications with modafinil as the active ingredient are readily accessible, can be purchased over the counter in pharmacies and do not require a prescription by specialist physicians. There is growing evidence that, in recent years, off-label use of modafinil has risen all over the world, notably among students, due to its reputation, created by certain websites, as a so-called “intelligence pill”<sup>3</sup>. The rate of use of modafinil and similar substances among university students in European countries is reported as being 0.8-16%<sup>4</sup>. Consequently, various countries are developing strategies and establishing commissions to address this problem<sup>5,6</sup>.

Modafinil use may lead to adverse effects such as insomnia, agitation, tachycardia, cardiac rhythm disorders, and increase in blood pressure<sup>7</sup>. Although rare, it can be associated with allergic reactions that may be fatal. Furthermore, indirect serious side effects such as full-blown manic episodes have also been reported<sup>8,9</sup>. Additionally, modafinil may induce hallucinations, paranoid ideation or behavior, depression, and anxiety<sup>10-13</sup>. The demand to increase the dosage is associated with its addictive potential<sup>14</sup>. Modafinil is a CNS-

activating medication and can lead to impairment in cognitive and motor skills. Reduced ability to use a motor vehicle safely can be observed. Modafinil interacts with the cytochrome system. It inhibits CYP 2C19, disrupts the function of CYP2C9 and induces CYP3A4, CYP2B6, and CYP1A2 enzymes. Due to these cytochrome interactions, modafinil interacts with many drugs other than psychotropic agents<sup>15</sup>.

Modafinil has been developed for the treatment of disorders associated with excessive daytime sleepiness, and efficacy studies were conducted for this indication. It has been licensed by the Ministry of Health (Turkey) with an indication of narcolepsy. Although potential to cause dependence has been reported, long-term side effects have not been investigated yet.

Rational use of modafinil is essential for preventing physical and mental health risks, restricting possible abuse by uncontrolled users. It is also necessary for the reduction of drug expenditures by social security institutions.

Relevant scientific and social evidence related to the use of modafinil can be summarized as risk for dose-dependent or independent, predictable or unpredictable side / adverse effects; potential for abuse and addiction; drug interactions with prescribed or over-the-counter agents; increasing uncontrolled use among young people due to its reputation as a so-called “intelligence pill” on the internet.

Cases of the medication’s off-label use or using it longer than indicated as well as exceeding the recommended doses by individuals who want to stay awake and alert are frequently recognized.

Thus, regulations must be urgently enacted to ensure the sale of modafinil in pharmacies only by appropriate prescription. We strongly suggest that over-the-counter purchase of modafinil be stopped immediately. The right to prescribe

medications with modafinil as the active ingredient must be restricted to psychiatrists, neurologists and pulmonologists and other physicians, based on continual drug use reports signed by these specialists.

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