SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Librium 5mg Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5mg capsule contains 5mg of the active ingredient chlordiazepoxide hydrochloride BP

Excipients with known effect: lactose
Each capsule contains 105.9 mg lactose.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Librium Capsules 5mg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term (2-4 weeks) symptomatic treatment of anxiety that is severe, disabling or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness.

Muscle spasm of varied aetiology.

Symptomatic relief of acute alcohol withdrawal.

4.2 Posology and method of administration

Posology:

Anxiety states--
Usual dose 10 mg, 2 – 3 times a day and up to 30 mg daily in divided doses. For severe symptoms 20 mg, 2 – 4 times a day. Maximun dose up to 100 mg daily in divided doses. Adjusted on an individual basis.
Generally, duration of treatment should not be more than 4 weeks, including a tapering-off process.

Insomnia associated with anxiety--
10 to 30 mg before retiring. Generally, duration of treatment varies from a few days to two weeks, with a maximum including a tapering-off process of four weeks.

Symptomatic relief of acute alcohol withdrawal--
25 to 100 mg and repeated if necessary in 2 to 4 hours.

Muscle spasm of varied aetiology--
10 to 30 mg daily in divided doses.

Paediatric patients
Librium is not for paediatric use.

Special patient groups
Elderly or debilitated patients, patients with organic brain damage, respiratory impairment and/or hepatic or renal dysfunction should normally not exceed half of the doses normally recommended.

The lowest dose which can control symptoms should be used. The dosage and duration of treatment should be determined on an individual basis dependent by the patient's response and severity of the disorder. Given that chlordiazepoxide is a long-acting benzodiazepine, the patient should be monitored regularly at the start of the treatment to decrease, if necessary, the dose or frequency of administration to prevent overdose due to accumulation.

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. Treatment should not be continued at the full dose beyond four weeks.

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 with special expertise. Little is known regarding the efficacy or safety of benzodiazepines in long-term use. Long-term chronic use is not recommended.

Treatment should always be tapered off gradually. Patients who have taken benzodiazepines for a prolonged time may require a longer period during which doses are reduced. Specialist help may be appropriate.

Method of administration:
Librium capsules are for oral administration and must be taken with water and not be chewed.

4.3 Contraindications

Librium is contraindicated for patients with:

-hypersensitivity to the active substance chlordiazepoxide or to any of the excipients listed in section 6.1

- myasthenia gravis
- severe pulmonary insufficiency
- respiratory depression
- severe hepatic insufficiency
- sleep apnoea syndrome
- phobic or obsessional states
- chronic psychosis
- spinal or cerebral ataxia

4.4 Special warnings and precautions for use

Tolerance: Some loss of efficacy to the hypnotic effects of benzodiazepines may develop after repeated use for a few weeks.

Dependence and withdrawal: The dependent potential of the benzodiazepines is low, particularly when limited to short-term use. Risk for physical and psychological dependence increases when high doses are used, especially when given over long periods. This is particularly so in patients with a history of alcoholism or drug abuse or in patients with marked personality disorders. Regular monitoring in such patients is essential. Routine repeat prescriptions should be avoided and treatment should be withdrawn gradually.

Symptoms such as headaches, muscle pain, extreme anxiety, restlessness, confusion, depression, nervousness, rebound insomnia, irritability, sweating and diarrhoea have been reported following abrupt cessation of treatment in patients receiving even normal therapeutic doses for short periods of time. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations, psychotic manifestations or epileptic seizures.

Abuse of benzodiazepines has been reported.

Rebound insomnia and anxiety: This is a transient syndrome whereby the symptoms that led to treatment with a benzodiazepine recur in an enhanced form, may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances 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 Posology) depending on the indication, but should not exceed 4 weeks, including tapering-off process. Routine repeat prescriptions should be avoided.

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 medicinal product is being discontinued.

When benzodiazepines with a long duration of action are being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

Amnesia: Amnesia may occur. Benzodiazepines may induce anterograde amnesia. The condition occurs most often several hours after ingesting the product and therefore to reduce the risk, patients should ensure that they will be able to have an uninterrupted sleep of 7 to 8 hours (see Undesirable effects).

