

**Expert Committee on Drug Dependence
Thirty-seventh Meeting
Geneva, 16-20 November 2015**



1. Comments based on the review report

a. Evidence on dependence and abuse potential

The Pre review material indicates that data on dependence potential (in humans) have not been described, but presumably fall – due to its high potency and duration of action - in the higher range of the conventional benzodiazepines. Data on dependence potential in animals is more clearly specified with data on tolerance and withdrawal syndrome indicating that valproate and alpha-methyl dopa abolish manifestations of the withdrawal syndrome and restore the disturbed equilibrium after long term administration an cessation of phenazepam in different degrees.

The potency of this substance is compared to that of diazepam and is indicated that as compared to it, in a double-blind clinical study, phenazepam (0.0025 mg/kg) showed a more pronounced and longer lasting sedation than diazepam (0.005 mg/kg), the evidence also indicates a 5- to 10-fold higher potency than diazepam, probably due to the bromine atom in the molecule.

In other parts of the document is indicated that:

- In the last decade, phenazepam gained increasing popularity as a recreational drug (page 19), the euphoric effect of phenazepam have led to its recreational effect. Accordingly, this substance may be used to enhance euphoric effects of opioids, to temper cocaine highs, and to augment the effects of alcohol.
- Similarly, an increase of unauthorized use of phenazepam has been observed over the past few years in the USA, New Zealand, and some European countries, particularly in Scandinavian countries including Finland, Norway, and Sweden.
- Phenazepam can be obtained via direct purchase from Internet. Illicit products of phenazepam have been sold in the USA as a powder, as tablets, and spiked in blotters similar to LSD. Phenazepam can be taken orally (most common), snorted, inhaled, administered transdermal or rectally, or injected (after crushing the tablet).
- As compared to other benzodiazepines agonists the discriminative stimuli of Phenazepam seems to be similar. In this sense, the discriminative

stimulus properties of phenazepam and lorazepam has been investigated and found similar by Kinina et al (Eksp Klin Farmakol 2008 Jan-Feb;71(1):3-7).

- Withdrawal symptoms have been described for phenazepam in humans.

The document report that no tolerance has been reported in humans, nevertheless the usual therapeutic oral dosage of phenazepam is reported as 0.5 mg two to three times per day, but doses up to 10 mg/day have been reported.

Limited information is reported for abuse potential in animals.

b. Risks to individual and society because of misuse

The Pre-Review Report indicates important information related to risks to individual and society because of misuse in different states in United States of America (Wisconsin, Georgia) and different countries around the world as Finland, Norway, UK, Turkey, Scotland and Russia This information include high levels of phenazepam in forensic samples associated to driving under influence, impaired drivers under the influence of phenazepam and multiple drugs, fatalities involving phenazepam alone or phenazepam combined with other drugs and poisoning in children.

Like other benzodiazepines, common signs of toxicity of phenazepam are CNS depression, impaired balance, amnesia, dizziness, loss of coordination, slurred speech, confusion, drowsiness, blurred vision, ataxia, muscle hypotonia, tachycardia (or bradycardia) and both auditory and visual hallucinations. However, unlike those caused by other benzodiazepines, the toxic effects of phenazepam may last for up to 5 days after ingestion, or up to 3 weeks after ingestion, and may fluctuate.

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

There is no information reported in the document for smuggling. The Pre-Review document states that according to a internet based questionnaire 9 respondent out of 1500 had misused phenazepam. Purchases via the internet are also reported. Seizures are also indicated in different parts of the world, Scotland, Germany, Turkey, New Zealand, South Korea, England and Wales.

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

According to the Pre – Review document Phenazepam is a long-acting benzodiazepine developed in the former Soviet Union during the 1970s. It has been in clinical use since 1978, primarily in Russia. As other benzodiazepines, phenazepam is reported to be used to treat epilepsy, insomnia, alcohol withdrawal syndrome, short-term treatment of anxiety disorders (panic attacks), as premedication prior to surgery and as an anticonvulsant. Not data available for veterinary use

e. Need of the substance for other purposes (e.g. industrial)

No data presented in the document.

f. Measures taken by countries to curb misuse

According to the Pre-Review document, neither USA nor EU have approved or controlled phenazepam but individual countries have taken different measures to curb misuse:

Individual member states have taken national measures to control it. Phenazepam is controlled in Estonia, Latvia, Lithuania, Moldova, Norway, Sweden, and the Republic of Ireland. Phenazepam is covered by prescription legislation (only available on a doctor's prescription) in Estonia, Latvia, Lithuania, the Russian Federation and Belarus.

