1 Name of the Medicinal Product

BACLOFEN TABLETS BP 10mg

2 Qualitative and Quantitative Composition

Each tablet contains 10mg Baclofen PhEur.

Excipient with known effect: Lactose PhEur 89.50mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White to off-white uncoated tablets.

White to off-white, circular, biconvex uncoated tablets impressed “C” on one face, and the identifying letters “B” “L” on either side of a central division line on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Baclofen is indicated for:

1) The relief of spasticity of voluntary muscle resulting from disorders such as multiple sclerosis and other spinal lesions, including tumours of the spinal cord, motor neurone disease, syringomyelia, transverse myelitis and traumatic partial section of the spinal cord.

2) Adults and children in the relief of spasticity of voluntary muscle arising from conditions such as cerebral palsy, cerebrovascular accidents, traumatic head injury and meningitis.

Treatment with Baclofen should not be initiated until the spastic state has become stabilised and it should be administered selectively; it is most likely to be of benefit to patients whose spasticity constitutes a handicap to activities or physiotherapy.

Paediatric population

Baclofen is indicated in patients 0 to <18 years for the symptomatic treatment of spasticity of cerebral origin, especially where due to infantile cerebral palsy, as well as following cerebrovascular accidents or in the presence of neoplastic or degenerative brain disease.

Baclofen is also indicated for the symptomatic treatment of muscle spasms occurring in spinal cord diseases of infectious, degenerative, traumatic, neoplastic, or unknown origin such as multiple sclerosis, spastic spinal paralysis, amyotrophic lateral sclerosis, syringomyelia, transverse myelitis, traumatic paraplegia or paraparesis, and compression of the spinal cord.
4.2 Posology and Method of Administration

Posology
Before commencing treatment the overall extent of clinical improvement that the patient may be expected to achieve must be realistically assessed. Careful titration of dosage is essential (particularly in the elderly) until the patient is stabilised. If the initial dosage is too high 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 incremented dosage regime is suggested but may need adjustment to suit individual patient requirements.
- 5mg three times daily for three days.
- 10mg three times daily for three days.
- 15mg three times daily for three days.
- 20mg three times daily for three days.
Satisfactory control of symptoms is usually obtained with doses up to 60mg daily but a careful adjustment is often necessary to meet the requirements of each individual patient. Dosage may be slowly increased where necessary to a maximum daily dose of not more than 100mg unless the patient is in hospital under careful medical supervision. Small frequent dosage regimes may prove to be more beneficial in some cases than larger spaced doses. Additionally, some patients may benefit from the administration of Baclofen at night only in order to counteract painful flexor spasm. Similarly, a single dose given approximately 1 hour prior to the performance of specific tasks such as washing, shaving, dressing and physiotherapy will often improve mobility.
Once the maximum recommended dosage has been reached and a therapeutic effect is not apparent within 6 weeks a decision should be made whether to continue treatment with Baclofen.

Paediatric population (0 to <18 years)
Treatment should usually be started with a very low dose (corresponding to approximately 0.3 mg/kg a day), in 2-4 divided doses (preferably in 4 divided doses).

The dosage should be raised cautiously, at about 1 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 weight. The total daily dose should not exceed a maximum of 40 mg/day in children below 8 years of age. In children over 8 years of age a maximum daily dose of 60 mg/day may be given.

Baclofen tablets are not suitable for use in children below 33 kg body weight.

Elderly
Elderly patients may be more susceptible to side-effects, especially during initial therapy. 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 dosage differs from that in younger patients.

**Renal impairment**

In patients with impaired renal function or undergoing chronic haemodialysis, a particularly low dosage of Baclofen should be selected *ie* approximately 5mg daily.

**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.

**Method of Administration**

For oral administration.

### 4.3 Contraindications

- Hypersensitivity to the active substance or any of the excipients listed in 6.1.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- Active peptic ulceration as Baclofen stimulates gastric acid secretion.
- Porphyria.

