Tapentadol

Expert peer review on pre-review report

35th Expert Committee on Drug Dependence, Hammamet, Tunisia
June 4-8, 2012
1. Comment based on the review report

a. Evidence on dependence and abuse potential

The evidence on dependence and abuse potential of tapentadol is far less developed than the evidence on pharmacology, toxicity and effectiveness in reducing pain. Its capacity to induce withdrawal seems to be in mid-range for pain-reducing opioids. The evidence on abuse potential is particularly scanty. There is just one study comparing “liking” to other opioids among opioid-experienced subjects, which found the liking equaled that for hydromorphone at equivalent pain-reducing doses. The few comments gleaned from the internet by experimenters with the substance are quite scattered, and the findings on nonmedical use of an initial uptake when the drug was first introduced in the US, falling off thereafter, suggest that the abuse potential may be limited so long as other opiates are de facto available for nonmedical use.

b. Consequences to individual and society because of misuse

Very little direct information is available specifically for tapentadol of the consequences to the individual from misuse. If its availability is limited to forms which cannot be easily injected, the adverse physical health consequences may well be limited. Government decisions appear to have been made up to now by analogy, with a bias toward the more restrictive side in scheduling decisions. One can certainly imagine a free-market situation in which there would be substantial adverse consequences if tapentadol were freely available while other opioids were kept in the current regime. Given the actions governments have already taken on scheduling, however, that seems unlikely to occur, whether or not tapentadol is scheduled internationally.

There is even less direct information available on potential consequences to society from tapentadol. If the Expert Committee is to make informed decisions on such dimensions, some work directly on these issues needs to be undertaken.

c. Magnitude of the problem in countries (misuse, illicit production, smuggling etc)

The problems appear to be small in countries in which tapentadol has been available as a psychopharmaceutical.

d. Need of the substance for medical (including veterinary) practice

The Australian Public Assessment Report for tapentadol (TGA, 2011, p. 127) concludes that tapentadol “has a favourable benefit to risk ratio” as a medication. The assessment continues, “the pharmacological profile, the dose- and time-independent pharmacokinetics, the improved gastrointestinal tolerability and the comparable efficacy to opioid standard
therapies suggest that tapentadol IR is a beneficial alternative for the treatment of moderate to severe acute pain.”
This is an endorsement of the medication as one more choice, but does not speak to a criterion of “need”, which would be required for consideration for WHO’s Essential Medicines list, for instance.

e. **Need of the substance for other purposes (e.g. industrial)**
   No known industrial use.

f. **Measures taken by countries to curb misuse**
The pre-review summary notes that tapentadol has been scheduled or recommended for scheduling in the US, UK, New Zealand and Australia, at the more restrictive end of the scheduling. These measures appear to have been taken preventively, rather than on the basis of substantial existing misuse. Other than that Risk Evaluation and Mitigation Strategies have been developed, no other information is available on other measures to curb misuse.

g. **Impact if this substance is scheduled**
   No information is available on this, but the impact in comparison with the present situation will be small. Given that availability of internationally scheduled substances for pain control in many low- and middle-income countries is extremely limited, there would also be potential health and welfare gains to be considered from not scheduling an effective pain medication such as tapentadol. Such gains would need to be weighed against potential harms from over availability.

2. **Additional information to the pre-review report**
The Australian assessment (TGA, 2011) is a useful further reference.

Reference

3. **Other comments or opinions**
Both at national and international levels, we have created systems of assessment and classification where review processes operate incrementally, and arguably with a bias towards restrictiveness, without a clear opportunity to take into account such balancing considerations as the resulting severe lack of pain medication in much of the world. The imbalance between richer and poorer countries in per-capita consumption of legal pain medications is in part a byproduct, in my view, of the international control system.
4. Expert reviewer’s recommendation for the need for a critical review

Yes, a critical review of tapentadol is recommended. In terms of how the international drug treaties are structured, and in terms of its dependence and abuse potential, it should be considered for classification under the 1961, or perhaps the 1971 Convention. I recommend that along with this review the Expert Committee consider what can be proposed about alterations in the international control regime, including its classification structure, which would ameliorate the severe undersupply of pain medications in poorer parts of the world.