1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S5

PROPRIETARY NAME AND DOSAGE FORM

TRANQIPAM - 0,5 (tablet)

TRANQIPAM - 1 (tablet)

TRANQIPAM - 2,5 (tablet)

COMPOSITION

Each tablet of TRANQIPAM - 0,5 contains 0,5 mg of lorazepam

Excipients:

Lactose, magnesium stearate, microcrystalline cellulose, polacrilin potassium.

Contains sugar: Lactose 33,875 mg

Each tablet of TRANQIPAM - 1 contains 1 mg of lorazepam

Excipients:

Lactose, magnesium stearate, microcrystalline cellulose, polacrilin potassium.

Contains sugar: Lactose 67,50 mg

Each tablet of TRANQIPAM - 2,5 contains 2,5 mg of lorazepam

Excipients:

Lactose, magnesium stearate, microcrystalline cellulose, polacrilin potassium

Contains sugar: Lactose 134,475 mg

CATEGORY AND CLASS

A 2.6 Tranquillizers

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Lorazepam is a benzodiazepine and has anxiolytic properties. Benzodiazepines presumably exert their effects by binding to specific receptors at several sites within the central nervous system, by potentiating the effects of synaptic or presynaptic inhibition mediated by gamma-aminobutyric acid.

Pharmacokinetic properties

Lorazepam is rapidly absorbed when given orally.

Peak plasma concentrations occur approximately 2 hours following administration. The half-life of unconjugated lorazepam in human plasma is approximately 12 to 16 hours. Lorazepam is about 90 % bound to plasma proteins. Conjugation with glucuronic acid to form the inactive glucuronide of lorazepam is the major metabolic pathway. Seventy to seventy five percent of the dose is excreted as the glucuronide in the urine. Metabolism is only subject to glucoronidation and is not linked to the action of the cytochrome P450 enzyme system. The plasma levels of lorazepam are proportional to the dose given.

INDICATIONS

TRANQIPAM is indicated for:

1. Anxiety disturbances or anxiety states:
   (a) general anxiety disturbances
   (b) panic disturbances
   (c) phobic anxiety disturbances
2. Anxiety associated with and caused by organic disease.
3. Adjustment disturbances with anxiety or stress reactions.

CONTRAINDICATIONS

Known hypersensitivity to benzodiazepines, and in patients with pre-existing CNS depression or coma.

The administration of TRANQIPAM is contraindicated in patients with porphyria.

WARNINGS AND SPECIAL PRECAUTIONS

Patients should be advised that their tolerance for alcohol and other central nervous system depressants will be diminished.

TRANQIPAM treatment should be avoided in general in psychotic patients and in those suffering from mental depression or suicidal tendencies unless there is a marked component of anxiety in their illness.

Care may be needed in epileptic patients, in whom the initiation or abrupt withdrawal of benzodiazepine therapy has provoked seizures.

Particular caution should be exercised with the elderly and debilitated who are at particular risk of over-sedation, respiratory depression, unsteadiness and ataxia. The initial dosage should be reduced in those patients.

Caution should be exercised in patients with pulmonary disease and limited pulmonary reserve, as well as in patients with acute narrow-angle glaucoma.

Caution is required in patients with impaired liver, kidney or respiratory function and in patients receiving other central nervous system depressant medicines in whom CNS depression may be potentiated. The pharmacokinetics of TRANQIPAM may change in impaired renal function.

There is potential for abuse and addiction-prone individuals, such as drug addicts and alcoholics, should be under careful surveillance when receiving TRANQIPAM.

The use of TRANQIPAM may lead to dependence. Withdrawal symptoms similar in character to those noted with barbiturates and alcohol have occurred following abrupt discontinuance of TRANQIPAM. These symptoms can range from mild dysphoria and insomnia to a major syndrome which may include convulsions, tremor, abdominal and muscle cramps, vomiting and sweating. These symptoms, especially the more serious ones, are more common in those patients who have received excessive doses over an extended period of time. However, withdrawal symptoms have also been reported following abrupt discontinuance of TRANQIPAM taken continuously at therapeutic levels. Accordingly, TRANQIPAM should be terminated gradually to help avoid occurrence of withdrawal symptoms.

Effects on ability to drive and use machines

Patients receiving TRANQIPAM should be warned not to operate dangerous machinery or motor vehicles, or climb dangerous heights until it is established that they do not become drowsy or dizzy or experience psychomotor impairment from TRANQIPAM therapy.

Excipients

TRANQIPAM 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 TRANQIPAM.

INTERACTIONS

TRANQIPAM produces additive central nervous system depressant effects when co-administered with other central nervous system depressants e.g. barbiturates or alcohol.

