

# **AUSTRALIAN PRODUCT INFORMATION – LIORESAL (BACLOFEN) TABLETS**

## **1 NAME OF THE MEDICINE**

The active ingredient of Lioresal is a gamma-aminobutyric acid derivative, baclofen, or  $\beta$ -(Aminomethyl)-p-chlorohydrocinnamic acid, a racemic mixture of the R(-) and S(+) isomers.

## **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Baclofen is a white or almost white, odourless or practically odourless, crystalline powder. It is slightly soluble in water, very slightly soluble in methanol and insoluble in chloroform.

Lioresal tablets contain 10 mg or 25 mg baclofen. The tablets also contain the following excipients: colloidal anhydrous silica, microcrystalline cellulose, magnesium stearate, povidone, wheat starch.

Excipient with known effect: wheat starch. Wheat starch may contain gluten, but only in trace amounts.

## **3 PHARMACEUTICAL FORM**

Tablets containing baclofen 10mg: white, round, flat with bevelled edges; marked with KJ and score, CG on reverse.

Tablets containing baclofen 25mg: white, round, flat with bevelled edges; marked with UR and score, CG on reverse.

## **4 CLINICAL PARTICULARS**

### **4.1 THERAPEUTIC INDICATIONS**

Suppression of voluntary muscle spasm in:

- Multiple sclerosis
- Spinal lesions of traumatic, infectious, degenerative, neoplastic and unknown origin, causing:
  - skeletal hypertonus
  - spastic and dyssynergic bladder dysfunction

Not recommended in Parkinson's disease or spasticity arising from strokes, cerebral palsy or rheumatoid disorders.

### **4.2 DOSE AND METHOD OF ADMINISTRATION**

Treatment with Lioresal should always be started in hospital, using small doses which are then gradually increased in a stepwise manner. The lowest dose compatible with an optimal response is recommended. The optimum daily dosage should be individualised so that clonus, flexor and extensor spasms, and spasticity are reduced, at the same time retaining enough muscle tone to permit active movements and avoiding adverse effects 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.

Abrupt discontinuation of treatment should be avoided (see section 4.4 special warnings and precautions for use).

In adults Lioresal should be given in at least three divided doses daily.

### **Dosage Regimen**

As a rule, treatment should be started with a dose of 5 mg three times daily, subsequently increased at 3-day intervals by 5 mg three times daily (i.e. the dosage regimen is 5 mg three times a day for 3 days, then 10 mg three times a day for 3 days, etc.) until the optimum response has been attained. In certain patients reacting sensitively to drugs, it may be advisable to begin with a lower daily dose (5 mg or 10 mg), increased by smaller steps at longer intervals (see section 4.4 special warnings and precautions for use). The optimum dosage generally ranges from 30 mg to 75 mg daily, although occasionally in hospitalised patients daily doses up to 100 mg may be necessary.

If no benefit is apparent within 6 to 8 weeks of achieving the maximum dosage, a decision should be taken whether or not to continue treatment with Lioresal.

Discontinuation of the treatment should always be gradual by successively reducing the dosage over a period of approximately 1 to 2 weeks, except in overdose-related emergencies, or where serious adverse effects have occurred (see section 4.4 Special warnings and precautions for use).

### **Special Populations**

#### Renal impairment:

In patients with impaired renal function or undergoing chronic haemodialysis, low doses (ie. approx. 5 mg daily) should be used. These patients should be closely monitored for prompt diagnosis of early signs and/or symptoms of toxicity (e.g. somnolence, lethargy) (see section 4.4 Special warnings and precautions for use and section 4.9 Overdose). Signs and symptoms of overdosage have been reported with doses at and above 5 mg daily in this setting (see section 4.9 Overdose).

Lioresal should be administered to end stage renal failure patients only if the expected benefit outweighs the potential risk.

#### Hepatic impairment:

No studies have been performed in patients with hepatic impairment under Lioresal therapy. Lioresal should be prescribed with caution in patients with hepatic impairment (see section 4.4 Special warnings and precautions for use).

#### Elderly patients (aged 65 years or above):

Since unwanted effects are more likely to occur in elderly patients (due to increased risk of renal function impairment and CNS toxicity), a very cautious dosage schedule should be adopted and the patient kept under appropriate surveillance.

Toxicity due to baclofen may be mistaken for uraemic encephalopathy.

