PACKAGE INSERT

SCHEDULING STATUS: S5

PROPRIETARY NAME (AND DOSAGE FORM):

Urbanol® 5 mg Capsules
Urbanol® 10 mg Tablets

COMPOSITION:

5 mg capsules and 10 mg tablets containing 7-chloro-1-methyl-5-phenyl-1H-1,5-benzodiazepine-2,4(3H-5H)-dione (clobazam)

PHARMACOLOGICAL CLASSIFICATION:

A. 2.6 Tranquillisers

PHARMACOLOGICAL ACTION:

Chemically **Urbanol** is a 1,5-benzodiazepine.

Animals:
After oral administration to dogs, maximum serum levels are reached within 2 – 4 hours. Drug elimination follows a biphasic pattern with a half-life of 3,3 ± 0,7 hours for the main (> 90 %) phase and about 24 hours for the other. (At the end of the study, the < 10 % in this phase was at the limits of detection).

Humans:
Peak serum concentrations were reached after a single administration of 10 – 40 mg between 1 and 5 hours irrespective of the dose given. The original substance was eliminated from the serum with an initial half-life of 5 hours, after the 8th hour the half-life was 41 hours.

INDICATIONS:

Urbanol is used in the treatment of anxiety in neurotic patients and for pre-operative medication. It may be effective in relieving the acute symptoms of the alcohol withdrawal syndrome, but has no specific usefulness in the treatment of psychotic patients.

Urbanol is only indicated when the disorder is severe, disabling or subjecting the individual to extreme stress.

CONTRA-INDICATIONS:

Urbanol is contra-indicated in myasthenia gravis, in infants and in patients with a known hypersensitivity to benzodiazepines.

DOSAGE AND DIRECTIONS FOR USE:

The normal adult dose ranges between 10 - 30 mg daily – doses of 20 mg and above should preferably be given at bedtime or in divided doses.

For elderly and debilitated patients as well as in children and light-weight patients, the daily dose should be halved.

Treatment should be started with the lowest recommended dose. The maximum dose should not be exceeded.

Treatment should be as short as possible. The patient should be reassessed regularly and the need for continued treatment should be evaluated, especially in case the patient is symptom free. The overall duration of treatment generally should not be more than 8 - 12 weeks, including a tapering off process.

In certain cases extension beyond the maximum treatment period may be necessary; if so, it should not take place without re-evaluation of the patient's status.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Urbanol is not recommended for the primary treatment of psychotic illness. **Urbanol** should not be used alone to treat depression or anxiety with depression (suicide may be precipitated in such patients). **Urbanol** should be used with extreme caution in patients with history of alcohol or drug abuse.

The side-effects most frequently encountered with **Urbanol** are drowsiness and over-sedation, dizziness, dry mouth and constipation. Drowsiness is more common in elderly and debilitated patients and in patients receiving high doses. Less common are depression of mood and affect, disorientation or confusion, lethargy, ataxia, tremor, increased motor activity, decreased motor activity and nausea/vomiting.

Paradoxical reactions such as acute hyperexcitable states with rage may occur – if these occur, **Urbanol** should be discontinued.

Blood dyscrasias and hepatic dysfunction have been reported.

Particular caution should be exercised with the elderly and debilitated – who are in particular risk of oversedation, respiratory depression and ataxia. (The initial oral dosage should be reduced in these patients).

Caution should also be observed in:

- patients suffering from impairment of renal or hepatic function.
- patients with pulmonary disease and limited pulmonary reserve.
- patients suffering from anxiety accompanied by underlying depressive disorders.
- patients receiving barbiturates, antihistamines, narcotics or other central nervous system depressants. There is an additive risk of central nervous system depression when these medicines are taken together. Large doses may produce syncope.
- patients should be cautioned regarding the additive effects of alcohol.
- **Urbanol** should be used judiciously during pregnancy and preferably avoided. Given during labour it crosses the placenta and may cause the floppy-infant syndrome characterised by central respiratory depression, hypotonia, hypothermia, poor sucking and an increase in foetal heart rate. It should not be administered to lactating mothers.
- patients should be advised particularly at the initiation of therapy, not to drive a motor-vehicle, climb dangerous heights, or operate dangerous machinery. In these situations, impaired decision making could lead to accidents.

Dependence:
There is a potential for abuse and the development of physical and psychic dependence, especially with prolonged use and high doses. The risk of dependence is also greater in patients with a history of alcohol or drug abuse. Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability.

In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.

Rebound effects:
A transient syndrome whereby the symptoms that led to treatment with **Urbanol** recur in an enhanced form may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety and restlessness. Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment it is recommended that the dosage is decreased gradually.

Duration of treatment:
The duration of treatment should be as short as possible (see dosage), but should not exceed eight to twelve weeks in case of anxiety, including the tapering-off process. Extension beyond these periods should not take place without re-evaluation of the situation. It may be useful to inform the patient when treatment is started that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. Moreover it is important that the patient should be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms, should they occur while the product is being discontinued.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

There is no known antidote. The most prominent symptom of overdosage is sedation and manifestations also include somnolence, confusion, coma, respiratory and cardiovascular depression and hypotension. The stomach should be emptied by gastric lavage. Treatment is symptomatic.

IDENTIFICATION:

Urbanol 5 mg – opaque blue and white capsules.
Urbanol 10 mg – white, bi-planar round tablet scored and engraved with "CBZ" on one side and plain on the other side.
10

PRESENTATION:

Urbanol is available as 5 mg capsules in blister packs of 100 and as 10 mg tablets in blister packs of 100.

STORAGE INSTRUCTIONS:

Store in a cool, dry place, below 25 °C.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

Urbanol 5 mg: L/2.6/52
Urbanol 10 mg: M/2.6/128

NAME AND BUSINESS ADDRESS OF THE APPLICANT:

sanofi-aventis south africa (pty) ltd
2 Bond Street
Midrand
1685, South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

26 November 1984