### 4.4 Special Warnings and Precautions for Use

- Severe psychiatric disorders may be exacerbated by treatment with Baclofen. Patients suffering from these conditions should therefore be treated cautiously and kept under close surveillance.
- Baclofen may also exacerbate epileptic manifestations but can be employed provided appropriate supervision and adequate anticonvulsive therapy are maintained.
- Baclofen should be used with extreme care in patients already receiving antihypertensive therapy (see “Interactions”).
- Baclofen should be used with caution in patients suffering from cerebrovascular accidents or from respiratory, hepatic or renal impairment.
- Baclofen stimulates gastric acid secretion and should be used with caution in patients with a history of peptic ulceration.
- Since under treatment with Baclofen neurogenic disturbances affecting emptying of the bladder may show an improvement, whereas in patients with pre-existing sphincter hypertonia acute retention of urine may occur, the drug should be used with caution in such patients.
- 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.
- **Withdrawal:** Anxiety and confusional states, hallucinations, psychotic, manic or paranoid states, convulsions (status epilepticus), tachycardia 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.

Paediatric population
There is very limited clinical data on the use of Baclofen in children under the age of one year. Use in this patient population should be based on the physician’s consideration of individual benefit and risk of therapy.

4.5 Interactions with other medicinal products and other forms of interaction

- Alcohol, anxiolytics and hypnotics: Alcohol and other CNS depressants may exacerbate the CNS effects of baclofen (daytime sedation, drowsiness) and should be avoided.
- Anaesthetics: Pre-treatment with baclofen may prolong the duration of fentanyl anaesthesia.
- Antidepressants, tricyclic: Tricyclic antidepressants can enhance the muscle relaxant effects of baclofen, resulting in profound muscle hypotonia so caution should be used if baclofen and tricyclic antidepressants are used concomitantly. In addition, tricyclic antidepressants can cause sedation and drowsiness which may be additive to the side effects of baclofen.
- Antihypertensives and diuretics: The hypotensive activity of baclofen may be potentiated by concomitant treatment with antihypertensive agents and diuretics. It may be necessary to adjust the dosage if baclofen is given to patients receiving antihypertensive therapy.
- Dopaminergics: It is recommended that levodopa and baclofen should not be given concomitantly. Reports of hallucination, confusion, headache and nausea developing in patients with parkinsonism shortly after baclofen was added to their medication. The interaction was thought to be due to an exacerbation of the side effects due to baclofen.
- Lithium: Patients receiving lithium and baclofen concomitantly should be monitored for severe aggravation of hyperkinetic symptoms, especially in patients with Huntington’s chorea.
- Memantine: Memantine may modify the effects of baclofen.
- NSAIDs: Because of their potential adverse effect on renal function, NSAIDs may indirectly be associated with decreased excretion of baclofen. (See section 4.2-patients with impaired renal function).

4.6 Fertility, pregnancy and Lactation

Pregnancy
Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown. However, during pregnancy, especially in the first 3 months, Baclofen 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 crosses the placental barrier.
**Breast-feeding**
In mothers taking Baclofen in therapeutic doses, the active substance passes into 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**

Baclofen may cause sedation, decreased alertness, dizziness and light-headedness. Patients should be warned that if affected they should not drive, operate machinery or take part in activities where these may put themselves or others at risk.

**4.8 Undesirable 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.

- **Central nervous system**: Particularly at the start of treatment, unwanted effects such as daytime sedation, drowsiness, and nausea may frequently occur. Also occasionally encountered are dryness of the mouth, respiratory depression, light-headedness, lassitude, exhaustion, mental confusion, dizziness, retching, vomiting, headache and insomnia. Should nausea persist following a reduction in dosage, it is recommended that Baclofen be ingested with food or a milk drink.

- **Neurological and/or psychiatric manifestations which have occasionally or rarely been reported include**: euphoria, depressive states, paraesthesia, myalgia, muscular weakness, ataxia, tremor, nystagmus, accommodation disorders, hallucinations, nightmares. It is often difficult to distinguish between these manifestations and those of the disease under treatment. Lowering of the convulsion threshold and attacks of convulsions may possibly occur, particularly in epileptic patients.

- **Gastrointestinal tract**: Frequently nausea. Occasionally, mild gastrointestinal disturbances (constipation, diarrhoea).

- **Cardiovascular system**: Occasionally, hypotension, cardiovascular depression.

- **Urogenital system**: Occasionally or rarely, dysuria, frequency of micturition and enuresis are reported frequently. It is often difficult to distinguish between these manifestations and those of the disease under treatment.

