

Scheduling status: **S4**

Proprietary names (and dosage forms)

LIORESAL 10® Tablets

LIORESAL 25® Tablets

Composition

LIORESAL 10®: Tablets containing 10 mg baclofen.

LIORESAL 25®: Tablets containing 25 mg baclofen.

Pharmacological classification

A 2.10 Centrally active muscle relaxants.

Pharmacological action

Baclofen displays pronounced muscle-relaxing activity. It acts on the motor system of the spinal cord in a distinctive segmental fashion. Baclofen inhibits both mono- and polysynaptic reflex transmission and reduces the activity of the gamma motor neurones. It does not, however influence neuromuscular impulse transmission in the motor endplates. In neurological diseases associated with skeletal muscle spasm Baclofen reduces spasticity. It also markedly relieves the associated pain, rigidity, automatism and clonus, with consequent improvement in the patient's mobility. Active and passive physiotherapy are thereby facilitated.

Indications

Spasticity of the skeletal muscle due to multiple sclerosis; spastic conditions occurring in spinal-cord diseases of infectious, degenerative, traumatic, neoplastic, or unknown aetiology – e.g. spastic spinal paralysis, amyotrophic lateral sclerosis, syringomyelia, transverse myelitis, traumatic paraplegia or paraparesis, and compression of the spinal cord.

Spasticity of cerebral origin, e.g. following cerebrovascular accidents or in the presence of

neoplastic or degenerative brain disease.

Contra-indications

Known hypersensitivity to baclofen or to any of the excipients. Porphyria.

Safety in pregnancy and lactation has not been established.

Warnings

LIORESAL may be associated with dizziness, sedation, somnolence, visual disturbances and impaired concentration which may impair the patient's reaction and may be aggravated by the simultaneous intake of alcohol or central nervous system depressant agents.

Patients experiencing these adverse reactions should be advised to refrain from driving or using machines. Lioresal tablets contain wheat starch. Wheat starch may contain gluten, but only in trace amounts. Taking Lioresal tablets is therefore considered safe for people with celiac disease.

Interactions

Where LIORESAL is taken concomitantly with other drugs acting on the CNS, with synthetic opiates or with alcohol, increased sedation may occur. The risk of respiratory depression is also increased. Careful monitoring of respiratory and cardiovascular functions is essential especially in patients with cardiopulmonary disease and respiratory muscle weakness.

During concurrent treatment with tricyclic antidepressants, the effect of LIORESAL may be potentiated, resulting in pronounced muscular hypotonia.

Since concomitant treatment with LIORESAL and antihypertensives are likely to increase the fall in blood pressure, the dosage of antihypertensive medication should be adjusted accordingly. Hypotension has been reported in one patient receiving morphine and intrathecal baclofen.

In patients with Parkinson's disease receiving treatment with LIORESAL and levodopa, there have been reports of mental confusion, hallucinations, headaches, nausea and agitation.

Pregnancy and lactation

Safety in pregnancy and lactation has not been established.

Dosage and directions for use

Treatment should always be initiated with small, gradually increasing doses of LIORESAL. The optimum daily dosage should be individually adapted to the patient's requirements in such a way that clonus, flexor and extensor spasms, and spasticity are reduced, but that a sufficient degree of muscle tone is maintained to permit active movements and adverse effects are avoided as far as possible.

In order to prevent excessive weakness and falling, LIORESAL should be used with caution when spasticity is needed to sustain upright posture and balance in locomotion or whenever spasticity is used to maintain function. It may be important to maintain some degree of muscle tone and allow occasional spasms to help support circulatory function.

LIORESAL should be taken during meals with a little liquid.

The daily dosage should be given in at least 3 divided doses in adults, and 3 to 4 in children.

