

BACLOFEN 5 MG/5 ML ORAL SOLUTION

PL 06464/2354

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted a Marketing Authorisation (licence) for the medicinal product Baclofen 5 mg/5 mL Oral Solution (product licence number: 06464/2354).

Baclofen 5 mg/5 mL Oral Solution contains the muscle relaxant baclofen. It is used to relieve muscle spasms that may occur during certain illnesses affecting the nervous system, such as multiple sclerosis, or following injuries to the head or spine.

Baclofen 5 mg/5 mL Oral Solution raised no clinically significant safety concerns and it was, therefore, judged that the benefits of using this product outweigh the risks; hence a Marketing Authorisation has been granted.

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Baclofen 5 mg/5 mL Oral Solution to Waymade Plc (Trading as Sovereign Medical) on 19 November 2008. This medicine is only available on prescription.

This standard abridged application was made under Directive 2001/83/EC Article 10.1, first paragraph, claiming that this medicinal product is a generic version of the reference product Lioresal Liquid (PL 00101/0503). This reference product was originally licensed to Ciba-Geigy PLC, (trading as Ciba Pharmaceuticals) on 5 February 1986 before a change of ownership to Novartis Pharmaceuticals UK Ltd (trading as Ciba Laboratories) on 21 September 1997. The 10-year rule is, therefore, adhered to and this is considered satisfactory.

Baclofen is a skeletal muscle relaxant that inhibits transmission at a spinal level and depresses the central nervous system. Baclofen is indicated for the treatment of chronic severe spasticity resulting from disorders such as multiple sclerosis or traumatic partial section of the spinal chord.

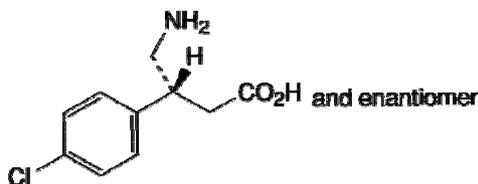
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE

Nomenclature

INN:	Baclofen
Chemical name (Ph.Eur.):	(3 <i>RS</i>)-4-amino-3-(4-chlorophenyl)butanoic acid
Chemical name (applicant):	(3 <i>RS</i>)-3-(4-aminomethyl)-4-chlorobutanoic acid
Other names:	b-(aminomethyl)-4-chlorobenzenepropanoic acid b-(aminomethyl)- <i>p</i> -chlorohydrocinnamic acid γ -amino-b-(Chlorophenyl) butyric acid b-(4-chlorophenyl) GABA
CAS number:	1134-47-0

Structure



Molecular formula:	C ₁₀ H ₁₂ ClNO ₂
Molecular weight:	213.7

Baclofen is a white or almost white powder. It is slightly soluble in water, very slightly soluble in alcohol and practically insoluble in acetone. It dissolves in dilute mineral acids and in dilute solutions of alkali hydroxides and shows polymorphism. The structure of Baclofen contains one asymmetric centre, meaning that two enantiomers are produced in the synthesis. The product used is a racemic mixture.

An appropriate specification in line with the Ph Eur monograph has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Full specifications are provided for the packaging used to store the baclofen, these are satisfactory.

Appropriate stability data have been generated supporting a retest period of 60 months.

DRUG PRODUCT

Description and Composition of the Drug Product

The product is presented as a clear, colourless to very slightly yellow solution with an odour of raspberries. Each 5 ml of the suspension contains 5 mg baclofen. Other ingredients are methylparahydroxybenzoate, propylparahydroxybenzoate, raspberry flavour, hydroxyethylcellulose, propylene glycol, sorbitol and purified water.

All excipients are controlled in line with the relevant Ph. Eur. monograph, with the exception the raspberry flavouring which is controlled according to an in-house specification (in the absence of a monograph for this excipient this is acceptable). Satisfactory certificates of analysis have been provided for all excipients.

The applicant has provided satisfactory certificates stating that neither the excipients nor the active substance contain substances of human or animal origin.

There were no novel excipients used and no overages.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on product batches and the results are satisfactory.

