1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S5

PROPRIETARY NAME AND DOSAGE FORM

BRAZEPAM-3 TABLETS (tablet)

BRAZEPAM-6 TABLETS (tablet)

COMPOSITION

Each tablet of BRAZEPAM-3 TABLETS contains 3 mg bromazepam

Excipients:

Colloidal silicon dioxide, croscarmellose sodium, erythrosine aluminium lake dye (red) (C.I. 45430), magnesium stearate, microcrystalline cellulose, tablettose

Contains sugar: Lactose 160,0 mg

Each tablet of BRAZEPAM-6 TABLETS contains 6 mg bromazepam

Excipients:

Colloidal silicon dioxide, colour lake green PB 21082 (C.I. 47005; 42090; 15985), colour yellow dye lennon lake yellow No.: 520 (C.I. 47005), croscarmellose sodium, magnesium

stearate, microcrystalline cellulose, tablettose

Contains sugar: Lactose 160,0 mg

CATEGORY AND CLASS

A 2.6 Tranquillisers

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Bromazepam is a benzodiazepine which has anxiolytic, sedative, muscle relaxant and anticonvulsant properties. In low doses it diminishes anxiety and tension. In higher doses the sedative and muscle-relaxant properties appear.

INDICATIONS

BRAZEPAM is used in the treatment of patients suffering from anxiety disturbances.

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

CONTRAINDICATIONS

BRAZEPAM is contraindicated in children and in patients with a known hypersensitivity to bromazepam and should not be given to patients with acute closed-angle glaucoma and myasthenia gravis.

BRAZEPAM should not be used for the treatment of chronic psychosis or for phobic or obsessional states.

Caution should be observed when giving BRAZEPAM to patients with impaired hepatic or renal function.

In elderly and debilitated patients, and patients with impaired obstructive airways disease large doses may produce syncope.

Use of BRAZEPAM in the first trimester of pregnancy has been associated with various congenital malformations in the infant and in the last trimester it has been associated with drowsiness, respiratory depression and intoxication in the new born infant. For these reasons BRAZEPAM is contraindicated in pregnancy.

BRAZEPAM is excreted in breast milk and is contraindicated by nursing mothers because of the side effects it can cause in the breastfed infant such as drowsiness, slow heartbeat and breathing problems.

WARNINGS AND SPECIAL PRECAUTIONS

Dependence

There is a potential for abuse and the development of physical and psychic dependence, especially with prolonged use and high doses. Prolonged use may lead to the development of dependence of the barbiturate-alcohol type. The risk of dependence is also greater in patients with a history of alcohol or drug abuse. Alcoholic drinks should be avoided, due to

the additive effect of BRAZEPAM with alcohol. Withdrawal of BRAZEPAM from patients who have been receiving it for prolonged periods of time should be gradual. 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 BRAZEPAM 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 AND DIRECTIONS FOR USE), but should not exceed eight to twelve weeks in case of anxiety, including tapering off process. Extension beyond this period 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 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.

BRAZEPAM should not be used in patients with pre-existing central nervous system depression or coma, acute pulmonary insufficiency, or sleep apnoea, and used with care in those with chronic pulmonary insufficiency.

Particular caution should be exercised in:

- the elderly and debilitated - who are at a particular risk of oversedation, respiratory depression and ataxia. (The initial oral dosage should be reduced in these patients);
- patients with pulmonary disease and limited pulmonary reserve;
- patients suffering from impairment of renal or hepatic function;
- patients suffering from anxiety accompanied by an underlying depressive disorder;
- patients receiving barbiturates or other central nervous system depressants since there is an additive risk of central nervous system depression when these medicines are taken together;
- patients with myasthenia gravis on account of pre-existing muscle weakness;
- patients with organic brain changes particularly arteriosclerosis.

BRAZEPAM is not recommended for the primary treatment of psychotic illness. BRAZEPAM should not be used alone to treat depression or anxiety with depression (suicide may be precipitated in such patients).