### Paediatric patients:

Lioresal should be given with extreme caution to children under 16 years of age, as only limited data are available. Lioresal tablets are not suitable for use in children with a body weight below 33 kg.

### **Method of administration**

Lioresal should be taken during meals with a little liquid.

### **Monitoring Advice**

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

Careful monitoring of respiratory and cardiovascular function is essential especially in patients with cardiopulmonary disease and respiratory muscle weakness.

### **4.3 CONTRAINDICATIONS**

Known hypersensitivity to baclofen or to any of the components of the formulation.

### **4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**

#### **Psychiatric and nervous system disorders**

Patients suffering not only from spasticity but also from psychotic disorders, schizophrenia, depressive or manic disorders or confusional states should be treated cautiously with Lioresal and kept under careful surveillance, because exacerbations of these conditions may occur.

Suicide and suicide-related events have been reported in patients treated with baclofen. In most cases, the patients had additional risk factors associated with an increased risk of suicide including alcohol use disorder, depression and/or a history of previous suicide attempts. Close supervision of patients with additional risk factors for suicide should accompany drug therapy. Patients (and caregivers of patients) should be alerted about the need to monitor for clinical worsening, suicidal behaviour or thoughts or unusual changes in behaviour and to seek medical advice immediately if these symptoms present.

Cases of misuse, abuse and dependence have been reported with baclofen. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of baclofen misuse, abuse or dependence e.g. dose escalation, drug-seeking behaviour, development of tolerance.

#### **Epilepsy or other potential convulsive conditions**

Caution is needed in patients with epilepsy or other convulsive conditions, cortical or subcortical brain damage or significant EEG abnormalities, since ingestion of baclofen may cause deterioration of seizure control and EEG changes and may precipitate convulsions. In patients with epilepsy and muscle spasticity, Lioresal can be employed under appropriate supervision, provided adequate anticonvulsive therapy is continued.

Lowering of the convulsion threshold may occur and seizures have been reported occasionally after cessation of Lioresal or with overdosage.

### **Encephalopathy**

Cases of encephalopathy have been reported in patients treated with Lioresal (see sections 4.8 Adverse effects (undesirable effects) and 4.9 Overdose). Symptoms included somnolence, depressed level of consciousness, confusion, myoclonus and coma which are usually reversible after treatment discontinuation. If any signs or symptoms of encephalopathy are observed, baclofen should be discontinued.

### **Others**

Lioresal should be used with caution in patients with:

- peptic ulcers or with a history of peptic ulcers
- cerebrovascular diseases or from respiratory or hepatic insufficiency.
- porphyria
- a history of alcoholism
- diabetes mellitus (baclofen may increase blood glucose concentrations)
- hypertension (see section 4.5 Interactions with other medicines)

Since unwanted effects are more likely to occur, a cautious dosage schedule should be adopted in elderly and patients with spasticity. Lioresal is not recommended in Parkinson's disease or spasticity arising from strokes, cerebral palsy or rheumatoid disorders.

### **Changes in muscle tone**

Lioresal should be used with caution in patients who use spasticity to maintain upright posture and balance in moving. If an undesirable degree of muscular hypotonia occurs, making it more difficult for patients to walk or fend for themselves, this can usually be relieved by adjusting the dosage (i.e. by reducing the doses given during the day and possibly increasing the evening dose).

During treatment with Lioresal, neurogenic disturbances affecting the emptying of the bladder may improve, whereas in patients with pre-existing sphincter hypertonia, acute retention of urine may occur. The drug should, therefore, be used with caution in such cases.

### **Abrupt discontinuation**

Anxiety and confusional states, delirium, hallucinations, psychotic disorders, mania, or paranoia, convulsion (status epilepticus), dyskinesia, tachycardia, hyperthermia and - as a rebound phenomenon - temporary aggravation of spasticity and hypertonia have been reported upon the abrupt withdrawal of Lioresal, especially after long-term medication.

Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intrauterine exposure to oral Lioresal. (See section 4.6 Fertility, pregnancy and lactation - Use in Pregnancy).

For the intrathecal formulation of Lioresal, it has been reported that clinical characteristics of withdrawal may resemble autonomic dysreflexia, infection (sepsis), malignant hyperthermia, neuroleptic-malignant syndrome, or other conditions associated with a hypermetabolic state or widespread rhabdomyolysis.

Except in overdose-related emergencies or where serious adverse effects have occurred, treatment should, therefore, always be gradually withdrawn by successive dosage reduction over a period of approximately 1 to 2 weeks.

