Final proposed clean copy of the professional information

SCHEDULING STATUS:

S5

PROPRIETARY NAME AND DOSAGE FORM:

DORMONOCT 2 mg TABLETS

COMPOSITION:

Each tablet contains: 2 mg loprazolam as loprazolam mesylate.

Other ingredients: colloidal anhydrous silica, lactose monohydrate, magnesium stearate, maize starch, microcrystalline cellulose and povidone.

Contains sugar (lactose monohydrate): 83,9 mg per tablet

CATEGORY AND CLASS:

A 2.2 Sedatives, hypnotics

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Loprazolam is a short-acting benzodiazepine with hypnotic properties. Loprazolam has little effect on paradoxical sleep patterns (REM).

Pharmacokinetic properties:

Absorption:

The absolute bioavailability following a single oral dose of 1 mg is 80 %. The maximum concentration (Cmax) is 5,5 – 6,0 µg/ml per one hour (Tmax) following a single oral dose of 1 mg loprazolam.

Distribution:

Plasma protein binding is 80 %.

Metabolism:

Loprazolam is metabolised in the liver. The principal metabolite is the piperazine N-oxide of loprazolam.

Elimination:

The half-life is 6 – 8 hours.

In the elderly, the plasma half-life is increased (approximately 1,5 fold). Loprazolam is excreted 40 % by the urinary route and 55 % in the faeces, while 3 - 25 % of the ingested dose is recovered in the bile.

INDICATIONS:

1) Short-term treatment of insomnia.
2) Sleep disturbances in the geriatric patient.
3) Pre-operative sleep disturbances.

DORMONOCT is only indicated when the disorder is severe, disabling or when the individual is subject to extreme stress.

CONTRAINDICATIONS:

- Hypersensitivity to loprazolam or to any of the other ingredients in DORMONOCT
- Severe respiratory insufficiency
- Myasthenia gravis
- Sleep apnoea syndrome
- Severe hepatic insufficiency
- Safety and efficacy in children have not been established.

WARNINGS AND SPECIAL PRECAUTIONS:

Caution should be exercised in the following patients:

In patients with pulmonary disease and limited pulmonary reserve.

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

Care should be taken to avoid aggravation of respiratory insufficiency and the dosage should be reduced (see DOSAGE AND DIRECTIONS FOR USE).

Caution should be exercised in the following patients:

- 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. There is an additive risk of central nervous system depression when these medicines are taken together
- patients should be cautioned regarding the additive effect of alcohol.

DORMONOCT is not recommended for the primary treatment of psychotic illness.

DORMONOCT should not be used alone to treat depression, or anxiety with depression, as suicide may be precipitated in such patients. DORMONOCT should be used with extreme caution in patients with a history of alcohol or drug abuse.

Dependence:

There is a potential for abuse and the development of physical and psychological 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: de-realisation, depersonalisation, hyperacusis, numbness and tingling of extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.

Rebound effects:

A transient syndrome, which may occur in withdrawal of treatment, whereby the symptoms that led to treatment with DORMONOCT recur in an enhanced form. It may be accompanied by other reactions including mood changes, anxiety and restlessness. Since the risk of withdrawal or rebound phenomena, is greater after abrupt discontinuation of treatment, it is recommended that the dosage be 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 four weeks for insomnia, including the tapering-off process. Extension beyond these periods should not take place without re-evaluation of the patient. 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 is aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms should they occur while the product is being discontinued.

There are indications that, in the case of benzodiazepines with a short duration of action like DORMONOCT, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high.

Tolerance:

Some loss of efficacy to the hypnotic effects of benzodiazepines, such as DORMONOCT, may develop after repeated use for a few weeks.

Amnesia:

Benzodiazepines, such as DORMONOCT, may induce anterograde amnesia. The condition occurs most often several hours after ingesting the medicine and therefore, to reduce the risk, patients should ensure that they will be able to have an uninterrupted sleep of 7 – 8 hours (see SIDE EFFECTS).

Psychiatric and "paradoxical" reactions:

Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should this occur, use of DORMONOCT should be discontinued. They are more likely to occur in children and the elderly.

Lactose Intolerance:

Since DORMONOCT tablets contain lactose, patients with rare hereditary problems of galactose intolerance e.g. galactosaemia, Lapp-lactase deficiency or glucose-galactose malabsorption, should not take DORMONOCT.