Adults

Treatment should as a rule be started with a dosage of 5 mg three times daily, which for the purpose of cautious dose titration should subsequently be increased at three-day intervals by 5 mg three times daily until the requisite daily dosage has been attained,

- i.e.:
- 5 mg three times daily for 3 days
 - 10 mg three times daily for 3 days
 - 15 mg three times daily for 3 days
 - 20 mg three times daily for 3 days

In certain patients reacting sensitively to medicines, it may be advisable to begin with a lower daily dosage (5 mg or 10 mg) and to raise this dosage more gradually. The optimum dosage generally ranges from 30 mg to 80 mg daily.

Doses of more than 80 mg to 100 mg daily are not generally recommended although higher doses have been given to carefully supervised patients in hospital.

Children

Treatment should usually be started with a very low dose, e.g. 0,3 mg/kg a day, in divided doses. The dosage should be raised cautiously, at about 1 to 2 week intervals, until it becomes sufficient for the child's individual requirements. The usual daily dosage for maintenance

therapy ranges between 0,75 and 2 mg/kg body mass. In children over 10 years of age, however, a maximum daily dosage of 2,5 mg/kg body mass may be given.

If no benefit is apparent within 6 to 8 weeks of achieving the maximum dosage, a decision whether to continue with LIORESAL should be taken.

In patients with impaired renal function or undergoing chronic haemodialysis, a particularly low dosage of LIORESAL should be selected, i.e. approximately 5 mg daily. Signs and symptoms of overdosage have been reported with doses above 5 mg daily in this setting.

Since unwanted effects are more likely to occur in elderly patients or in patients with spastic states of cerebral origin, in such cases it is recommended that a very cautious dosage schedule be adopted and that the patient be kept under appropriate surveillance.

Withdrawal of LIORESAL should be gradual.

Abrupt discontinuation of the treatment should be avoided (see "Side-effects and special precautions").

Side-effects and special precautions

Side-effects

Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: very common ($\geq 1/10$); common ($\geq 1/100$, $< 1/10$); uncommon ($\geq 1/1,000$, $< 1/100$); rare ($\geq 1/10,000$, $< 1/1,000$); very rare ($< 1/10,000$), including isolated reports.

Unwanted effects occur mainly at the start of treatment (e.g. sedation, somnolence, drowsiness, fatigue and nausea), if the dose is raised too rapidly, if large doses are employed, or if the patient is an elderly person. In patients with a case history of psychiatric illness or with cerebrovascular disorders (e.g. stroke), as well as in elderly patients, adverse reactions may assume a more serious form.

Lowering of the convulsion threshold and attacks of convulsions may possibly occur, particularly in epileptic patients.

Certain patients have shown increased muscle spasticity as a paradoxical reaction to the medication.

Many of the adverse CNS and genitourinary effects reported are known to occur in association with the underlying conditions being treated.

An undesirable degree of muscular hypotonia - making it more difficult for patients to walk or fend for themselves - may occur and may be relieved by re-adjusting the dosage (i.e. by reducing the doses given during the day and possibly increasing the evening dose).

Table 1

Nervous system disorders	
<i>Very common:</i>	Sedation, somnolence, drowsiness, fatigue and nausea. Dryness of the mouth, respiratory depression, light-headedness, lassitude, exhaustion, mental confusion, dizziness, headache, insomnia, euphoria, depressive states, myalgia, muscular weakness, ataxia, tremor, nystagmus, hallucinations, nightmares.
<i>Rare:</i>	Paraesthesia, dysarthria, dysgeusia.
<i>Very rare:</i>	Hypothermia.
Eye disorders	
<i>Common:</i>	Accommodation disorders, visual disturbances.
<i>Uncommon:</i>	Tinnitus
Cardiac disorders	
<i>Common</i>	Cardiac output decreased
Vascular disorders	
<i>Common:</i>	Hypotension
Gastrointestinal disorders	
<i>Very common:</i>	Nausea. Gastrointestinal disturbances, retching, vomiting, constipation, diarrhoea.
<i>Rare:</i>	Abdominal pain.