HUMAN REPRODUCTION

TRANQIPAM should be used judiciously during pregnancy and preferably avoided.
In humans, blood levels obtained from umbilical cord indicate placental transfer of TRANQIPAM and its glucuronide. Neonates appear to conjugate TRANQIPAM slowly, the glucuronide being detectable in the urine for more than seven days. Glucuronidation of TRANQIPAM may competitively inhibit the conjugation of bilirubin, leading to hyperbilirubinaemia in the newborn.

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

It should not be administered to nursing mothers since there is evidence that TRANQIPAM is excreted in human breast milk.

DOSAGE AND DIRECTIONS FOR USE

Anxiety or tension associated with everyday life does not require treatment with an

anxiolytic.

It is recommended that the need for continued therapy with TRANQIPAM be determined periodically.

Dosage for children under 12 years has not been established.
Dosage should be individualised for optimal beneficial effect.

The average dosage for the treatment of anxiety is 2 mg to 3 mg daily administered in two to four portions: however, this may range between 1 mg and 6 mg daily.

For elderly or debilitated patients, an initial dosage of 1 mg or 2 mg per day in two to four portions is recommended to be adjusted as needed and tolerated.

SIDE EFFECTS

The most frequent adverse reactions reported are drowsiness and over-sedation followed by dizziness, weakness, unsteadiness, confusion and lethargy.

Vertigo, light-headedness, mental depression, slurred speech or dysarthria, changes in libido, ataxia, tremor, urinary retention or incontinence, changes in salivation and jaundice may also occur.

Respiratory depression and hypotension may occur with high doses.

Other adverse reactions reported include nausea, change in appetite, headache sleep disturbance, agitation, dermatological symptoms and eye-function disturbance.

Transient amnesia or memory impairment has been reported. Some patients on

benzodiazepines have developed blood dyscrasias and some have had elevations in liver enzymes.

Periodic blood counts and liver-function tests are recommended for patients on long-term therapy.

Paradoxical reactions such as acute hyperexcitable states with rage may occur.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

Overdosage of TRANQIPAM is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma, respiratory and cardiovascular depression. In mild cases, symptoms include drowsiness, mental confusion and lethargy. In more serious cases, symptoms may include ataxia, hypotension, hypnosis, coma and death.

Treatment

Treatment is symptomatic and supportive.

IDENTIFICATION

TRANQIPAM - 0,5: A white, round tablet.

TRANQIPAM - 1: A flat, white to off-white, round tablet with bevelled edges bisected on one side and imprinted C11 on the other side.

TRANQIPAM - 2,5: A flat, white to off-white, round tablet with bevelled edges, bisected on one side and imprinted C18 on the other side.

PRESENTATION

TRANQIPAM - 0,5: 100, 250, 500 and 1 000 tablets are packed into a round, amber Type III

glass bottle with a plastic screw-on cap together with a white cotton wool insert or a silica gel sachet and a leaflet.

10 tablets are packed in aluminium foil blister strips. There are 10 tablets per blister strip and six or ten blister strips are packed into an outer cardboard carton together with a leaflet.

TRANQIPAM – 1 : 100 tablets are packed into a round, amber Type III glass bottle with a white polypropylene snap cap together with a white rayon insert or a silica gel sachet and a leaflet.

TRANQIPAM – 2,5: 100 tablets are packed into a round, amber Type III glass bottle with a white polypropylene screw-on cap with expanded polyethylene liner together with a round white foam insert and white desiccant disk or a silica gel sachet and a leaflet.

100 tablets are packed into a round, amber Type III glass bottle with a white urea screw-cap with expanded polyethylene liner together with a round white foam insert and white desiccant disk or a silica gel sachet and a leaflet.

TRANQIPAM - 1 and 2,5: 100 tablets are packed into a round, amber Type III glass bottle with a white polypropylene child resistant wadded cap together with a silica gel sachet and a leaflet.

Not all strengths, packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C, in a cool dry place.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS

TRANQIPAM - 0,5: X/2.6/83

TRANQIPAM - 1: U/2.6/38

TRANQIPAM - 2,5: U/2.6/39

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:

TRANQIPAM - 0,5: 09 January 1990

TRANQIPAM - 1: 22 February 1989

TRANQIPAM - 2,5: 22 February 1989

Date of the most recent amendment to the professional information as approved by the Authority: 05 February 1990

Botswana:	S1C
0,5 mg	B9322955
1 mg:	B9322950
2,5 mg:	B9322945

Namibia:	NS3
1 mg:	90/2.6/001239
2,5 mg:	90/2.6/001240

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