Effects on ability to drive and use machines

BRAZEPAM may cause drowsiness. If affected, patients should not drive or operate machinery.

Excipients

Lactose warning:

BRAZEPAM contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take BRAZEPAM.

INTERACTIONS

Grapefruit juice has been found to increase the bio-availability of certain medicines (those metabolised by the cytochrome P450 3A4 enzyme), by inhibiting their metabolism in the liver and gut. Because BRAZEPAM might potentially be affected, patients taking this are advised not to drink grapefruit juice, as potentially serious adverse effects may occur.

The effects of BRAZEPAM may be enhanced by alcohol, barbiturates, narcotics, mono-amine oxidase (MAO) inhibitors and other depressants of the central nervous system.

The response to treatment with oral anticoagulants may be variable in patients taking BRAZEPAM. Cimetidine may inhibit the metabolism of BRAZEPAM.

HUMAN REPRODUCTION

Use of BRAZEPAM in the first trimester of pregnancy has been associated with various congenital malformations in the infant and in the last trimester it has been associated with drowsiness, respiratory depression and intoxication in the new born infant. For these reasons BRAZEPAM is contraindicated in pregnancy.

BRAZEPAM is excreted in breast milk and is contraindicated by nursing mothers because of the side effects it can cause in the breastfed infant such as drowsiness, slow heartbeat and breathing problems.

Given during labour it crosses the placenta and may cause the floppy-infant syndrome characterised by central respiratory depression, hypothermia and poor sucking.

DOSAGE AND DIRECTIONS FOR USE

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

The usual dose is 3 mg twice or three times daily. In severe conditions up to 6 mg to 12 mg twice or three times daily.

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 to

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

The side effects most commonly encountered are drowsiness and oversedation. Drowsiness is more common in elderly and debilitated patients and in patients receiving high doses.

Less common are depression of mood, disorientation or confusion, lethargy and ataxia.

Paradoxical reactions such as acute hyperexcitable states with hostility and rage, may occur. If these occur, the medicine should be discontinued.

Other side effects observed include hypotension, respiratory depression, gastro-intestinal disturbances such as nausea and constipation, changes in salivation, visual disturbances such as blurred vision and diplopia, dysarthria, skin rashes, urinary retention, incontinence, tremor, headache, slurred speech, vertigo, confusion and changes in libido.

There have been reports of blood disorders and jaundice.

During long-term treatment regular blood counts and liver function tests should be performed.

The product can induce amnesia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

Manifestations of overdosage include somnolence, confusion, coma, respiratory depression and hypotension.

Treatment

In acute severe overdosage the stomach should be emptied with aspiration and lavage.

Treatment is symptomatic and supportive.

IDENTIFICATION

BRAZEPAM-3 TABLETS: A flat, round, pink tablet with bevelled edges, bisected on one side and embossed C13 on the other side.

BRAZEPAM-6 TABLETS: A flat, round, green tablet with bevelled edges, bisected on one side and embossed C17 on the other side.

PRESENTATION

BRAZEPAM-3 TABLETS and BRAZEPAM-6 TABLETS:

30 tablets are packed in a polyvinylchloride blister strip sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

100 tablets are packed into a white polypropylene securitainer with a white round flat topped low density polyethylene closure with a tamper evident seal, together with a white rayon

insert or a white foam insert and a leaflet.

BRAZEPAM-6 TABLETS:

30 or 120 tablets are packed into polyethylene grip bags and metallised lay flat bags sealed with a lay-flat zip (for tender purposes).

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C.

Protect from light and moisture.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

BRAZEPAM-3 TABLETS: W/2.6/407

BRAZEPAM-6 TABLETS: W/2.6/408

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead

2191

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Date of registration: 26 November 1990

Date of the most recent amendment to the professional information as approved by the Authority: 21 May 1997

Namibia:	NS3
BRAZEPAM-3 TABLETS:	04/2.6/0083
BRAZEPAM-6 TABLETS:	04/2.6/0054

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