

Therapeutic Products Programme  
Holland Cross, Tower "B"  
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00-103441-951

September 19, 2000

Pharmaceutical Issues Committee  
Deans of Pharmacy  
Registrars of Medicine  
Registrars of Pharmacy  
Provincial Deputy Ministers of Health  
Health and Trade Associations  
Pharmaceutical Manufacturers  
Solicitor General  
Attorney General  
Customs Agency

Dear Sir/Madam:

**Re: Schedule 1243 - Amendments to *Food and Drug Regulations*;  
*Controlled Drugs and Substances Act*; and *Benzodiazepines and  
Other Targeted Substances Regulations* regarding the  
Scheduling of Zaleplon, Zolpidem and Zopiclone**

This is to provide you with an opportunity to comment on the Therapeutic Products Programme's intention to remove Zolpidem and Zopiclone from Schedule F of the *Food and Drug Regulations*; and to add Zaleplon, Zolpidem and Zopiclone to Schedule IV of the *Controlled Drugs and Substances Act*, and to the *Benzodiazepines and Other Targeted Substances Regulations*.

Zaleplon, Zolpidem, and Zopiclone are all indicated for the short-term treatment of insomnia. While the chemical structures of these compounds are unrelated to benzodiazepines, they share a common site of action with benzodiazepines at the GABA<sub>A</sub> receptor complex. It is binding to this receptor complex that is

believed to be responsible for the hypnotic efficacy of both benzodiazepines, as well as Zaleplon, Zolpidem, and Zopiclone. While these three latter compounds may have some higher selectivity for specific subunits of the GABA<sub>A</sub> receptor complex (as demonstrated in non-clinical tests), the clinical significance of preferential subunit selectivity has not been established.

This recommendation reflects the clinical evidence that while these drugs are not benzodiazepines, they are hypnotics, and they share many of the pharmacological properties of the benzodiazepines and have a similar abuse potential.

In addition, the American Hospital Formulary System, a therapeutic classification system developed by the American Society of Health-System Pharmacists, has grouped these drugs with benzodiazepines in their classification standards according with their therapeutic use.

At the time of their approval for use within Canada, Zolpidem and Zopiclone were recommended to be scheduled in the same way as benzodiazepines, on Schedule F of the *Food and Drug Regulations*, until the implementation of the *Benzodiazepines and Other Targeted Substances Regulations*. Schedule F of the *Food and Drug Regulations* is a list of drugs which must only be dispensed upon receipt of a prescription. The *Benzodiazepines and Other Targeted Substances Regulations* were approved June 1, 2000, and came into effect September 1, 2000. At this time the benzodiazepines currently listed on Schedule F of the *Food and Drug Regulations* will be moved to Schedules 1 and 2 of the *Benzodiazepines and Other Targeted Substances Regulations*.

Once Zaleplon, Zolpidem, and Zopiclone have been moved over to Schedule IV of the *Controlled Drugs and Substances Act*, and to Schedules 1 and 2 of the *Benzodiazepines and Other Targeted Substances Regulations*, a greater degree of control will be warranted and a number of changes will have to be made in regards to the manufacturing, labelling, distributing, storing and dispensing of these medications. Please refer to Schedule 1091, *Benzodiazepines and Other Targeted Substances Regulations*, to see a detailed description of modifications that will be required. This information can be obtained from the Therapeutic Products Website at <http://www.hc-sc.gc.ca/hpb-dgps/therapeut/>.

Any comments regarding this proposed amendment should be addressed to Alixandria Clymans, Policy Division, Bureau of Policy and Coordination, Therapeutic Products Programme, 1600 Scott Street, Holland Cross, Tower 'B', 2<sup>nd</sup> Floor, Address

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Locator: 3102C5, Ottawa, Ontario, K1A 1B6, or by e-mail to [alixanderia\\_clymans@hc-sc.gc.ca](mailto:alixanderia_clymans@hc-sc.gc.ca) within **thirty** days.

Yours sincerely,

*Original Signed by:*

Robert G. Peterson, M.D. PhD. MPH  
A/Director General