SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Baclofen 10 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg of Baclofen.

Excipients with known effect:
Each tablet contains 65.2 mg lactose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet
White, plain flat bevelled edged tablet. Engraving: Breakline: 3K2

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Baclofen tablets are indicated to relieve the spasticity of voluntary muscle which may arise when suffering from disorders such as multiple sclerosis and other spinal lesions eg: motor neurone disease, syringomyelia, transverse myelitis, tumours and traumatic partial section of the spinal cord.

Baclofen is also indicated for the relief of voluntary muscle spasticity arising from, for example, cerebrovascular accidents, cerebral palsy, meningitis and traumatic head injury.

Treatment with baclofen is likely to be most beneficial in patients whose spasticity makes activity and/or physiotherapy difficult. Treatment should not be started until the spastic state has stabilised.

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

Baclofen is given orally in either tablet or liquid form. These two formulations are bioequivalent. The liquid may be particularly suitable for children or those adults who are unable to take tablets. Dosage titration can be more precisely managed with the liquid. The lowest dose compatible with an optimal response is recommended.

The overall degree of clinical improvement that the patient may expect to achieve with baclofen therapy should be evaluated before treatment is initiated. Increases in dosage **must** be carefully considered whilst the patient's condition stabilises and particular care is necessary in the elderly. Side effects may occur if the dosage is increased too rapidly or if the starting dose is too high. This is particularly pertinent if the patient is ambulant in order to minimise muscle weakness in unaffected limbs or where spasticity is necessary for support.
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 should be taken.
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).

Adults

The following incremental dosage schedule is suggested; however, the dosage should be adjusted to suit the individual patient.

5 mg three times daily for three days
10 mg three times daily for three days
15 mg three times daily for three days
20 mg three times daily for three days

Satisfactory control of symptoms is usually attained with doses up to 60 mg daily. Nevertheless, careful adjustment is usually needed to suit the requirements of each individual. If necessary, the dose may be slowly increased but the maximum daily dose (100 mg) should not be exceeded unless the patient is in hospital under careful medical supervision. Small and frequent doses may prove better in some cases than larger infrequent ones.

Some patients may benefit from a nightly dose of baclofen to counteract painful flexor spasm. Also, a single dose given approximately 1 hour before a specific activity such as washing, dressing, physiotherapy or shaving may improve mobility.

If the therapeutic effect of baclofen is not apparent within 6 weeks of achieving the maximum recommended dose, cessation of therapy should be considered.

Special populations

Elderly (aged 65 years or above)

These patients may be more prone to side effects, especially during the early stages of treatment. Therefore, small doses should be used at the beginning of treatment. Under careful supervision, the dose may be gradually increased in line with the patient's response. There is no evidence to suggest that the final maximum dose will differ from that seen in younger patients.

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.

Patients with impaired renal function

For those patients with impaired renal function or those undergoing chronic haemodialysis, a low dose of baclofen should be chosen i.e.: approximately 5 mg per day.

Baclofen should only be administered to end stage renal failure patients when benefit outweighs risk. 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).

Patients with hepatic impairment

No studies have been performed in patients with hepatic impairment receiving Baclofen therapy. The liver does not play a significant role in the metabolism of baclofen after oral administration (see section 5.2). However, Baclofen has the potential of elevating liver enzymes. Baclofen should be prescribed with caution in patients with hepatic impairment

Patients with spastic states of cerebral origin

Adverse effects are more likely to occur in these patients. Therefore, a cautious dosage regimen is recommended and patients should be kept under suitable surveillance.

Method of administration

For oral administration. Baclofen should be taken during meals with a little liquid.

4.3. Contraindications

Baclofen is contra-indicated in peptic ulceration.
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use

Psychiatric and nervous system disorders
Psychotic disorders, schizophrenia, depressive or manic disorders, confusional states or Parkinson's disease may be exacerbated by treatment with baclofen.
Patients suffering from these conditions should therefore be treated cautiously and kept under close surveillance.

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
Baclofen may also exacerbate epileptic manifestations, but can be employed provided appropriate supervision and adequate anticonvulsive therapy are maintained.

Encephalopathy
Cases of encephalopathy have been reported in patients receiving baclofen at therapeutic doses, which were reversible after treatment discontinuation. Symptoms included somnolence, depressed level of consciousness, confusion, myoclonus and coma.

If signs of encephalopathy are observed, baclofen should be discontinued.

Others
Baclofen should be used with extreme care inpatients already receiving antihypertensive therapy (see section 4.5).

Baclofen should be used with caution in patients suffering from cerebrovascular accidents or from respirator or hepatic impairment.

Since unwanted effects are more likely to occur, a cautious dosage schedule should be adopted in elderly and patients with spasticity of cerebral origin (see section 4.2).

Renal impairment
Baclofen 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 Posology and method of administration).