Finished product specification

The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System

The finished product is packed amber, 300 mL, Type III glass bottles with polypropylene tamper evident caps with expanded polyethylene liners. The proposed packaging is standard for oral liquids and includes amber glass to provide light protection for the product. Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food. Stability results are considered acceptable to demonstrate the compatibility of the product with the proposed packaging.

Stability

Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 2 years before opening and of 60 days once the product is first opened are appropriate. The storage precautions are "Protect from light", "Do not store above 25°C" and "Do not refrigerate."

Bioequivalence / Bioavailability

No bioequivalence study is required as the product is an aqueous oral solution at the time of administration and contains the active substance in the same concentration as an oral solution currently approved as a medicinal product.

Essential similarity

The active substance in the product is controlled to Ph.Eur. standards and the finished product specification is in line with that of the innovator and of the BP monograph for Baclofen oral solution. The claim of essential similarity and the biowaiver for this oral solution may be supported.

Product literature

All product literature (SPCs, PILs and labelling) are satisfactory. The package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

Conclusions

A marketing authorisation may be granted for this application.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none is required for an application of this type.

CLINICAL ASSESSMENT

Overview

An appropriate clinical overview has been included in the dossier. The clinical overview contains a sufficient outline of the published literature concerning the clinical pharmacology, efficacy and safety of baclofen.

Biowaver

The product proposed for marketing authorisation is an aqueous oral solution containing the active substance in the same concentration as the UK reference product, Lioresal Liquid. Thus, in accordance with the "Note for Guidance on the Investigation of Bioavailability and Bioequivalence" (CPMP/EWP/QWP/ 1401/98), the applicant is not required to submit a bioequivalence study.

Clinical study reports

This application is a generic application referring to the reference medicinal product Lioresal Liquid, which has been authorised for more than 10 years in the UK. According to Article 10(1) of Directive 2001/83/EC, in this type of application the applicant is not required to provide results of clinical trials.

Product literature

All product literature (SPCs, PILs and labelling) are satisfactory. The package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

Assessor's overall conclusions

It is recommended that a marketing authorisation can be granted.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Baclofen 5 mg/5 mL Oral Solution are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

The efficacy of baclofen is well established.

The SPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable, no significant preclinical or clinical safety concerns were identified, and benefit has been shown to be associated with Baclofen 5 mg/5 mL Oral Solution. The risk: benefit ratio is therefore considered to be acceptable.

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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the marketing authorisation application on 28 March 2006
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 11 May 2006
3	Following assessment of the application the MHRA requested further information relating to the quality dossier on 26 October 2006
4	The applicant responded to the MHRA's requests, providing further information on the quality dossier on 10 May 2007
5	Following assessment of the response the MHRA requested further information relating to the quality dossier on 19 December 2007
6	The applicant responded to the MHRA's requests, providing further information on the quality dossier on 29 January 2008
7	Following assessment of the response the MHRA requested further information relating to the quality dossier on 8 April 2008
8	The applicant responded to the MHRA's requests, providing further information on the quality dossier on 21 May 2008
9	The application was determined on 19 November 2008

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Baclofen 5 mg/5 mL Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 5 mg Baclofen.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral Solution

A colourless to pale yellow solution with a raspberry flavour.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Baclofen 5 mg/5 mL Oral Solution is indicated for the relief of spasticity of voluntary muscle resulting from such disorders as: multiple sclerosis, other spinal lesions, e.g. tumours of the spinal cord, syringomyelia, motor neurone disease, transverse myelitis, traumatic partial section of the cord.

Baclofen 5 mg/5 mL Oral Solution is also indicated in adults and children for the relief of spasticity of voluntary muscle arising from e.g. cerebrovascular accidents, cerebral palsy, meningitis, traumatic head injury.

Patient selection is important when initiating Baclofen 5 mg/5 mL Oral Solution therapy; it is likely to be of most benefit in patients whose spasticity constitutes a handicap to activities and/or physiotherapy. Treatment should not be commenced until the spastic state has become stabilised.

4.2 Posology and method of administration

Before starting treatment with Baclofen 5 mg/5 mL Oral Solution it is prudent to realistically assess the overall extent of clinical improvement that the patient may be expected to achieve. Careful titration of dosage is essential (particularly in the elderly) until the patient is stabilised. If too high a dose is initiated or if the dosage is increased too rapidly side effects may occur. This is particularly relevant if the patient is ambulant in order to minimise muscle weakness in the unaffected limbs or where spasticity is necessary for support.