Effects on ability to drive and use machines:

Patients should be advised, particularly at the initiation of therapy, not to drive a motor vehicle or perform potentially hazardous tasks where impaired decision making could lead to accidents.

INTERACTIONS:

Concomitant use not recommended:

Concomitant intake with alcohol: the sedative effect may be enhanced when DORMONOCT is used in combination with alcohol. This affects the ability to drive or use machines (see WARNINGS AND SPECIAL PRECAUTIONS).

Combinations to be taken into account:

Combination with central nervous system depressants: enhancement of the central depressive effect of DORMONOCT may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant medicines, narcotic analgesics, anti-epileptic medicines, anaesthetics and sedative antihistamines (see WARNINGS AND SPECIAL PRECAUTIONS).

In the case of narcotic analgesics, enhancement of the euphoria may also occur, leading to an increase in psychic dependence.

Additive synergy has been observed with neuromuscular depressants (curare-like medicines and muscle relaxants).

The risk of a withdrawal syndrome occurring is increased when DORMONOCT is combined with other benzodiazepines prescribed as anxiolytics or hypnotics.

HUMAN REPRODUCTION:

Safety in pregnancy has not been established.

Pregnancy: During labour it crosses the placenta and may cause the “floppy-infant” syndrome characterised by central respiratory depression, hypothermia and poor sucking.

Lactation: It should not be administered to mothers breastfeeding their babies. Infants born to mothers who took benzodiazepines chronically during the later stages of pregnancy may develop physical dependence and may be at risk for developing withdrawal symptoms in the postnatal period.

DOSAGE AND DIRECTIONS FOR USE:

Dosage:

The usual adult dose is 1 – 2 mg at bedtime, the higher dose being recommended for patients who have previously been treated with benzodiazepines for severe persistent insomnia. An initial dose of 0,5 mg – 1,0 mg is recommended in elderly and debilitated patients. The 2 mg tablet may not be suitable for use as initiation, in elderly patients and patients with renal, hepatic or moderate respiratory insufficiency.

Duration of treatment:

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

Treatment should be as short as possible. Generally, the duration of treatment varies from a few days to two weeks, with a maximum of four weeks including the 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.

Discontinuation of treatment:

It is strongly recommended that after prolonged treatment DORMONOCT is not withdrawn suddenly but rather that the dose is reduced gradually under medical supervision; otherwise withdrawal symptoms may occur (see WARNINGS AND SPECIAL PRECAUTIONS).

Administration:

DORMONOCT should be taken half an hour before bedtime.

Tablets are to be swallowed without chewing, with sufficient amount of liquids.

SIDE EFFECTS:

The following CIOMS frequency rating is used, when applicable: Very common: (≥ 1/10); common: (≥ 1/100, < 1/10 ; uncommon: (≥ 1/1000, < 1/100); rare: (≥ 1/10 000, < 1/1000); very rare: (< 1/10000), including isolated reports.

Nervous system disorders:

Very common: drowsiness, over-sedation. Drowsiness is most common in elderly and debilitated patients, and those receiving high doses.

Uncommon: depression of mood and affect, disorientation or confusion, lethargy, ataxia

Frequency unknown: anterograde amnesia may occur using therapeutic dosages, with the risk increasing at higher dosages.

Psychiatric disorders:

Uncommon: changes in libido

Frequency unknown: paradoxical reactions such as acute hyper-excitability with rage. If these occur, DORMONOCT should be discontinued.

Pre-existing depression may be unmasked by benzodiazepine use.

There is a potential for abuse. Withdrawal symptoms (including convulsions) have occurred following abrupt cessation, especially in patients who have received large doses for prolonged periods.

Gastrointestinal disorders:

Uncommon: constipation, nausea, diarrhoea

Immune system disorders:

Frequency unknown: hypersensitivity reactions such as rash and pruritus

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

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

Intravenous fluids should be administered and an adequate airway maintained. Treatment is supportive and symptomatic and gastric lavage may be of use if performed within 12 hours of ingestion.

IDENTIFICATION:

Light yellow, biconvex round tablets. "B" and "026" are engraved and separated by a score line on one side. The other side is neutral.

PRESENTATION:

2 mg tablets packed in blister packs of 30's and 100's.

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light, heat and humidity. Keep tablets in blister pack until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

Q/2.2/355

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

sanofi-aventis south africa (pty) ltd

2 Bond Street

Midrand

1685

South Africa

Final proposed clean copy of the professional information

DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION:

Date registered: 15.01.1984

Date revised: To be allocated