Teva Pharmaceuticals (Pty) Ltd.
TEVA BACLOFEN 10, tablets
Each tablet contains 10 mg baclofen

APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE:

TEVA BACLOFEN 10 (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 breakline on one side and engraved 3K2 on the reverse. The breakline 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 etiology, 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 TEVA BACLOFEN 10. 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, TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 should be taken.

Withdrawal of TEVA BACLOFEN 10 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 section 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 ~~75 mg~~ 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 TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 therapy. Liver does not play significant role in the metabolism of baclofen after oral administration of TEVA BACLOFEN 10.

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

Method of administration:

For oral use.

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

4.3 Contraindications

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

4.4 Special warnings and precautions for use:

Parkinsonism:

TEVA BACLOFEN 10 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 TEVA BACLOFEN, 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 TEVA BACLOFEN 10. As a precautionary measure, TEVA

BACLOFEN 10 administration to neonates with gradual tapering can help in controlling and preventing the withdrawal reactions (See section 4.6).

Renal impairment:

TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 with medicines that can significantly affect renal function. Renal function should be closely monitored and the TEVA BACLOFEN 10 daily dose adjusted to prevent baclofen toxicity.

Cases of baclofen toxicity, contained in TEVA BACLOFEN 10, 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 TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 and kept under careful surveillance, because exacerbation of these conditions may occur.

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

Epilepsy

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

Hyperacidity

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

Other

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

TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 poorly.

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

Posture and balance

TEVA BACLOFEN 10 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.

TEVA BACLOFEN 10 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 TEVA BACLOFEN 10.

4.5 Interaction with other medicines and other forms of interaction

Medicines that cause central nervous system depression, opioids and alcohol

Where TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 may be potentiated, resulting in pronounced muscular hypotonia.

Antihypertensives

Since concomitant treatment with TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 and levodopa/carbidopa.

Lithium

Severe aggravation of hyperkinetic symptoms may occur in patients taking lithium.

Thus caution should be exercised when TEVA BACLOFEN 10 is used concomitantly with lithium.

Medicines reducing renal function

Medicines that can significantly affect renal function may reduce TEVA BACLOFEN 10 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 TEVA BACLOFEN 10 (see section 4.4)

Fertility

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

4.7 Effects on ability to drive and use machines

The use of TEVA BACLOFEN 10 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 udesirable 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 TEVA BACLOFEN 10 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	Gastro-intestinal 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 intra-uterine exposure to oral TEVA BACLOFEN 10.

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 TEVA BACLOFEN 10 10 (see section 4.2 and section 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 adiuretic. Haemodialysis (sometimes unscheduled) may be useful in severe poisoning associated with renal failure (seesection 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 neurones. 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 about 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

Teva Pharmaceuticals (Pty) Ltd.
TEVA BACLOFEN 10, tablets
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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

18 August 2023