If withdrawal symptoms occur, restarting baclofen therapy and withdrawing over a longer period may help to resolve withdrawal problems.

### **Switching from oral to intrathecal baclofen and vice versa**

An attempt should be made to discontinue concomitant antispastic medication to avoid possible overdose or adverse drug interactions. This should preferably be done before switching from oral to intrathecal baclofen or vice versa and requires careful monitoring by the physician. Abrupt reduction or discontinuation of concomitant antispastics during chronic therapy with baclofen should be avoided.

### **Posture and balance**

Lioresal should be used with caution when spasticity is needed to sustain upright posture and balance in locomotion (see section 4.2 Dose and method of administration).

### **Wheat starch**

Lioresal tablets contain wheat starch. Wheat starch may contain gluten, but only in trace amounts.

### **Use in hepatic impairment**

Because baclofen is partially metabolised in the liver, patients with impaired liver function should be periodically monitored with laboratory tests (see section 4.2 Dose and method of administration - Monitoring Advice”).

### **Use in renal impairment**

Since baclofen is largely eliminated by the kidneys, a dosage reduction is advised to avoid drug accumulation. Lioresal should be used with caution in patients with renal impairment and should be administered to end stage renal failure patients only if the expected benefit outweighs the potential risk (see section 4.2 Dose and method of administration - Renal impairment”).

Neurological signs and symptoms of overdose including clinical manifestations of toxic encephalopathy (e.g. confusion, somnolence, hallucination) have been observed in patients with renal impairment taking Lioresal at doses at and above 5 mg daily. Patients with renal impairment should be closely monitored for prompt diagnosis of early signs and symptoms of toxicity (see section 4.9 Overdose).

Particular caution is required when combining Lioresal to drugs or medicinal products that can significantly impact renal function. Renal function shall be closely monitored and Lioresal daily dosage adjusted accordingly to prevent baclofen toxicity.

Besides discontinuing treatment, unscheduled haemodialysis might be considered as a treatment alternative in patients with severe baclofen toxicity. Haemodialysis effectively removes baclofen from the body, alleviates clinical symptoms of overdose and shortens the recovery time in these patients.

### **Use in the elderly**

Since unwanted effects are more likely to occur in elderly patients (due to increased risk of renal function impairment and CNS toxicity), a very cautious dosage schedule should be adopted and the patient kept under appropriate surveillance.

Toxicity due to baclofen may be mistaken for uraemic encephalopathy.

### **Paediatric use**

Lioresal should be given with extreme caution to children under 16 years of age, as only limited data are available. Lioresal tablets are not suitable for use in children with a body weight below 33 kg.

### **Effects on laboratory tests**

No data available

## **4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS**

### **Levodopa/Dopa Decarboxylase (DDC) inhibitor (Carbidopa):**

In patients with Parkinson's disease receiving treatment with Lioresal and levodopa (alone or in combination with DDC inhibitor, carbidopa), there have been reports of mental confusion, hallucinations, headaches, nausea and agitation. Worsening of the symptoms of Parkinsonism has also been reported. Hence, caution should be exercised during concomitant administration of Lioresal and levodopa/carbidopa.

### **Drugs causing Central Nervous System (CNS) depression:**

Increased sedation may occur when Lioresal is taken concomitantly with other drugs causing CNS depression including other muscle relaxants (such as tizanidine), with synthetic opiates or with alcohol (see section 4.4 Special warnings and precautions for use). The risk of respiratory depression is also increased. In addition, hypotension has been reported with concomitant use of morphine and intrathecal baclofen. Careful monitoring of respiratory and cardiovascular functions is essential, especially in patients with cardiopulmonary disease and respiratory muscle weakness.

### **Antidepressants:**

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

### **Lithium:**

Concurrent use of oral Lioresal and lithium resulted in aggravated hyperkinetic symptoms. Thus, caution should be exercised when Lioresal is used concomitantly with lithium.

### **Antihypertensives and other drugs known to lower blood pressure:**

Since concomitant treatment with drugs that lower blood pressure is likely to increase the fall in blood pressure, the dosage of concomitant medications should be adjusted accordingly.

### **Agents reducing renal function:**

Drugs or medicinal products that can significantly impact renal function may reduce baclofen excretion leading to toxic effects (see section 4.4 Special warnings and precautions for use, Impaired renal function).