Adults: The following gradually increasing dosage regimen is suggested, but should be adjusted to suit individual patient requirements.

5mg three times a day for three days

10mg three times a day for three days

15mg three times a day for three days

20mg three times a day for three days

Satisfactory control of symptoms is usually obtained with doses of up to 60mg daily, but a careful adjustment is often necessary to meet the requirements of each individual patient. The dose may be increased slowly if required, but a maximum daily dose of more than 100mg is not advised unless the patient is in hospital under

careful medical supervision. Small frequent dosage may prove better in some cases than larger spaced doses. Also some patients benefit from the use of Baclofen 5 mg/5 mL Oral Solution only at night to counteract painful flexor spasm. Similarly a single dose given approximately 1 hour prior to performance of specific tasks such as washing, dressing, shaving, physiotherapy, will often improve mobility.

Once the maximum recommended dose has been reached, if the therapeutic effect is not apparent within 6 weeks a decision whether to continue with Baclofen 5 mg/5 mL Oral Solution should be taken.

Elderly:

Elderly patients may be more susceptible to side effects, particularly in the early stages of introducing Baclofen 5 mg/5 mL Oral Solution. Small doses should therefore be used at the start of treatment, the dose being titrated gradually against the response, under careful supervision. There is no evidence that the eventual average maximum dose differs from that in younger patients.

Children:

A dosage range of 0.75-2mg/kg body weight should be used. In children over 10 years of age, however a maximum daily dosage of 2.5mg/kg body weight may be given. Treatment is usually started with 2.5mg given 4 times daily. The dosage should be cautiously raised at about 3 day intervals, until it becomes sufficient for the child's individual requirements. The recommended daily dosages for maintenance therapy are as follows:

Children aged: 12 months - 2 years: 10-20mg

2 years - 6 years: 20-30mg

6 years - 10 years: 30-60mg

Patients with impaired renal function:

In patients with impaired renal function or undergoing chronic haemodialysis, a particularly low dosage of Baclofen 5 mg/5 mL Oral Solution should be selected i.e. approx. 5mg daily. Signs of overdose have been observed in patients with renal impairment taking oral Baclofen at doses of more than 5mg per day.

Patients with spastic states of cerebral origin:

Unwanted effects are more likely to occur in these patients. It is therefore recommended that a very cautious dosage schedule be adopted and that patients be kept under appropriate surveillance.

4.3 Contraindications

Hypersensitivity to baclofen, peptic ulceration.

4.4 Special warnings and precautions for use

Psychotic disorders, schizophrenia, depressive or manic disorders, confusional states or Parkinson's disease may be exacerbated by treatment with Baclofen 5 mg/5 mL Oral Solution. Patients suffering from these conditions should therefore be treated cautiously and kept under close surveillance.

Baclofen 5 mg/5 mL Oral Solution may also exacerbate epileptic manifestations but can be employed provided appropriate supervision and adequate anticonvulsive therapy are maintained. Baclofen 5 mg/5 mL Oral Solution should be used with extreme care in patients already receiving antihypertensive therapy, (see Interactions).

Baclofen 5 mg/5 mL Oral Solution should be used with caution in patients suffering from cerebrovascular accidents or from respiratory, hepatic or renal impairment.

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Signs of overdose have been observed in patients with renal impairment taking oral baclofen at doses of more than 5mg per day.

Under treatment with Baclofen 5 mg/5 mL Oral Solution neurogenic disturbances affecting emptying of the bladder may show an improvement. In patients with pre-existing sphincter hypertonia, acute retention of urine may occur; the drug should be used with caution in such cases.

Abrupt withdrawal:

Anxiety and confusional states, hallucinations, psychotic, manic or paranoid states, convulsions (status epilepticus), dyskinesia, tachycardia, hyperthermia and as rebound phenomenon temporary aggravation of spasticity have been reported with abrupt withdrawal of baclofen, especially after long term medication. Treatment should always, (unless serious adverse effects occur), therefore be gradually discontinued by successively reducing the dosage over a period of about 1-2 weeks.