Psychiatric and paradoxical reactions: Rare behavioural effects including restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should these effects occur, use of the medicinal product should be discontinued. They are more likely to occur in children and the elderly.

Risk from concomitant use of opioids:

Concomitant use of Librium and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines such as benzodiazepines with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Librium concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible (see also general dose recommendation in section 4.2).

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers (where applicable) to be aware of these symptoms (see section 4.5).

Specific patient groups:
Elderly patients should be given a reduced dose (see section 4.2) A lower dose is also recommended for patients with chronic respiratory insufficiency due to the risk of respiratory depression. Benzodiazepines are contraindicated to treat patients with severe hepatic insufficiency as they may precipitate encephalopathy and reduced doses should be given to patients with renal or hepatic disease.

Benzodiazepines are not recommended for the primary treatment of psychotic illness, phobia or obsessive-compulsive diseases.

Librium should not be used alone to treat depression or anxiety associated with depression, since it may uncover depression with suicidal tendencies. Extreme caution should be used in prescribing benzodiazepines to patients with personality disorders. Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse.

In cases of loss or bereavement, psychological adjustment may be inhibited by benzodiazepines.

Due to the myorelaxant effect there is a risk of falls and consequently fractures in the elderly.

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

If Librium is combined with centrally-acting drugs such as neuroleptics, tranquilisers, antidepressants, hypnotics, analgesics, anaesthetics, and sedative antihistamines the central depressive effects are likely to be intensified. In the case of narcotic analgesics, enhancement of the euphoria may also occur leading to an increase in psychic dependence. The elderly require special supervision.

Librium in combination with 4-hydroxybutanoic acid (sodium oxybate) may cause an increased respiratory depression.

Concomitant intake with alcohol should be avoided. The sedative effect may be enhanced when the product is used in combination with alcohol. This adversely affects the ability to drive or use machines.

Concurrent treatment with tranquilisers may increase the effects of relaxing the muscles – especially elderly patients receiving higher doses of Librium should be well monitored (higher risk of falling).

When Librium is used in conjunction with anti-epileptic drugs, side-effects and toxicity may be more evident, particularly with hydantoins or barbiturates or combinations including them. This requires extra care in adjusting dosage in the initial stages of treatment.

The concomitant use of sedative medicines such as benzodiazepines with opioids increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section 4.4).

Known inhibitors of hepatic enzymes, eg cimetidine, omeprazole, macrolide antibiotics (erythromycin) and disulfiram have been shown to reduce the clearance of benzodiazepines and may potentiate their action. The same applies to the use of contraceptive agents. Known inducers of hepatic enzymes, e.g. rifampicin, may increase the clearance of benzodiazepines.

In patients receiving long-term treatment with other medicines (such as centrally acting antihypertensive agents, beta receptor blockers, anticoagulant

agents and cardiac glycosides), nature and extent of interactions cannot safely be foreseen.

Benzodiazepines possibly antagonise the effect of levodopa.

Sedative effects are possibly increased when benzodiazepines are given with moxonidine.

Benzodiazepines enhance effects of sodium oxybate. Concomitant use should be avoided.

Effects of benzodiazepines are possibly reduced by theophylline.

4.6 Fertility, pregnancy and lactation

Contraception in males and females:
Due to the genotoxic potential of Chlordiazepoxide (see section 5.3), women of childbearing potential should use effective contraceptive measures while being treated with Librium and for 7 months following completion of treatment.

If the patient suspects to be pregnant or intends to become pregnant, she should be warned to contact her physician to discuss discontinuation of Librium.

Men are recommended to use effective contraceptive measures and to not father a child while receiving Librium and for 4 months following completion of treatment.

Pregnancy:
Chlordiazepoxide crosses the placenta.

There is a limited amount of data from the use of chlordiazepoxide in pregnant women.

Studies in animals have shown reproductive toxicity (see section 5.3).

Librium should not be used during pregnancy, especially during the first and last trimester unless the clinical condition of the woman requires treatment with chlordiazepoxide.