### **Others:**

Concurrent use of baclofen with monoamine oxidase (MAO) inhibitors may result in increased CNS-depressant and hypotensive effects. Caution is recommended and dosage of one or both agents may require reduction.

Since baclofen may increase blood glucose concentrations, dosage adjustments of insulin and/or oral hypoglycaemic agents may be necessary during and after concurrent therapy.

Studies in rats indicate that the agonistic effects of baclofen on gastric acid secretion are potentiated by diazepam.

## **4.6 FERTILITY, PREGNANCY AND LACTATION**

### **Effects on fertility**

There are no data available on the effect of baclofen on fertility in humans.

### **Use in pregnancy – Pregnancy Category B3**

#### Risk summary

There are no adequate and well-controlled studies in pregnant women. Animal data showed that baclofen crosses the placental barrier. Therefore, Lioresal should not be used during pregnancy unless the expected benefit outweighs the potential risk to the foetus.

Drug withdrawal reactions including postnatal convulsions in neonates following intra-uterine exposure to oral baclofen, have been reported. In one suspected case of postnatal baclofen withdrawal, the convulsions were refractory to various anticonvulsants, but responsive to the administration of baclofen to the affected neonate (See section 4.4 Special warnings and precautions for use, Abrupt discontinuation).

### **Use in lactation.**

Studies in lactating women are limited to one (1) patient. In this particular case, available evidence suggests that baclofen is found in quantities so small that adverse effects in the infant would have been unlikely.

## **4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES**

Lioresal may be associated with adverse effects such as dizziness, sedation, somnolence and visual impairment (see section 4.8 Adverse effects) which may impair the patient's reaction. Patients experiencing these adverse reactions should be advised to refrain from driving or using machines.

The patient's ability to react may be adversely affected by sedation and decreased alertness caused by Lioresal. Patients should, therefore, exercise due caution when driving a vehicle or operating machinery.

## 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

### Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at [www.tga.gov.au/reporting-problems](http://www.tga.gov.au/reporting-problems).

Adverse effects occur mainly at the start of treatment (e.g. sedation, somnolence), if the dosage is increased too rapidly, if large doses are employed or if the patient is elderly. They are often transitory and can be attenuated or eliminated by reducing the dosage. They may necessitate withdrawal of the medication. In patients with a history of psychiatric illness, cortical or organic brain disorders or with cerebrovascular disorders (eg. stroke), as well as in elderly patients, adverse reactions may be more serious.

It is often difficult to distinguish whether some of these are drug effects or manifestations of the diseases under treatment. Psychiatric manifestations can occur in acute or chronic toxicity due to baclofen.

Lowering of the convulsion threshold and convulsions may occur, particularly in epileptic patients (see section 4.4 Special warnings and precautions for use).

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

Within each system organ class, adverse reactions are ranked by frequency, with the most frequent reactions 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 ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

#### Immune system disorders

Not known                      Hypersensitivity

#### Psychiatric disorders

Common                        Confusional state, hallucination, depression, insomnia, euphoric mood, nightmare

#### Nervous system disorders

Very common:                Sedation, somnolence

Common:                      Dizziness, personality changes, vertigo, headache, ataxia, tremor, nystagmus, tinnitus

Rare:                            Paraesthesia, dysarthria, dysgeusia, syncope, dyskinesia, coma, taste disturbances

Not known:                    Cases of misuse, abuse and dependence have been reported with baclofen. Suicide and suicide-related events have been reported in patients treated with baclofen (see section 4.4 Special warnings and precautions for use – Psychiatric and nervous system disorders), encephalopathy

#### Eye disorders

Common:                      Accommodation disorder, visual impairment

#### Cardiac disorders

Rare:                            Arrhythmias, palpitations, chest pain



Not known: Bradycardia

**Vascular disorders**

Common: Hypotension

Rare: Dyspnoea, ankle oedema

**Gastrointestinal disorders**

Very common: Nausea (particularly at the start of treatment)

Common: Gastrointestinal disorder, retching, vomiting, constipation, diarrhoea, dry mouth