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

4.5 Interaction with other medicinal products and other forms of interaction

Where Baclofen 5 mg/5 mL Oral Solution 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 Baclofen 5 mg/5 mL Oral Solution may be potentiated, resulting in pronounced muscular hypotonia.

Since concomitant treatment with Baclofen 5 mg/5 mL Oral Solution and anti-hypertensives is 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.

Drugs that may produce renal insufficiency e.g. ibuprofen may reduce baclofen excretion leading to toxic effects. In patients with Parkinson's disease receiving treatment with baclofen and levodopa plus carbidopa, there have been reports of mental confusion, hallucinations, nausea and agitation.

4.6 Pregnancy and lactation

During pregnancy, especially in the first 3 months, Baclofen 5 mg/5 mL Oral Solution should only be employed if its use is of vital necessity. The benefits of the treatment for the mother must be carefully weighed against the possible risks for the child.

Baclofen 5 mg/5 mL Oral Solution crosses the placental barrier.

In mothers taking Baclofen 5 mg/5 mL Oral Solution in therapeutic doses, the active substance passes into the breast milk, but in quantities so small that no undesirable effects on the infant are to be expected.

4.7 Effects on ability to drive and use machines

The patient's reactions may be adversely affected by Baclofen 5 mg/5 mL Oral Solution induced sedation or decreased alertness, patients should therefore exercise due caution. Operating equipment or machinery may be hazardous.

4.8 Undesirable effects

Side effects:

Unwanted effects occur mainly at the start of treatment, if the dosage is raised too rapidly, if large doses are employed, or in elderly patients. They are often transitory and can be attenuated or eliminated by reducing the dosage; they are seldom severe enough to necessitate withdrawal of the medication.

Should nausea persist following a reduction in dosage, it is recommended that Baclofen 5 mg/5 mL Oral Solution be ingested with food or a milk beverage.

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.

Frequency estimates: frequent > 10%, occasional > 1% - 10%, Rare > 0.001% - 1%, isolated cases < 0.001%.

Central Nervous System:

Frequent: particularly at the start of treatment daytime sedation, drowsiness, and nausea may frequently occur.

Occasional: respiratory depression, light-headedness, lassitude, exhaustion, mental confusion, dizziness, headache, insomnia, euphoria, depression, muscular weakness, ataxia, tremor, hallucinations, nightmares, myalgia, nystagmus, dry mouth.

Rare: paraesthesia, dysarthria. Lowering of the convulsion threshold and convulsions may occur, particularly in epileptic patients.

Sense organs:

Occasional: accommodation disorders, visual disturbance.

Rare: dysgeusia.

Gastro-intestinal tract:

Frequent: nausea.

Occasional: mild gastro-intestinal disturbances, constipation, diarrhoea, retching and vomiting.

Rare: abdominal pain

Cardiovascular system:

Occasional: hypotension, diminished cardiovascular function.

Urogenital system:

Frequent: frequency of micturition, enuresis, dysuria.

Rare: urinary retention, impotence.

Liver:

Rare: disorders of hepatic function.

Skin:

Occasional: hyperhidrosis, skin rash.

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

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

4.9 Overdose

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, bradycardia; hypothermia; nausea, vomiting, diarrhoea, hypersalivation; elevated LDH, SGOT and AP values. Patients with renal impairment can develop signs of overdose even on low doses of oral Baclofen 5 mg/5 mL Oral Solution (see section 4.2 Posology and Method of administration and 4.4 Special warnings and special precautions for use.)

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 patients should be intubated prior to gastric lavage), administration of activated charcoal; if necessary, saline aperient; in respiratory depression, administration of artificial respiration, also measures in support of cardiovascular functions. Since the drug is excreted chiefly via the kidneys, generous quantities of fluid should be given, possibly together with a diuretic. In the event of convulsions diazepam should be administered cautiously i.v.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Baclofen is an antispastic agent acting at the spinal level. A gamma-aminobutyric acid (GABA) derivative, baclofen is chemically unrelated to other antispastic agents. Baclofen depresses monosynaptic and polysynaptic reflex transmission, probably by stimulating the GABA_B receptors, this stimulation in turn inhibiting the release of the excitatory amino acids glutamate and aspartate. Neuromuscular transmission is unaffected by baclofen.

