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:
Each tablet contains 65.2 mg lactose

For a 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

For oral administration.

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.

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.

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.

The Elderly
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.

**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: 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 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.

4.3. **Contraindications**

Baclofen is contra-indicated in peptic ulceration and where there is a known hypersensitivity to baclofen or to any of its excipients.

4.4 **Special warnings and precautions for use**

**Psychotic and nervous system disorders**

The signs of psychotic disorders, schizophrenia, depressive or manic disorders, confusional states or Parkinson’s disease may be intensified during baclofen therapy. Patients suffering from these conditions should therefore be treated cautiously and closely monitored.

**Epilepsy**

Baclofen may also exacerbate attacks of epilepsy, but can still be used so long as adequate supervision and anti-convulsive therapy are maintained.

**Others**

Care should be exercised when treating patients already receiving anti-hypertensive therapy (see section 4.5).

Caution should be used when treating patients suffering from cerebrovascular accidents or from respiratory, hepatic impairment.

**Renal impairment**

Signs of overdose have been observed in patients with renal impairment taking oral baclofen at doses of more than 5 mg per day. Baclofen should be used with caution in patients with renal insufficiency and should only be administered to patients with end-
stage renal failure (CKD stage 5, GFR <15 mL/min) when benefit outweighs risk (see Section 4.2).

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

Particular caution is required when combining baclofen with medicines that can significantly affect renal function. Renal function should be closely monitored and the baclofen daily dosage adjusted 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.

**Urinary disorders**
Neurogenic disturbances which affect the emptying of the bladder may show signs of improvement during baclofen therapy. However, in patients with pre-existing sphincter hypertonia, baclofen therapy may result in acute retention of urine. Therefore, caution should be employed when prescribing baclofen in both these groups of patients.

**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.

Neonatal convulsions 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 AST, alkaline phosphatase and glucose levels in serum have been recorded. Therefore, in patients with liver diseases or diabetes mellitus, the appropriate laboratory tests should be performed to ensure that drug induced changes to the underlying disease have not occurred.

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

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 **Interaction with other medicinal products and other forms of interaction**
Increased sedation may occur when baclofen is taken concurrently with alcohol, synthetic opiates or other drugs that affect the CNS.

Treatment with baclofen increases the risk of respiratory depression. Careful monitoring of respiratory and cardiovascular functions is essential especially in patients with cardiopulmonary disease and respiratory muscle weakness.
Concomitant treatment with tricyclic antidepressants may potentiate the effect of baclofen. This may result in pronounced muscular hypotonia.

Simultaneous treatment with baclofen and anti-hypertensives is likely to increase the fall in blood pressure. Therefore, the dosage of anti-hypertensive medication should be altered appropriately. ACE inhibitors also potentiate the hypotensive effects of baclofen. Hypotension has been reported in one patient receiving morphine and intrathecal baclofen.

Ibuprofen and other drugs which may produce renal insufficiency may decrease baclofen excretion and may lead 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.

Medicinal products that can significantly affect renal function may reduce baclofen excretion leading to toxic effects (see Section 4.4).

### 4.6 Pregnancy and lactation

**Pregnancy**: During pregnancy, particularly the first trimester, baclofen should only be used if considered essential. The possible benefits of the treatment for the mother must be carefully weighed against the possible any possible risks to the unborn child. Baclofen crosses the placenta.

In rat foetuses, the incidence of omphaloceles (ventral hernia) increases when baclofen is used at high doses. No teratogenic effects have been noted in mice or rabbits.

One case of suspected withdrawal reaction (generalised convulsions) has been reported in a week-old infant whose mother had taken oral baclofen 80 mg daily throughout her pregnancy. The convulsions, which were refractory to standard anticonvulsant treatment, ceased within 30 minutes of giving baclofen to the infant.

**Lactation**: In mothers taking baclofen 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

Patients should be advised that effects such as dizziness, sedation, somnolence, decreased alertness, visual disturbances (see section 4.8 Undesirable effects), ataxia and tremor may affect their ability to drive or operate machinery. Patients experiencing these adverse reactions should be advised to refrain from driving or using machines.

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

Unwanted effects (e.g. sedation, somnolence and nausea) usually occur at the start of therapy, if the dosage is increased too rapidly, large doses are used or in patients who are elderly. They are often transitory and can be attenuated or eliminated by reducing the dosage. They are seldom severe enough to require withdrawal of treatment.