Rare: Colicky abdominal pain, anorexia

**Hepatobiliary disorders**

Rare: Hepatic function abnormal

**Skin and subcutaneous tissue disorders**

Common: Hyperhidrosis, rash, pruritus

Not known: Urticaria, alopecia

**Musculoskeletal and connective tissue disorders**

Common: Muscle weakness, myalgia

**Renal and urinary disorders**

Common: Pollakiuria, enuresis, dysuria

Rare: Urinary retention, nocturia, haematuria

**Reproductive system and breast disorders**

Rare: Erectile dysfunction, inability to ejaculate

Not known: Sexual dysfunction

**Respiratory, thoracic and mediastinal disorders**

Common: Respiratory depression

**General disorders and administration site conditions**

Common: Fatigue

Very rare: Hypothermia

Not known: Drug withdrawal syndrome\*, swelling face and peripheral oedema

**Investigations**

Common: Cardiac output decreased

Not known: Blood glucose increase

**Miscellaneous**

Rare: nasal congestion, weight gain

\*Drug withdrawal syndrome including postnatal convulsions has also been reported after intra-uterine exposure to oral Lioresal

## 4.9 OVERDOSE

### Signs and symptoms

Prominent features are signs of central nervous depression or encephalopathy: somnolence, depressed level of consciousness, respiratory depression due to absent respiratory movement, coma.

Also liable to occur are: confusion, hallucinations, agitation, abnormal electroencephalogram (burst suppression pattern and triphasic waves), accommodation disorders, impaired pupillary reflex; generalised muscular hypotonia, myoclonus, hyporeflexia or areflexia; convulsions; peripheral vasodilatation, hypotension or hypertension, bradycardia, tachycardia or cardiac arrhythmias, hypothermia, nausea, vomiting, diarrhoea, salivary hypersecretion; increased hepatic enzymes, sleep apnoea, rhabdomyolysis, tinnitus.

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.

Adult patients have ingested up to 1125 mg of baclofen and survived. Ingestion of 1250 to 2500 mg by one patient was fatal. Serious poisoning has occurred with doses of 150 and 300 mg in adults.

### Treatment

No specific antidote is known.

Supportive measures and symptomatic treatment should be given for complications such as hypotension, hypertension, convulsions, gastrointestinal disturbances, and respiratory or cardiovascular depression.

Symptomatic treatment should include the following:

- elimination of the drug from the gastrointestinal tract e.g. administration of activated charcoal; if necessary, saline laxatives
- since the drug is excreted chiefly via the kidneys, generous quantities of fluid should be given, possibly together with a diuretic.
- measures in support of cardiovascular functions
- in the case of respiratory muscle weakness, administration of artificial respiration
- in the event of convulsions, diazepam should be administered cautiously i.v., paying attention to increased muscle relaxation and possible respiratory insufficiency, if the patient is not already being artificially ventilated.
- Haemodialysis (some times unscheduled) may be useful in severe poisoning associated with renal failure (see section 4.4 Special warnings and precautions for use)

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 PHARMACODYNAMIC PROPERTIES

#### Mechanism of action

Lioresal is an effective antispastic agent with a spinal site of action. Its mechanism of action and pharmacological properties are different from those of other antispastic agents.

Baclofen also has central sites of action given the adverse event profile and general CNS depressant properties.

Baclofen depresses monosynaptic and polysynaptic reflex transmission, probably by various actions, including stimulation of GABA<sub>β</sub>-receptors. This stimulation in turn inhibits the release of excitatory amino acids (glutamate and aspartate) in guinea pig preparations. Neuromuscular transmission is not affected by baclofen.

Baclofen exerts an antinociceptive effect. The clinical significance of this awaits clarification. In neurological diseases associated with spasm of the skeletal muscles, the clinical effects of Lioresal take the form of a beneficial action on reflex muscle contractions and of marked relief from painful spasm, automatism and clonus. Lioresal, where indicated, improves the patient's mobility, making for greater independence and facilitating passive and active physiotherapy. Baclofen stimulates gastric acid secretion.

#### Clinical trials

No data available.

### 5.2 PHARMACOKINETIC PROPERTIES

#### Absorption

Baclofen is rapidly and completely absorbed from the gastro-intestinal tract. Maximum concentrations of unchanged drug are attained in plasma in 2 to 4 hours after an oral dose. The bioavailability of oral baclofen is 70 to 80%.

Following oral administration of a single dose of 40 mg baclofen, peak serum concentrations of 500 to 600 nanogram/mL are reached. The serum concentration remains above 200 nanogram/mL for 8 hours. The onset of action is highly variable and may range from hours to weeks.

#### Distribution

The distribution volume of baclofen amounts to 0.7 litre/kg. In cerebrospinal fluid, the active substance attains concentrations approx. 8.5 times lower than in the plasma.

Baclofen is bound to plasma proteins to the extent of about 30%.