- **Other unwanted effects**: In rare or isolated cases visual disturbances, alterations in the taste sensation, hyperhidrosis, skin rash, deterioration in liver function tests. There have been rare reports of hypothermia.

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 (ie by reducing the doses given during the day and possibly increasing the evening dose).

**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; website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Symptoms: Prominent features are signs of central nervous depression eg 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 vasodilation, hypotension, bradycardia; 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 CNS eg alcohol, diazepam, tricyclic antidepressants, have been taken at the same time. Symptoms may occur at lower dosages in patients with impaired renal function or in the elderly.

Treatment: No specific antidote is known. Elimination of the drug from the gastrointestinal tract (induction of vomiting, gastric lavage; comatose, drowsy or hyporeflexic 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; inducing artificial or assisted respiration and possibly aggressive maintenance of cardiovascular function. 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 iv.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Muscle relaxant, other centrally acting agent.
ATC CODE: M03B X01

Baclofen, a GABA (gamma-aminobutyric acid) derivative, is chemically unrelated to other antispastic agents and acts at spinal level, reducing spasticity and spasm. Baclofen depresses monosynaptic and polysynaptic reflex transmission, probably by simulating the GABA\textsubscript{B}-receptors, this simulation in turn inhibiting the release of the excitatory amino acids glutamate and aspartate. Neuromuscular transmission is unaffected by Baclofen. Baclofen also exerts an antinociceptive effect. Baclofen may act at supraspinal sites producing CNS depression.

5.2 Pharmacokinetic properties

- Absorption
Baclofen is rapidly and almost completely absorbed from the gastrointestinal tract. The peak plasma concentration occurs about from 1 to 3 hours following ingestion.
• **Distribution**
Baclofen crosses the blood-brain barrier and concentrations in the CSF are about 12% of those in plasma. Protein binding is about 30%.

• **Biotransformation**
Baclofen is metabolised by deamination to a small extent. The main metabolite, β-(p-chlorophenyl)-4-hydroxobutyric acid, is pharmacologically inactive.

• **Elimination**
The elimination half-life of baclofen is about 3 to 4 hours in plasma and about 5 hours in CSF. This half life may increase to 35 hours in overdose. About 70 to 80% of a dose is excreted in the urine mainly as unchanged drug and about 15% is metabolised in the liver.

5.3. **Preclinical safety data**

There is no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.
Baclofen increases the incidence of omphaloceles (ventral hernias) in the foetuses of rats at high doses. A dose related increase in the incidence of ovarian cysts, and less marked increase in enlarged and/or hemorrhagic adrenals have been observed in female rats treated for 2 years. No teratogenic effects have been noted in mice or rabbits. The clinical relevance of these findings is not known.

6. **PHARMACEUTICAL PARTICULARS**

6.1. **List of excipients**

Also contains: lactose, pregelatinised maize starch, maize starch, magnesium stearate, water.

6.2. **Incompatibilities**

None known.

6.3. **Shelf-life**

Shelf-life
Three years from the date of manufacture.
6.4. Special precautions for storage

Store below 25°C.
Protect from light.

6.5. Nature and contents of container

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene tablet containers with polyfoam wad or polyethylene ullage filler and snap-on polyethylene lids; in case any supply difficulties should arise the alternative is amber glass bottles with screw caps and polyfoam wad or cotton wool. An alternative closure for polyethylene containers is a polypropylene, twist on, push down and twist off child-resistant, tamper-evident lid.

The product may also be supplied in blister packs in cartons:

a) Carton: Printed carton manufactured from white folding box board.

b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil with 5-7g/M² PVC and PVdC compatible heat seal lacquer on the reverse side.

Pack sizes: 28s, 30s, 50s, 56s, 60s, 84s, 90s, 100s, 112s, 120s, 168s, 180s, 250s, 500s, 1000s.

Product may also be supplied in bulk packs for reassembly purposes only, in polybags contained in tins, skillets or polybuckets filled with suitable cushioning material. Maximum size of bulk packs: 50,000.

6.6. Instruction for use and handling

Not applicable.
8. MARKETING AUTHORISATION NUMBER(S)

PL 00142/0344

9 Date of First Authorisation/Renewal of Authorisation

Date of first authorisation: 24th June 1993
Date of latest renewal: 27th January 2005

10 DATE OF REVISION OF THE TEXT

06/05/2016