The major benefits of baclofen stem from its ability to reduce painful flexor spasms and spontaneous clonus thereby facilitating the mobility of the patient, increasing independence and helping rehabilitation.

Baclofen also exerts an antinociceptive effect. General well being is often improved and sedation is less often a problem than with centrally acting drugs.

Baclofen stimulates gastric acid secretion.

5.2 Pharmacokinetic properties

Absorption:

Baclofen is rapidly and completely absorbed from the gastro-intestinal tract. No significant difference between the solution and tablet formulations is observed in respect of t_{max} , c_{max} and bioavailability. Following oral administration of single doses (10-30mg) peak plasma concentrations are recorded after 0.5 to 1.5 hours and areas under the serum concentration curves are proportional to the dose.

Distribution:

The volume of distribution of baclofen is 0.7 l/kg and the protein binding rate is approximately 30%. In cerebrospinal fluid active substance concentrations are approximately 8.5 times lower than in the plasma.

Biotransformation:

Baclofen is metabolised to only a minor extent. Deamination yields the main metabolite, -(p-chlorophenyl)-4-hydroxybutyric acid, which is pharmacologically inactive.

Elimination/excretion:

The plasma elimination half-life of baclofen averages 3 to 4 hours. The serum protein binding rate is approximately 30%.

Baclofen is eliminated largely in unchanged form. Within 72 hours, about 75% of the dose is excreted via the kidneys with about 5% of this amount as metabolites.

Elderly:

The pharmacokinetics of baclofen in elderly patients are virtually the same as in young subjects. The peak plasma concentrations of baclofen in elderly patients are slightly lower and occur later than in healthy young subjects but the AUCs are similar in the two groups.

5.3 Preclinical safety data

Baclofen increases the incidence of omphaloceles (ventral hernias) in the foetuses of rats given approximately 13 times the maximum oral dose (on a mg/kg basis) recommended for human use. This was not seen in mice or rabbits.

An apparently dose related increase in the incidence of ovarian cysts, and a less marked increase in enlarged and/or haemorrhagic adrenals have been observed in female rats treated for 2 years. The clinical relevance of these findings is not known. Experimental evidence to date suggests that baclofen does not possess either carcinogenic or mutagenic properties.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methylparahydroxybenzoate (E218)
Propylparahydroxybenzoate (E216)
Raspberry flavour (containing propylene glycol (E490/E1520))
Hydroxyethylcellulose (E1525)
Propylene glycol (E490/E1520)
Sorbitol (E420)
Purified water.

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

2 years

In Use Shelf Life

60 days

6.4 Special precautions for storage

Protect from light. Do not store above 25°C. Do not refrigerate.

6.5 Nature and contents of container

Amber 300 mL Type III glass bottles with polypropylene tamper evident caps with expanded polyethylene liners.

Pack size: 300 mL.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Waymade Plc
Trading as
Sovereign Medical
Sovereign House
Miles Gray Road
Basildon
Essex
SS14 3FR

8 MARKETING AUTHORISATION NUMBER(S)

PL 06464/2354

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

19/11/2008

10 DATE OF REVISION OF THE TEXT

19/11/2008

PATIENT INFORMATION LEAFLET

Baclofen 5 mg/5 mL Oral Solution

Baclofen

Read all of this leaflet carefully before you start taking this medicine.

- Please keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What Baclofen 5 mg/5 mL Oral Solution is and what it is used for
2. Before you take Baclofen 5 mg/5 mL Oral Solution
3. How to take Baclofen 5 mg/5 mL Oral Solution
4. Possible side effects
5. How to store Baclofen 5 mg/5 mL Oral Solution
6. Further information

1. WHAT BACLOFEN 5 MG/5 ML ORAL SOLUTION IS AND WHAT IT IS USED FOR

The name of your medicine is Baclofen 5 mg/5 mL Oral Solution. The active ingredient is baclofen.

Baclofen is a muscle-relaxant.

Baclofen 5 mg/5 mL Oral Solution is used to relieve muscle spasms that may occur during certain illnesses affecting the nervous system, such as multiple sclerosis, or following injuries to the head or spine.