#### Metabolism

About 15% of a dose of baclofen is metabolised in the liver. Deamination yields the main metabolite, β-chlorophenyl-γ-hydroxybutyric acid, which is pharmacologically inactive.

#### Excretion

Approximately 70% of baclofen is eliminated in the urine in unchanged form. The plasma elimination half-life of baclofen averages 3 to 4 hours. Within 72 hours, approximately 75% of the dose is

excreted via the kidneys, approximately 5% of this quantity being in the form of metabolites. The remainder of the dose, including 5% as metabolites, is excreted in the faeces.

### **5.3 PRECLINICAL SAFETY DATA**

#### **Genotoxicity**

Baclofen did not induce mutations in bacterial or mammalian cells in vitro, lacked DNA damaging activity in the sister chromatid exchange assay and had no clastogenic activity in the nuclear anomaly test.

#### **Animal data**

In two teratogenic studies in pregnant rats, baclofen has been shown to increase the incidence of omphaloceles (ventral hernias) in fetuses at a dose of 20 mg/kg/day, which is maternotoxic. The relevance of this finding to humans is unknown. At the same dose there was also an increased incidence of incomplete sternebral ossification in the fetuses.

In mice, no teratogenic effects were observed at a dose of 81.5 mg/kg/day given via the diet or up to 40 mg/kg/day given by gavage. At 40 mg/kg/day by gavage, a delay in fetal growth was associated with maternal anorexia. The lack of maternotoxicity seen in the dietary study suggests that the dose used was inadequate.

In pregnant rabbits, oral doses up to 10 mg/kg/day were manifested as a sedative effect. Skeletal examination of fetuses revealed a marked increase in the absence of ossification of the phalangeal nuclei of fore-limbs and hind-limbs.

#### **Carcinogenicity**

A two year carcinogenicity study in rats found no evidence that baclofen had carcinogenic potential at oral doses up to 100 mg/kg/day. An apparently dose-related increase in the incidence of ovarian cysts and enlarged and/or haemorrhagic adrenals at the highest two doses (50 and 100 mg/kg/day) was observed in female rats. The clinical relevance of these findings is not known.

Ovarian cysts have been found by palpation in about 5% of the multiple sclerosis patients who were treated with oral Lioresal for up to one year. In most cases these cysts disappeared spontaneously while patients continued to receive the drug. Ovarian cysts are known to occur spontaneously in a proportion of the normal female population.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 LIST OF EXCIPIENTS**

Refer to Section 2 - Qualitative and quantitative composition.

### **6.2 INCOMPATIBILITIES**

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

### 6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

### 6.4 SPECIAL PRECAUTIONS FOR STORAGE

10 mg tablet blister pack: Store below 30°C.

10 mg tablet bottle and 25 mg tablet blister pack and bottles: Store below 25°C.

Medicines should be kept out of the reach of children.

### 6.5 NATURE AND CONTENTS OF CONTAINER

10 mg tablet: HDPE bottles and PVC/PE/PVDC/Al of 100.

25 mg tablet: HDPE bottles of 100 and PVC/PE/PVDC/Al blister packs of 50 and 100.

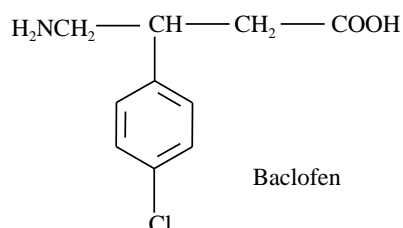
### 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

### 6.7 PHYSICOCHEMICAL PROPERTIES

#### Chemical structure

The chemical structure of baclofen is:



**CAS number** 1134-47-0

**Empirical formula** C<sub>10</sub>H<sub>12</sub>ClNO<sub>2</sub>

**Molecular weight** 213.67

## 7 MEDICINE SCHEDULE (POISONS STANDARD)

**Poison schedule:** 4 – Prescription Only Medicine

## 8 SPONSOR

NOVARTIS Pharmaceuticals Australia Pty Limited

ABN 18 004 244 160

54 Waterloo Road

Macquarie Park NSW 2113

Telephone 1 800 671 203

Web site: [www.novartis.com.au](http://www.novartis.com.au)

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## 9 DATE OF FIRST APPROVAL

31 August 2001

## 10 DATE OF REVISION

21 January 2025

### SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
2, 6.4, 6.5	Addition of 10 mg blister pack presentation.

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