The administration of high doses or prolonged administration of low doses of benzodiazepines in the last trimester of pregnancy or during labour have been reported to produce irregularities in the foetal heart rate, moderate respiratory depression, hypotonia, poor sucking and hypothermia in the neonate. Moreover, infants born to mothers who chronically took benzodiazepines during the later stages of pregnancy may have developed physical dependence and may be at some risk for developing withdrawal symptoms in the postnatal period.

Breast-feeding:
Chlordiazepoxide may appear in breast milk. If possible the use of Librium should be avoided during breast-feeding.

4.7 Effects on ability to drive and use machines

Patients should be advised that, like all medicaments of this type, Librium may modify patients' performance at skilled tasks. Sedation, amnesia, impaired concentration and impaired muscle function may adversely affect the ability to drive or use machinery. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased. Patients should further be advised that alcohol may intensify any impairment, and should, therefore, be avoided during treatment.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

- The medicine is likely to affect your ability to drive
- Do not drive until you know how the medicine affects you
- It is an offence to drive while under the influence of this medicine
- However, you would not be committing an offence (called 'statutory defence') if:
  - The medicine has been prescribed to treat a medical or dental problem and
  - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and

It was not affecting your ability to drive safely

4.8 Undesirable effects

Common adverse effects include drowsiness, sedation, dizziness, somnolence, fatigue, balance disorder, unsteadiness and ataxia; these are dose-related and may persist into the following day even after a single dose. However, these phenomena occur predominantly at the start of therapy and usually disappear with repeated administration. The elderly are particularly sensitive to the effects of centrally-depressant drugs and may experience confusion, especially if organic brain changes are present; and the dosage of Librium should not exceed one-half that recommended for other adults.

Evaluation of undesirable effects is based on the following frequency information: very common (≥ 1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (frequency cannot be estimated from available data).

Blood and lymphatic system disorders:

Rare: Bone marrow depression (e.g. thrombocytopenia, leukopenia, agranulocytosis, pancytopenia)

Immune system disorders:
Very rare: Anaphylactic reaction, angioedema
Frequency not known: Hypersensitivity

Metabolism and nutrition disorders:
Frequency not known: Increased appetite

Psychiatric disorders:
Frequency not known: Amnesia, hallucinations, dependence, depression, restlessness, agitation, irritability, depressed level of consciousness, aggression, delusion, nightmares, psychotic disorder, abnormal behaviour, emotional disturbances, paradoxical drug reaction (e.g. anxiety, sleep disorders, insomnia, suicide attempt, suicidal ideation)

Nervous system disorders:
Common: Sedation, dizziness, unsteadiness, somnolence, ataxia, balance disorder, confusional states
Rare: Headache, vertigo
Frequency not known: Dysarthria, gait disturbance, extrapyramidal disorder (e.g. tremor, dyskinesia)

Eye disorders:
Rare: Visual impairment including diplopia

Vascular disorders:
Rare: Hypotension

Respiratory, thoracic and mediastinal disorders:
Frequency not known: Respiratory depression

Gastrointestinal disorders:
Rare: Gastrointestinal upsets

Hepatobiliary disorders:
Frequency not known: Jaundice, blood bilirubin increased, transaminases increased, blood alkaline phosphatase increased

Skin and subcutaneous tissue disorders:
Rare: Skin reaction (e.g. rash)

Musculoskeletal and connective tissue disorders:
Due to the myorelaxant effect there is a risk of falls and consequently fractures in the elderly
Frequency not known: Muscle weakness

Renal and urinary disorders:
Rare: Urinary retention, incontinence

Reproductive system and breast disorders:
Rare: Libido disorders, erectile dysfunction, menstrual disorder

General disorders and administration site conditions:
Common: Fatigue
Frequency not known: Changes in salivation

Amnesia
Anterograde amnesia may occur at the therapeutic doses, with increasing risk at higher doses. This may be associated with inappropriate behavior (see section 4.4)

Depression
Pre-existing depression may be unmasked by benzodiazepines.

Psychiatric and paradoxical reactions
Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behavior and other adverse behavioural effects are known to occur when using benzodiazepine-like agents. They may be quite severe with this product. They are more likely to occur in children and the elderly.