2. BEFORE YOU TAKE BACLOFEN 5 MG/5 ML ORAL SOLUTION

Do not take this medicine if:

- you have ever had an **allergic reaction** to any of the ingredients of Baclofen 5 mg/5 mL Oral Solution or any other medicines that you may have taken to relieve muscle spasms. The signs of an allergic reaction may have been itching, reddening of the skin or difficulty in breathing
- you have or have ever had a **stomach ulcer**.

Take special care with this medicine and tell your doctor or pharmacist if:

- you suffer from epilepsy
- you have difficulties in passing water
- you suffer from any serious liver, kidney or lung disease
- you suffer from mental illness, for example: depression, manic disorders, schizophrenia, psychotic disorders or confused states
- you suffer from diabetes
- you suffer from Parkinson's disease
- you are pregnant, trying to become pregnant or are breast-feeding
- you have breathing problems
- you have had a stroke, a "mini stroke" (transient ischaemic attack) or have been told you may be at risk of these.

Tell your doctor before taking this medicine if you have been told that you have an **intolerance to some sugars**.

This is because Baclofen 5mg/5 mL Oral Solution contains sorbitol, a type of sugar.

Taking other medicines

Tell your doctor if you are taking any other medicines, especially the following:

- medicines for depression, e.g. tricyclic antidepressants
- medicines for high blood pressure
- medicines for arthritis or pain, e.g. ibuprofen
- medicines which slow down the nervous system, e.g. antihistamines
- sedatives or sleeping tablets e.g. diazepam
- medicines for pain relief e.g. morphine or codeine
- medicines for epilepsy e.g. phenytoin or carbamazepine
- medicines for Parkinson's disease e.g. levodopa or carbidopa

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without prescription.

Other special warnings

- Be careful when drinking **alcohol** - it may affect you more than usual.
- Whilst you are taking this medicine, your doctor may want to give you a **check up** from time to time.
- Tell your doctor that you are taking Baclofen 5 mg/5 mL Oral Solution if you are going to have an **operation** of any kind.

Pregnancy and breast-feeding

Tell your doctor if you become pregnant, or if you are breast-feeding.

Driving and using machines

This medicine can make you feel drowsy or cause blurred vision. Do not drive or operate machinery if you are affected.

3. HOW TO TAKE BACLOFEN 5 MG/5 ML ORAL SOLUTION

Always take your medicine exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. In all patients the dose is increased gradually, usually every 3 days, starting with doses of 5-15 mg (5-15 mL) per day. The final dose depends on how you respond.

The usual doses of Baclofen 5 mg/5 mL Oral Solution are as follows:

Adults

20 mg (20 mL) three times a day. The maximum daily dose is 100 mg (100 mL). However some patients take it only at night or about one hour before doing a task such as washing, dressing, shaving or having physiotherapy.

If you are in hospital, a higher dose may be used.

The dose may be reduced for elderly patients.

Children

The dosage depends on the weight of the child. It will be worked out using the range 0.75-2 mg per kg of body weight. A starting dose of 2.5 mg (2.5 mL) four times a day is often used. The dose may be increased every three days depending on the child's response, until a dose is found which works well (maintenance dose).

Guidelines for maintenance doses in children are:

Age 12 months - 2 years:	10 - 20 mg a day	(10 - 20 mL a day)
Age 2 - 6 years:	20 - 30 mg a day	(20 - 30 mL a day)
Age 6 - 10 years:	30 - 60 mg a day	(30 - 60 mL a day)

If you have kidney problems

A lower dose of 5 mg (5 mL) daily may be used.

If you are not sure about how much medicine to take, please speak to your doctor or pharmacist.
Shake the bottle well before you take your medicine.
If you feel sick after taking this medicine, you may find it helps to take it with food or a milk drink.

Do not stop taking your medicine suddenly; unwanted effects such as muscle spasms and increased muscle rigidity, fast heart rate, fever, confusion, hallucinations, changes in mood and emotion, mental disorders, feeling persecuted or convulsions (fits) may occur. Ask your doctor how to reduce the dose gradually.