Neurological signs and symptoms of overdose including clinical manifestations of toxic encephalopathy (e.g. confusion, disorientation, somnolence and depressed level of consciousness) have been observed in patients with renal impairment taking oral baclofen at doses of more than 5mg per day and at doses of 5mg per day n patients with end-stage renal failure being treated with chronic haemodialysis. Patients with impaired renal function should be closely monitored for prompt diagnosis of early symptoms of toxicity (see section “Overdose”).

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

Cases of baclofen toxicity have been reported in patients with acute renal failure (see section 4.9).

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.

Urinary disorders
Under treatment with Baclofen neurogenic disturbances affecting emptying of the bladder may show signs of improvement. In patients with pre-existing sphincter hypertonia, acute retention of urine may occur; the drug should be used with caution in such cases.

Posture and balance
Baclofen should be used with caution when spasticity is needed to sustain upright posture and balance in locomotion (see section 4.2).

Abrupt withdrawal
Treatment should always, (unless serious adverse effects occur), be gradually discontinued by successively reducing the dosage over a period of about 1-2 weeks. Anxiety and confusional state, delirium, hallucination, psychotic disorder, mania or paranoia, convulsion (status epilepticus), dyskinesia, tachycardia, hyperthermia, rhabdomyolysis and temporary aggravation of spasticity have been reported with abrupt withdrawal of baclofen, especially after long term medication.

Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intrauterine exposure to oral baclofen (see Section 4.6).

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.

Laboratory tests
In rare instances elevated aspartate aminotransferase, blood alkaline phosphatase and blood 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.

Paediatric patients
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.

Excipients

Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5. Interaction with other medicinal products and other forms of interaction

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

Drugs causing Central Nervous System (CNS) depression
Increased sedation may occur when baclofen is taken concomitantly with other drugs causing CNS depression including other muscle relaxants (such as tizanidine), with synthetic opiates or with alcohol (see section 4.7).

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 baclofen may be potentiated, resulting in pronounced muscular hypotonia.

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

Antihypertensives
Since concomitant treatment with baclofen and anti-hypertensives is likely to increase the fall in blood pressure, the dosage of anti-hypertensive medication should be adjusted accordingly. ACE inhibitors

also potentiate the hypotensive effects of baclofen. Hypotension has been reported in one patients receiving morphine and intrathecal baclofen.

Agents reducing renal function

Drugs or medicinal products that can significantly affect renal function may reduce baclofen excretion leading to toxic effects (see Section 4.4).4.6. Fertility, pregnancy and lactation

4.6 Fertility, pregnancy and lactation

Pregnancy:
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.

Foetal/neonatal adverse reactions
Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intra-uterine exposure to oral Baclofen (see section 4.4).

Breastfeeding:
In mothers taking baclofen at therapeutic doses, the active substance passes into the breast milk, but in quantities so small that no undesirable effects in the infant are to be expected.

4.7. Effects on ability to drive and use machines

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

4.8. Undesirable effects

Adverse effects occur mainly at the start of treatment (e.g. sedation, somnolence and nausea), 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 be ingested with food or a milk beverage.

In patients with a 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 convulsions may occur, particularly in epileptic patients. 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).

Adverse reactions (Table 1) are ranked under heading of frequency, the most frequent first, using the following convention: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000) very rare (< 1/10,000) and not known (cannot be estimated from the available data).

Table 1: Tabulated summary of adverse drug reactions

Frequency and System Organ Classes	*Very common (≥ 1/10)*	*Common (≥ 1/100, < 1/10)*	*Rare (≥ 1/10,000, < 1/1,000)*	*Very rare (< 1/10,000), including isolated reports*	*Not known* (cannot be estimated from the available data)
Immune system disorders					Hypersensitivity
Nervous System Disorders	Sedation, somnolence	Respiratory depression, light-headedness, exhaustion, confusional state, dizziness, headache, insomnia, fatigue, euphoric mood, depression, muscular weakness, ataxia, tremor, hallucinations, nightmares, myalgia, nystagmus, dry mouth	Paraesthesia, dysarthria, dysgeusia		Sleep apnoea syndrome*, encephalopathy
Eye disorders		Accommodation disorders, visual impairment			
Cardiac disorders		Cardiac output decreased			Bradycardia
Vascular disorders		Hypotension			
Gastrointestinal disorders	Nausea	Gastrointestinal disorder, retching, vomiting, constipation, diarrhoea	Abdominal pain		
Hepatobiliary disorders			Hepatic function abnormal		
Skin and subcutaneous tissue disorders		Hyperhidrosis, rash			Urticaria, alopecia
Renal and urinary disorders		Pollakiuria, enuresis, dysuria	Urinary retention		
Reproductive system & breast disorders			Erectile dysfunction		Sexual dysfunction
General disorders and administration site conditions				Hypothermia	Drug withdrawal syndrome** (see section 4.4), swelling

					face and peripheral oedema
Investigations					Blood glucose increased

**Drug withdrawal syndrome including postnatal convulsions in neonates has also been reported after intra-uterine exposure to oral Baclofen.