Hepatobiliary disorders	
<i>Rare:</i>	Hepatic function abnormal.
Skin and subcutaneous tissue disorders	
<i>Common:</i>	Hyperhidrosis, rash.
Renal and urinary disorders	
<i>Common:</i>	Pollakiuria, enuresis, dysuria.
<i>Rare:</i>	Urinary retention
Reproductive system and breast disorders	
<i>Rare:</i>	Erectile dysfunction.

Precautions

Patients suffering from psychotic disorders, schizophrenia, depressive or manic disorders, confusional states or Parkinson's disease should be treated cautiously with LIORESAL and kept under careful surveillance, because exacerbations of these conditions may occur.

Special attention should be given to patients known to suffer from epilepsy since lowering of the convulsion threshold may occur and seizures have occasionally been reported in connection with the discontinuation of LIORESAL or with overdosage. Adequate anticonvulsive therapy should be continued and the patient carefully monitored.

Anxiety and confusional states, hallucinations, psychotic, manic or paranoid states, convulsions (status epilepticus), dyskinesia, tachycardia, hyperthermia and - as a rebound phenomenon - temporary aggravation of spasticity have been reported upon the abrupt withdrawal of LIORESAL, especially after long-term medication. Except in overdose - related emergencies or where serious adverse effects have occurred, treatment should therefore always be gradually discontinued by successively reducing the dosage (over a period of approximately one to two weeks).

LIORESAL should be used with caution in patients with, or with a history of, peptic ulcers, as well as in those suffering from cerebrovascular diseases or from respiratory, hepatic, or renal failure. Patients with stroke tolerate LIORESAL poorly.

LIORESAL should be used with caution in patients with pre-existing sphincter hypertonia as acute retention of urine may occur.

In rare instances, elevated SGOT, alkaline phosphatase, and glucose levels in the serum have been recorded. Appropriate laboratory tests should therefore be performed periodically in patients with liver disease or diabetes mellitus in order to ensure that no drug-induced changes in these underlying diseases have occurred.

Known symptoms of overdosage and particulars of its treatment

Signs and symptoms

Prominent features are signs of central nervous depression: drowsiness, impairment of consciousness, respiratory depression, coma. Also liable to occur are: confusion, hallucinations, agitation, accommodation disorders, absent pupillary reflex; generalised muscular hypotonia, myoclonia, hyporeflexia or areflexia; convulsions; peripheral vasodilatation, hypotension or hypertension, bradycardia or tachycardia; hypothermia; nausea, vomiting, diarrhoea, hypersalivation; elevated LDH, SGOT, and AP values.

A deterioration in the condition may occur if various substances or drugs acting on the central nervous system (e.g. alcohol, diazepam, tricyclic antidepressants) have been taken at the same time.

Treatment

No specific antidote is known. Elimination of the drug from the gastro-intestinal tract (induction of vomiting, gastric lavage; comatose or convulsing patients should be incubated prior to gastric lavage). Supportive measures and symptomatic treatment should be given for complications such as hypotension, hypertension, convulsions, gastrointestinal disturbances, and respiratory or cardiovascular depression.

Identification

LIORESAL 10®:

White to faintly yellowish, round, flat tablets with a slightly bevelled edge. Imprinted CG on one side, KJ and a score on the other. Diameter approximately 7 mm. Thickness approximately 3 mm.

LIORESAL 25®:

White to faintly yellowish, round, flat tablets with a slightly bevelled edge. Imprinted CG on one side, UR and a score on the other. Diameter approximately 8 mm.

Thickness approximately 3.2 mm.

Presentation

LIORESAL is supplied as uncoated tablets of 10 mg and 25 mg in packs of 30.

Storage instructions

Store at or below 30 °C and protect from moisture.

KEEP OUT OF THE REACH OF CHILDREN.

Registration numbers

LIORESAL 10 mg® Tablets: E/2.10/227

LIORESAL 25 mg® Tablets: E/2.10/228

Name and business address of the holder of the certificate of registration

NOVARTIS SOUTH AFRICA (PTY) LTD

Magwa Crescent

West, Waterfall

City, Jukskei View

Johannesburg

2090

Date of publication of this package insert

15 August 2008

® Registered Trademark