Dependence
Use (even therapeutic doses) may lead to the development of physical dependence: discontinuation of the therapy may result in the withdrawal or rebound phenomena. Psychological dependence may occur. Abuse of benzodiazepines has been reported

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

When taken alone in overdosage, Librium presents few problems in management. When taken with centrally-acting drugs, especially alcohol, the effects of overdose are likely to be more severe and in the absence of supportive measures may prove fatal.

Symptoms:
Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy, in more serious cases, symptoms

may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death.

Management:
In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken.
Treatment is symptomatic.

The benefit of gastric decontamination is uncertain. Consider activated charcoal (charcoal dose: 50 g for an adult, 1 g/kg for a child) in adults or children who have taken more than a potentially toxic amount within 1 hour, provided the airway can be protected.

The value of dialysis has not been determined. Flumazenil, a benzodiazepine antagonist, is available but should rarely be required. It may be required in children who are naïve to benzodiazepines or patients with COPD as an alternative to ventilation. Flumazenil has a short half-life (about an hour) and in this situation an infusion may therefore be required. Flumazenil should not normally be used in patients with a history of seizures, head injury, chronic benzodiazepine use, co-ingestion of a benzodiazepine and tricyclic antidepressant or other proconvulsant.

If excitation occurs, barbiturates should not be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeiutic group: Psycholeptics, anxiolytics, benzodiazepine derivatives.
ATC code: N05BA02

Chlordiazepoxide is a psychotropic substance from the class of 1,4-benzodiazepines with tension, excitement, anxiety attenuating properties and sedative and hypnotic effects. Chlordiazepoxide shows muscle relaxant and anticonvulsant effects.

Chlordiazepoxide has low affinity as an agonist at specific benzodiazepine receptors located on GABA-ergic neurones. Stimulation of benzodiazepine receptors potentates the actions of GABA. GABA-ergic neurones are inhibitory in the nervous system. This results in diminution of various 5-HT, dopamine and noradrenergic neurotransmitter system effects.

5.2 Pharmacokinetic properties

Absorption:

Librium is well absorbed, with peak blood levels being achieved one or two hours after administration.

Steady-state levels are usually reached within three days.

Distribution:

Chlordiazepoxide is metabolised to desmethyl-chlordiazepoxide. Demoxepam and desmethyldiazepam are also found in the plasma of patients on continuous treatment. The active metabolite desmethyl-chlordiazepoxide has an accumulation half-life of 10 – 18 hours; that of demoxepam has been recorded as 21 – 78 hours

Steady-state levels of these active metabolites are reached after 10-15 days, with metabolite concentrations which are similar to those of the parent drug.

Elimination:

The drug has a half-life is of 6 - 30 hours.

Pharmacokinetic / pharmacodynamic relationship:

No clear correlation has been demonstrated between the blood levels of Librium and its clinical effects.

5.3 Preclinical safety data

Mutagenic and tumourigenic potential:

In in-vivo and in-vitro studies with chlordiazepoxide, there are indications for a mutagenic effect. Nevertheless, in similar test systems results are negative. The relevance of the positive findings is currently unclear.
In carcinogenicity studies in mice an increase of liver tumours was seen at high doses, especially in males, whereas no increase of tumour incidence was seen in rats.

Reproductive toxicity:

In animal studies increased resorption rates, increased incidence of stillbirth and neonatal death, malformation of the scull (exencephaly, cleft palate), lung anomalies and changes in the urogenital tract as well as behavioural disorders and neurochemical changes have been observed in the offspring.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

5mg capsules contain the following excipients: gelatine, starch maize white, talc purified, lactose, yellow iron oxide E172, indigo carmine E132, titanium dioxide E171, quinoline yellow E104 and erythrosine E127.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Librium capsules should not be stored above 30ºC

6.5 Nature and contents of container

Amber glass bottle with screw cap containing 100 capsules

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordence with local requirements.

7 MARKETING AUTHORISATION HOLDER

Viatris Products Limited,
Station Close,
Potters Bar,
EN6 1TL,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 46302/0175

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/03/1998 / 18/03/2003

10 DATE OF REVISION OF THE TEXT

29/09/2025