* Cases of central sleep apnoea syndrome have been observed with baclofen at high doses (≥ 100 mg) in patients who are alcohol dependent.

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

4.9. Overdose

Symptoms:
Prominent features are signs of central nervous depression or encephalopathy: somnolence, depressed level of consciousness, respiratory depression, coma and tinnitus.

Also liable to occur are: confusion, hallucinations, agitation, convulsion, abnormal electroencephalogram (burst suppression pattern and triphasic waves, generalised slowing on EEG), accommodation disorder, impaired pupillary reflex; generalised muscular hypotonia, myoclonia, hyporeflexia or areflexia; convulsions; peripheral vasodilation, hypotension or hypertension, bradycardia or tachycardia, or cardiac arrhythmia; hypothermia, nausea, vomiting, diarrhoea, salivary hypersecretion; increased hepatic enzymes, sleep apnoea and rhabdomyolysis. Patients with renal impairment can develop signs of overdose even on low doses of oral baclofen. (see Section 4.2 and Section 4.4).

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

Treatment:
No specific antidote is known.

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

After ingestion of a potentially toxic amount, activated charcoal should be considered. In the early period after ingestion charcoal should be considered in adults who ingested more than 100mg baclofen within 1 hour, and in children who have ingested more than 5mg/kg baclofen within 1 hour. Gastric decontamination (e.g. gastric lavage) should be considered in individual cases, especially in the early period (60 minutes) after ingestion of a potentially life-threatening overdose. Comatose or convulsing patients should be intubated prior to the initiation of gastric decontamination.

Since the drug is excreted chiefly via the kidneys, generous quantities of fluid should be given, possibly together with a diuretic. Haemodialysis (sometimes unscheduled) may be useful in severe poisoning associated with renal failure (see Section 4.4). In the event of convulsions, diazepam should be administered intravenously with caution.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antispastic with spinal site attack, ATC code: M03B X01

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 his 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 (baclofen) is rapidly and completely absorbed from the gastro-intestinal tract. No significant difference between the liquid 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. The protein binding rate is approximately 30 % and is constant in the concentration range of 10 nanogram/mL to 300 microgram/mL.. 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, β-(p-chlorophenyl)-4-hydroxybutyric acid, which is pharmacologically inactive.

Elimination/excretion: The plasma elimination half-life of baclofen averages 3 to 4 hours.

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

Special populations

Elderly patients (aged 65 years or above)
The pharmacokinetics of baclofen in elderly patients are virtually the same as in in patients below 65 years of age. Following a single oral dose, elderly patients have slower elimination but a similar systemic exposure of baclofen compared to adults below 65 years of age. Extrapolation of these

results to multi-dose treatment suggests no significant pharmacokinetic difference between patients below 65 years of age and elderly patients.

Paediatric patients
Following oral administration of 2.5 mg Baclofen tablet in children (aged 2 to12 years), Cmax of 62.8±28.7 nanogram/mL, and Tmax in the range of 0.95-2 h have been reported. Mean plasma clearance (Cl) of 315.9 mL/h/kg; volume of distribution (Vd) of 2.58 L/kg; and half-life (T½) of 5.10 h have been reported.

Hepatic impairment
No pharmacokinetic data are available in patients with hepatic impairment after administration of Baclofen. However, as the liver does not play a significant role in the disposition of baclofen, it is unlikely that baclofen pharmacokinetics would be altered to a clinically significant level in patients with hepatic impairment.

Renal impairment
No controlled clinical pharmacokinetic study is available in patients with renal impairment after administration of Baclofen. Baclofen is predominantly eliminated unchanged in urine. Sparse plasma concentration data collected only in female patients under chronic hemodialysis or compensated renal failure indicate significantly decreased clearance and increased half-life of baclofen in these patients. Dosage adjustment of baclofen based on its systemic levels should be considered in renal impairment patients, and prompt hemodialysis is an effective means of reversing excess baclofen in systemic circulation.

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

Lactose
Microcrystalline cellulose
Sodium starch glycolate
Magnesium stearate

6.2. Incompatibilities

Not applicable

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store below 25°C.
Store in the original package.

6.5. Nature and contents of container

HDPE or polypropylene tablet containers with caps or child resistant closures in packs of 28, 30, 50, 56, 60, 100, 250, 500 or 1000 tablets.

Blister strips in packs of 10, 28, 30, 56, 60, 84 or 100 tablets.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

Not applicable.

7. MARKETING AUTHORISATION HOLDER

Teva UK Limited,
Ridings Point,
Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom.

8. MARKETING AUTHORISATION NUMBER

PL 00289/0243

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27/02/1995 / 13/03/2009

10. DATE OF REVISION OF THE TEXT

19/12/2024