If you take more solution than you should

If you accidentally take too much of your medicine, tell your doctor **at once** or contact your nearest hospital casualty department. Take your medicine with you.

If you forget to take your medicine

If you forget to take a dose, just take the next dose at the usual time. DO NOT take a double dose.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Baclofen 5 mg/5 mL Oral Solution can cause side effects, although not everybody gets them.

You are unlikely to get any of the following, but if you do, **tell your doctor immediately**:

- Skin reddening, itching, difficulty in breathing or swelling. These could be signs of an allergic reaction and might be due to some of the ingredients. These might not happen immediately - they can be delayed.
- Excessive weakness of the limbs or feeling tired and exhausted
- Difficulty in passing water
- Hallucinations (seeing or hearing things which are not there)
- Fits
- Blurred or double vision, difficulty in focussing, trembling or flicking of the eyes
- Symptoms similar to the effects of alcohol
- Fainting
- Breathing difficulties
- Mood changes
- Skin rash

If you notice any side effects mentioned above, please **tell your doctor or pharmacist**.

Other side effects may include:

- Feeling sleepy, dizzy, light-headed or slightly confused
- Feeling or being sick, retching, constipation or diarrhoea
- Headache or sleeplessness
- Unsteadiness, trembling or other problems with muscle control
- Pain in your muscles or abdomen
- Numbness or tingling in hands or feet; increased muscle spasm
- Sexual problems in men, e.g. impotence
- Increased sweating
- Dry mouth or changes in the way things taste, slurred speech
- Increased need to pass water
- Nightmares
- Changes in blood sugar or blood levels of certain liver enzymes
- Slow heart rate.

These effects are often mild and may wear off after a few days' treatment. If they are severe or last for more than a few days, tell your doctor. Older people may be at more risk of these effects, particularly at the start of treatment.

If any of the side effects get severe, or if you notice any side effects not listed in this leaflet, please **tell your doctor or pharmacist immediately**.

5. HOW TO STORE BACLOFEN 5 MG/5 ML ORAL SOLUTION

Do not use after the expiry date that is stated on the carton and bottle labels.

Once opened, the solution should be used within 60 days.

Store the solution so that it is protected from light. Do not store above 25°C. Do not put it in the fridge.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

Return any unused medicine to your pharmacist.

6. FURTHER INFORMATION

What Baclofen 5 mg/5 mL Oral Solution contains:

Each 5 mL of solution contains 5 mg of the active substance, baclofen.

The other ingredients are: methylparahydroxybenzoate (E218); propylparahydroxybenzoate (E216); raspberry flavour; hydroxyethylcellulose (E1525); propylene glycol (E490/E1520); sorbitol (E420) and purified water.

What Baclofen 5 mg/5 mL Oral Solution looks like and the contents of the pack:

Baclofen 5 mg/ 5 mL Oral Solution is a clear, colourless to pale yellow solution, which is available in amber glass bottles with tamper-evident caps.

Each bottle contains 300 mL oral solution.

Each bottle is packed singularly in a carton.

Marketing Authorisation Holder and Manufacturer

Waymade Plc trading as Sovereign Medical, Sovereign House, Miles Gray Road, Basildon, Essex, SS14 3FR.

This leaflet does not contain all the available information about your medicine.

If you have any questions or are not sure about anything, ask your doctor or pharmacist.

The information in this leaflet applies only to Baclofen 5 mg/5 mL Oral Solution.



Date of preparation of leaflet: August 2007

LABELLING

Label:

5mg/5mL

Baclofen
5mg/5mL
Oral Solution

Baclofen
300mL

Each 5mL of solution contains 5mg of Baclofen,
Also contains E218, E216, E1525, E490/E1520
and E420.
Please read leaflet for further information.
Use as directed by your doctor,
Once opened the solution should be used within 60
days, Protect from light, Do not store above 25°C,
Do not refrigerate.
Further information is provided in the patient
information leaflet.

**KEEP OUT OF THE REACH AND SIGHT OF
CHILDREN.**

PL 06464/2354
Waymade PLC, trading as Sovereign Medical,
Sovereign House, Miles Gray Road, Basildon,
Essex, SS14 3FR

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 **SOVEREIGN**
M E D I C A L

Carton:

