Applicant: Teva Pharmaceuticals (Pty) Ltd	**Product name:** Baclofen 10 Teva **Dosage form & strength:** Each tablet contains 10 mg baclofen

PROFESSIONAL INFORMATION:

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

BACLOFEN 10 TEVA (tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains baclofen 10 mg.

Excipient with known effect:

Contains sugar (lactose monohydrate 65,2 mg per tablet)

For the full list of excipients, see **section 6.1**.

3. PHARMACEUTICAL FORM:

Tablets.

White, round, plain, flat, bevelled edged tablets with break line on one side and engraved '3K2' on the reverse. The break line can be used to divide the tablet into equal halves.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

Spasticity of the skeletal muscle due to multiple sclerosis; spastic conditions occurring in spinal-cord diseases of infectious, degenerative, traumatic, neoplastic, or unknown aetiology, e.g. spastic spinal paralysis, amyotrophic lateral sclerosis, syringomyelia, transverse myelitis, traumatic paraplegic or paraparesis, and compression of the spinal cord.

Spasticity of cerebral origin, e.g. following cerebrovascular accidents or in the presence of neoplastic or degenerative brain disease.

4.2 Posology and method of administration:

Posology:

Treatment should always be initiated with small, gradually increasing doses of BACLOFEN 10 TEVA. The optimum daily dosage should be individually adapted to the patient's requirements in such a way that clonus, flexor and extensor spasms, and spasticity are reduced, but that a sufficient degree of muscle tone is maintained to permit active movements and adverse effects are avoided as far as possible.

In order to prevent excessive weakness and falling, BACLOFEN 10 TEVA should be used with caution when spasticity is needed to sustain upright posture and balance in locomotion or whenever spasticity is used to maintain function. It may be important to maintain some degree of muscle tone and allow occasional spasms to help support circulatory function.

The daily dosage should be given in at least 3 divided doses in adults, and 3 to 4 in children.

If no benefit is apparent within 6 to 8 weeks of achieving the maximum dosage, a decision whether to continue with BACLOFEN 10 TEVA should be taken.

Withdrawal of BACLOFEN 10 TEVA should be gradual.

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.

Abrupt discontinuation of the treatment should be avoided (see **sections 4.4** and **4.8**).

Adults:

Treatment should as a rule be started with a dosage of 5 mg (half a tablet) three times daily, which - for the purpose of cautious dose titration - should subsequently be increased at three-day intervals by 5 mg (half a tablet) three times daily until the requisite daily dosage has been attained,

i.e. 5 mg (half a tablet) three times daily for 3 days,

10 mg (one tablet) three times daily for 3 days,

15 mg (one and a half tablets) three times daily for 3 days,

20 mg (two tablets) three times daily for 3 days.

In certain patients reacting sensitively to medicines, it may be advisable to begin with a lower daily dosage of 5 mg or 10 mg (half to one tablet) and to raise this dosage more gradually. The optimum dosage generally ranges from 30 mg to 80 mg daily.

Doses of more than 80 mg to 100 mg daily are not generally recommended although higher doses have been given to carefully supervised patients in hospital.

Children:

Treatment should usually be started with a very low dose, e.g. 0,3 mg/kg a day, in divided doses. The dosage should be raised cautiously, at about 1 to 2 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 mass. In children over 10 years of age, however, a maximum daily dosage of 2,5 mg/kg body mass may be given.

Impaired renal function:

In patients with impaired renal function BACLOFEN 10 TEVA should be given with caution and at lower doses.

These patients should be closely monitored for prompt diagnosis of early signs and/or symptoms of toxicity (e.g. somnolence, lethargy). Patients undergoing chronic haemodialysis, baclofen concentrations in plasma are elevated and therefore a particularly low dosage of BACLOFEN 10 TEVA should be selected, i.e. approximately 5 mg daily.

Elderly patients:

Since unwanted effects are more likely to occur in elderly patients or in patients with spastic states of cerebral origin, in such cases it is recommended that a very cautious dosage schedule be adopted in these patients and that they be kept under appropriate surveillance.

Hepatic impairment:

No studies have been performed in patients with hepatic impairment under BACLOFEN 10 TEVA therapy. Liver does not play a significant role in the metabolism of baclofen after oral administration of BACLOFEN 10 TEVA.

However, BACLOFEN 10 TEVA has the potential of elevating liver enzymes. BACLOFEN 10 TEVA should be prescribed with caution in patients with hepatic impairment.

Method of administration:

For oral use.

BACLOFEN 10 TEVA should be taken during meals with a little liquid.

4.3 Contraindications:

- Known hypersensitivity to baclofen, or any of the excipients of BACLOFEN 10 TEVA listed in **section 6.1**.
- Porphyria.
- Pregnancy and lactation (see **section 4.6**).

4.4 Special warnings and precautions for use:

Parkinsonism:

BACLOFEN 10 TEVA is not suitable for use in Parkinson's disease or in athetotic conditions.

Abrupt withdrawal:

Anxiety and confusional state, delirium, hallucinations, psychotic disorder, manic or paranoid states, convulsions (status epilepticus), dyskinesia, tachycardia, hyperthermia, rhabdomyolysis and - as a rebound phenomenon - temporary aggravation of spasticity have been reported upon the abrupt withdrawal of BACLOFEN 10 TEVA, especially after long-term medication. Therefore, except where serious adverse effects have occurred, the treatment should be gradually discontinued by successively reducing the dosage (over a period of approximately one or two weeks).

Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intrauterine exposure to oral BACLOFEN 10 TEVA. As a precautionary measure, BACLOFEN 10 TEVA administration to neonates with gradual tapering can help in controlling and preventing the withdrawal reactions (see **section 4.6**).

Renal impairment:

BACLOFEN 10 TEVA should be used with caution in patients with renal impairment. 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 10 TEVA at doses of more than 5 mg per day and at doses of 5 mg per day in 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 4.9**).

Patients with renal impairment may need a reduced dose.

Special caution is required when co-administering BACLOFEN 10 TEVA with medicines that can significantly affect renal function. Renal function should be closely monitored and the BACLOFEN 10 TEVA daily dose adjusted to prevent baclofen toxicity.

Cases of baclofen toxicity, with baclofen as contained in BACLOFEN 10 TEVA, have been reported in patients with acute renal failure (see **section 4.9**).

Besides discontinuing treatment, haemodialysis might be considered as a treatment alternative in patients with severe BACLOFEN 10 TEVA toxicity. Haemodialysis effectively eliminates baclofen from the body, relieving clinical symptoms of overdose and shortens the recovery time in these patients.

Psychiatric and nervous system disorders:

Patients suffering not only from spasticity but also from psychotic disorders, schizophrenia, depressive or manic disorders, confusional states or Parkinson’s disease should be treated cautiously with BACLOFEN 10 TEVA and kept under careful surveillance, because exacerbation of these conditions may occur.

Suicide and suicide-related events have been reported in patients treated with BACLOFEN 10 TEVA. 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 medicine 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 10 TEVA. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of BACLOFEN 10 TEVA misuse, abuse or dependence e.g. dose escalation, drug-seeking behaviour, development of tolerance.

Epilepsy:

BACLOFEN 10 TEVA may exacerbate seizures in epileptic patients. In spastic patients with epilepsy, BACLOFEN 10 TEVA can be employed under appropriate supervision, provided adequate anticonvulsive therapy is continued.

Hyperacidity:

BACLOFEN 10 TEVA should be used with caution in patients with a history of peptic ulcers.

Other:

BACLOFEN 10 TEVA should be administered with caution in patients with cerebrovascular disease, respiratory, hepatic or renal failure.

BACLOFEN 10 TEVA should be used with extreme care in patients already receiving antihypertensive therapy (see **section 4.5**).

Care is also required in the elderly in whom adverse effects may be more common and in patients with a history of psychiatric illness and patients with stroke who tolerate BACLOFEN 10 TEVA poorly.

BACLOFEN 10 TEVA may be associated with dizziness, sedation, somnolence, visual disturbances and impaired concentration which may impair the patient's reaction and may be aggravated by the simultaneous intake of alcohol or central nervous system depressant agents.
Patients experiencing these adverse reactions should be advised to refrain from driving or using machines (see **section 4.7**).

Urinary disorders:

Under treatment with BACLOFEN 10 TEVA neurogenic disturbances affecting emptying of the bladder may show an improvement. In patients with pre-existing sphincter hypertonia, acute retention of urine may occur; BACLOFEN 10 TEVA should be used with caution in such cases.

Posture and balance:

BACLOFEN 10 TEVA should be used with caution when spasticity is needed to sustain upright posture and balance in locomotion (see **section 4.2**).

Laboratory tests:

In less frequent instances elevated aspartate aminotransferase, blood alkaline phosphatase and blood glucose levels have been recorded. Appropriate laboratory tests should be performed in patients with liver diseases or diabetes mellitus, in order to ensure that no medicinal-induced changes in these underlying diseases have occurred.
BACLOFEN 10 TEVA contains lactose monohydrate as an excipient, and patients with rare hereditary problems of galactose intolerance total lactase deficiency or glucose-galactose malabsorption should not take BACLOFEN 10 TEVA.

4.5 Interaction with other medicines and other forms of interaction:

Medicines that cause central nervous system depression, opioids and alcohol:

Where BACLOFEN 10 TEVA is taken concomitantly with other medicines acting on the central nervous system including other muscle relaxants (such as tizanidine), with synthetic opiates or with alcohol, increased sedation may occur.
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 concurrent treatment with tricyclic antidepressants, the effect of BACLOFEN 10 TEVA may be potentiated, resulting in pronounced muscular hypotonia.

Antihypertensives:

Since concomitant treatment with BACLOFEN 10 TEVA and antihypertensives is likely to increase the fall in blood pressure, the dosage of antihypertensive medication should be adjusted accordingly.

Levodopa/dopa-decarboxylase (DDC inhibitor) Carbidopa:

In patients with Parkinson's disease receiving treatment with BACLOFEN 10 TEVA 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 10 TEVA and levodopa/carbidopa.

Lithium:

Severe aggravation of hyperkinetic symptoms may occur in patients taking lithium.
Thus, caution should be exercised when BACLOFEN 10 TEVA is used concomitantly with lithium.

Medicines reducing renal function:

Medicines that can significantly affect renal function may reduce BACLOFEN 10 TEVA excretion leading to toxic effects (see **section 4.4**).

4.6 Fertility, pregnancy and lactation:

Pregnancy and lactation:

Safety in pregnancy and lactation has not been established. There are no adequate and well-controlled studies in pregnant women. Baclofen crosses the placental barrier and should not be used during pregnancy.
Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intrauterine exposure to oral BACLOFEN 10 TEVA (see **section 4.4**).

Fertility:

No data on the effect of BACLOFEN 10 TEVA on human fertility is available.

4.7 Effects on ability to drive and use machines:

The use of BACLOFEN 10 TEVA may be associated with undesirable effects such as dizziness, sedation, somnolence and visual impairment (see **section 4.8**) which may impair the patient's reaction. Patients experiencing these undesirable effects should be advised to refrain from driving or using machines.

4.8 Undesirable effects:

a. Summary of the safety profile:

Undesirable 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 if the patient is an elderly person. Side effects are often transient and dose related; they are seldom severe enough to necessitate withdrawal of the medication.
Should nausea persist following a reduction in dosage, it is recommended that BACLOFEN 10 TEVA 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, undesirable effects may assume a more serious form.

Lowering of the seizure 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).

b. Tabulated list of adverse reactions:

Adverse reactions identified in clinical studies and post-marketing	
(MedDRA) SYSTEM ORGAN CLASS	**ADVERSE REACTION AND FREQUENCY**
Nervous system disorders:	
Frequent	Sedation, somnolence, confusional state, dizziness, hallucination, depression, fatigue, insomnia, euphoric mood, muscular weakness, ataxia, tremor, nightmare, myalgia, headache, dry mouth, nausea, exhaustion, nystagmus, nightmare
Less frequent	Paraesthesia, dysarthria, dysgeusia, lassitude, exhaustion
Frequency unknown	Sleep apnoea syndrome*
Eye disorders:	
Frequent	Visual impairment, accommodation disorder, nystagmus
Ear and labyrinth disorders:	
Less frequent	Tinnitus
Cardiac disorders:	
Frequent	Decreased cardiac output
Frequency unknown	Bradycardia
Vascular disorders:	

Frequent	Hypotension
Respiratory, thoracic and mediastinal disorders:	
Frequent	Respiratory depression
Gastrointestinal disorders:	
Frequent	Gastrointestinal disorder, constipation, diarrhoea, nausea, retching, vomiting
Less frequent	Abdominal pain
Hepato-biliary disorders	
Less frequent	Disorders of hepatic function
Skin and subcutaneous tissue disorders:	
Frequent	Rash, hyperhidrosis
Less frequent	Allergic skin reactions, pruritus
Frequency unknown	Urticaria
Renal and urinary disorders:	
Frequent	Pollakiuria, enuresis, dysuria
Less frequent	Urinary retention
Reproductive system and breast disorders:	
Less frequent	Erectile dysfunction
General disorders and administration site conditions:	
Less frequent	Hypothermia
Frequency unknown	Medicine withdrawal syndrome* (see **section 4.4**)
Investigations:	
Frequency unknown	Increased blood glucose

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

* Medicine withdrawal syndrome including postnatal convulsions in neonates has also been reported after intrauterine exposure to oral BACLOFEN 10 TEVA.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the 6.04 Adverse Drug Reactions Reporting Form, found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose:

Signs and symptoms:

Prominent features are signs of central nervous system depression: drowsiness, impairment of consciousness, respiratory depression, coma and tinnitus. Also liable to occur are: confusion, hallucinations, agitation, accommodation disorders, absent pupillarly reflex; generalised muscular hypotonia, myoclonia, hyperflexia or areflexia, convulsions, abnormal electroencephalogram (burst suppression pattern and triphasic waves), peripheral vasodilatation, hypotension, hypertension, bradycardia, tachycardia or cardiac dysrhythmia, hypothermia, nausea, vomiting, diarrhoea, hypersalivation, elevated LDH, SGOT and AP values and rhabdomyolysis. Patients with renal impairment can develop signs of overdose even on low doses of oral BACLOFEN 10 TEVA (see **sections 4.2** and **4.4**).

A deterioration in the condition may occur if various substances or medicines acting on the central nervous system (e.g. alcohol, diazepam, tricyclic antidepressants) are taken concomitantly.

Treatment:

No specific antidote is known. The drug can be eliminated from the gastrointestinal tract by induction of vomiting.

Treatment is symptomatic and supportive for complications such as hypotension, hypertension, convulsions, gastrointestinal disorders and respiratory or cardiovascular depression.

Since baclofen 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**).

5. PHARMACOLOGICAL PROPERTIES:

5.1 Pharmacodynamic properties:

Pharmacological classification: A 2.10 Centrally active muscle relaxant.

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

Baclofen is an analogue of aminobutyric acid and displays pronounced muscle-relaxing activity. It acts on the motor system of the spinal cord in a distinctive segmental fashion. Baclofen inhibits both mono- and polysynaptic reflex transmission and reduces the activity of the gamma motor neurons. It does not however, influence neuromuscular impulse transmission in the motor endplates.

5.2 Pharmacokinetic properties:

Absorption:

Baclofen is rapidly and almost completely absorbed from the gastrointestinal tract after an oral dose. Peak plasma concentrations occur about 0,5 to 3 hours after ingestion, but the

rate and extent of absorption vary between patients, and may vary inversely with the dose. Baclofen is rapidly absorbed after oral administration and the extent of absorption is not significantly altered by the presence of food.

Distribution:

Approximately 30 % of baclofen is bound to plasma proteins.

Biotransformation:

After oral doses some baclofen crosses the blood-brain barrier, with concentrations in CSF 12 % of those in the plasma. About 70 to 80 % of a dose is excreted in the urine mainly as unchanged drug; about 15 % is metabolised in the liver. Baclofen crosses the placenta and is distributed into breast milk.

Elimination:

The elimination half-life of baclofen is about 3 to 4 hours in plasma and about 1 to 5 hours in the CSF.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Lactose monohydrate

Magnesium stearate

Microcrystalline cellulose

Sodium starch glycollate

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

2 years.

6.4 Special precautions for storage:

Store at or below 25 °C.

Store in a dry place and protect from light and moisture.

Keep blister in carton until required for use.

6.5 Nature and contents of container:

Blister strips of 10 tablets in pack sizes of 30 and 100. Blister strips are packed into an outer cardboard carton.

Tampertainers with 30, 100 and 500 tablets.

6.6 Special precautions for disposal and other handling:

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

Teva Pharmaceuticals (Pty) Ltd

Maxwell Office Park

Magwa Crescent West

Waterfall City, Midrand

2090

South Africa

8. REGISTRATION NUMBER:

30/2.10/0392

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

10 October 2008

10. DATE OF REVISION OF THE TEXT:

13 September 2024