UK: Phenazepam is not listed in the British National Formulary and has not received marketing authority in the UK (that is it is not a medicine licensed by the Medicines and Healthcare Products Regulatory Agency). Following the UK Advisory Council on the Misuse of Drugs (ACMD) advice, the Home Office imposed a ban (dated 22 July 2011) under the Open General Import License on the importation of phenazepam. Following the recommendation of the (ACMD), phenazepam is controlled in the UK, like other benzodiazepines (such as diazepam), as a Class C drug since June 2012.

Germany: In July 2013, phenazepam was controlled via List III of the 'Betäubungsmittelgesetz' (BtMG, Narcotics Act).

Estonia: According to Narcotic Drugs and Psychotropic Substances Act, phenazepam is a Schedule IV substance. Schedule IV is the lowest classification of psychoactive substances in Estonia and includes prescription drugs, including other benzodiazepines. It appears to be concordant with Schedule IV in the UN Convention on Psychotropic Substances.

Latvia: According to Cabinet Regulation N 35, phenazepam is a Schedule III substance. Schedule III is the lowest classification of active psychoactive substances in Latvia and includes prescription drugs, including other benzodiazepines and barbiturates.

Lithuania: According to 'The Law on the Control of Narcotic and Psychotropic Substances' phenazepam is a Schedule III substance. Schedule III is the lowest classification of psychoactive substances in Lithuania and includes prescription drugs.

Republic of Ireland: Since August 2010, phenazepam falls under the Criminal Justice (Psychoactive Substances) Act of 2010 which makes it illegal to 'sell or supply for

human consumption substances which are not specifically prescribed under the Misuse of Drugs Acts, but which have psychoactive effects.

Sweden: In 2008, phenazepam was classified as a narcotic under the ‘The Ordinance on Prohibition of Certain Goods Dangerous to Health’.

Norway: Since March 2010, phenazepam is considered a 'narcotic', in common with most other benzodiazepines. It cannot be prescribed by physicians.

Finland: Phenazepam was classified as a narcotic in Finland in July, 2014.

Russian Federation: Phenazepam does not appear in this list of controlled substances, dated 2008 and is available by a physician's prescription. However, it has been reported that it is available at some pharmacies without a prescription.

Moldova: Since 2008, phenazepam is regulated by ‘The Resolution of the Government of the Republic of Moldova No 79’ which prohibits the possession of drugs which is considered a 'drug-related crime or a drug-related administrative offence'.

Australia: In Australia, the states of Victoria and South Australia have passed an Analog Act under which phenazepam is a controlled substance (analogue to existent benzodiazepines).

Canada: Phenazepam is not listed in the Controlled Drugs and Substances Act.

China: Phenazepam is not reported to be controlled in China.

India: Phenazepam is not listed among ‘narcotics, drugs, psychotropic substances & precursor chemicals’ that are controlled.

g. Impact if this substance is scheduled

Most benzodiazepines are under international control. If Phenazepam is scheduled it should not represent a problem. Countries should already have the laboratory capacity to identify the substance.

2. Are there absent data that would be determinative for scheduling?

There is no absent data that would be determinative for scheduling

3. Other comments or opinions

No additional comments

4. Expert reviewer's view on scheduling with rationale

Evidence presented is consistent with the characterization of phenazepam as a benzodiazepine. There is information on its liability to abuse and to induce significant harm effects in humans, including death. It does not meet the criteria for inclusion in any Schedule pertaining to the 1961 Convention, but it does meet criteria to be included in Schedule IV, 1971 Convention: “*Substances whose liability to abuse constitutes a smaller but still significant risk to public health and which have a therapeutic usefulness from little too great.*” On the view of this, I consider that current information justify that the Expert Committee should proceed to the critical review.