It is recommended that baclofen be administered with food or a milk beverage should nausea persist following a reduction in dosage.

Adverse effects may assume a more serious form in patients with a history of psychiatric illness, or with cerebrovascular disorders (e.g. stroke) as well as in elderly patients.

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

Table 1

<table>
<thead>
<tr>
<th>Frequency and System Organ Classes</th>
<th>Very common ($\geq 1/10$)</th>
<th>Common ($\geq 1/100$, $&lt; 1/10$)</th>
<th>Rare ($\geq 1/10,000$, $&lt; 1/1,000$) very rare ($&lt; 1/10,000$), including isolated reports</th>
<th>Not known (cannot be estimated from the available data)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous System Disorders</td>
<td>Sedation, somnolence</td>
<td>Respiratory depression, lightheadedness, lassitude, exhaustion, confusional state, dizziness, headache, insomnia, euphoric mood, depression, muscular weakness, ataxia, tremor, hallucinations, nightmares, myalgia, nystagmus, dry mouth</td>
<td>Paraesthesia, dysarthria, dysgeusia</td>
<td>Hypothermia</td>
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<tr>
<td>Eye disorders</td>
<td></td>
<td>Accommodation disorders, visual disturbances</td>
<td></td>
<td></td>
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<tr>
<td>Cardiac disorders</td>
<td></td>
<td>Cardiac output decreased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Hypotension</td>
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<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea</td>
<td>Gastrointestinal disturbances, retching, vomiting, constipation, diarrhoea</td>
<td>Abdominal pain</td>
<td></td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td></td>
<td>Hepatic function abnormal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Hyperhidrosis, rash</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal and urinary disorders</td>
<td>Polyuria, enuresis, dysuria</td>
<td>Urinary retention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive system &amp; breast disorders</td>
<td></td>
<td>Erectile dysfunction</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Some 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 - can 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).

An increase in the incidence of ovarian cysts and enlarged and/or haemorrhagic adrenals has been seen in female rats treated for two years. Although these effects are dose related the clinical significance of these findings is not known.

**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](http://www.mhra.gov.uk/yellowcard).

### 4.9 Overdose

The most common symptoms of overdosage are signs of central nervous depression: coma, drowsiness, impairment of consciousness and respiratory depression. The following may also occur: accommodation disorders, agitation, absent pupillary reflex, confusion, generalised muscular hypotonia, myoclonia, hallucinations, hyporeflexia or areflexia; convulsions; EEG changes (burst suppression pattern and triphasic waves), peripheral vasodilation, hypotension or hypertension, bradycardia, tachycardia or cardiac arrhythmias; hypothermia, nausea, vomiting, diarrhoea, hypersalivation, elevated LDH, AST, SGOT and AP values. 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, 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

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 is a skeletal muscle relaxant used in the management of spasticity. It is indicated for the symptomatic relief of spasticity caused by conditions such as multiple sclerosis and lesions of the spinal cord.

Baclofen depresses monosynaptic and polysynaptic reflex transmission, probably by stimulating the GABA<sub>B</sub>-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 is structurally similar to the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). However, its mode of action is not fully understood. It is known that baclofen interfaces with the release of excitatory neurotransmitters and inhibits monosynaptic and polysynaptic transmission at spinal level.
Adverse effects include drowsiness, dizziness, nausea, confusion and hypotension. Abrupt withdrawal of treatment should be avoided.

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

When given orally, baclofen is quickly and almost completely absorbed from the gastrointestinal tract. Peak plasma concentrations occur 1-3 hours after oral administration, but the rate and extent of absorption may vary between patients. Approximately 15% of the active is metabolised in the liver and converted to β-(p-chlorophenyl)-gamma-hydroxybutyric acid by deamination. Approximately 70-80% of a single dose is excreted in the urine, mainly as the unmetabolised drug.

Absorption: Baclofen (baclofen) is rapidly and completely absorbed from the gastrointestinal tract. No significant difference between the liquid and tablet formulations is observed in respect of $t_{\text{max}}$, $c_{\text{max}}$ 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, β-(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
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
Brampton Road
Hampden Park
Eastbourne
East Sussex
BN22 9AG
8 MARKETING AUTHORISATION NUMBER
PL 00289/0243

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
13/03/2009

10 DATE OF REVISION OF THE TEXT
14/07/2015