SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSE FORM

BACLOFEN 10 BIOTECH

BACLOFEN 25 BIOTECH

COMPOSITION

Each tablet contains 10 mg or 25 mg of baclofen respectively.

Excipients

Dibasic Calcium Phosphate anhydrous, Colloidal silicon dioxide, Magnesium stearate, Microcrystalline cellulose, and Sodium carboxymethyl starch.

Contains sugar (Lactose Monohydrate 40 mg & 60 mg respectively per tablet).

PHARMACOLOGICAL CLASSIFICATION

A. 2.10 Centrally acting muscle relaxants.

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Baclofen is an analogue of gamma-aminobutyric acid (GABA).

Baclofen exerts its antispastic effects by depressing monosynaptic and polysynaptic transmission in the spinal cord.

Baclofen inhibits both mono- and polysynaptic reflex transmission and reduces the activity of the gamma motor neurones.

These effects superficially resemble those of GABA, which is released by interneurons in the spinal cord and depolarises the axonal terminals of primary afferent fibres.

This results in presynaptic inhibition of motor neurons.

Baclofen does not cause depolarisation of primary afferent nerve terminals.

Pharmacokinetic properties

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.

After oral doses some baclofen crosses the blood-brain barrier, with concentrations in CSF about 12% of those in the plasma.

About 30% of baclofen is bound to plasma

proteins. About 70 to 80 % of a dose is excreted in the urine mainly as unchanged drug; about 15 % is metabolised in the liver.

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

Baclofen crosses the placenta and is distributed into breast milk.

INDICATIONS

BACLOFEN 10/25 BIOTECH is used in adults to treat spasticity of the skeletal muscle due to multiple sclerosis; spastic conditions occurring in spinal cord diseases of infectious, degenerative, traumatic, neoplastic, or unknown etiology.

CONTRAINDICATIONS

Galactose - lactose intolerance.

Active peptic ulcer.

Hypersensitivity to Baclofen or to any of the excipients of BACLOFEN 10/25 BIOTECH

BACLOFEN 10/25 BIOTECH should not be administered to pregnant or breastfeeding women. *(See Pregnancy and Lactation*)

Porphyria.

WARNINGS AND SPECIAL PRECAUTIONS

Extreme caution is needed if BACLOFEN 10/25 BIOTECH is combined with anti-hypertensive therapy because of the risk of potentiating the hypotensive effect.

The use of BACLOFEN 10/25 BIOTECH may lead to drowsiness, visual disturbances and impaired concentration which may be aggravated by the simultaneous intake of alcohol or central nervous system depressants agents.

Concomitant treatment of BACLOFEN 10/25 BIOTECH and levodopa (alone or in combination with carbidopa) in patients with Parkinson's, will result in mental confusion, hallucinations, headaches, nausea and agitation, manic or paranoid states (see "INTERACTIONS"). Worsening of the symptoms of Parkinsonism has also been reported.

Psychiatric disorders, schizophrenia, depression and manic disorders, confusional states and Parkinson's disease may be exacerbated by treatment with BACLOFEN 10/25 BIOTECH. Patients suffering from these conditions should be treated cautiously and kept under surveillance.
BACLOFEN 10/25 BIOTECH may also result in or exacerbate epileptic manifestations, but can be employed provided appropriate supervision and adequate anti-convulsive therapy are maintained.

BACLOFEN 10/25 BIOTECH should be used with caution in patients with renal insufficiency.
Particular caution is required when combining BACLOFEN 10/25 BIOTECH with medicines that affect renal function. Renal function should be closely monitored and BACLOFEN 10/25 BIOTECH daily dosage adjusted accordingly to prevent baclofen toxicity.

BACLOFEN 10/25 BIOTECH stimulates gastric acid secretion and should be used with caution in patients with a history of peptic ulcer and avoided in those with active peptic ulcer disease (*see "Contraindications"*).
BACLOFEN 10/25 BIOTECH should be used with caution in patients with cerebrovascular disease.

BACLOFEN 10/25 BIOTECH can cause increased blood sugar concentrations, caution is advised in patients with diabetes mellitus.

Urine retention may be exacerbated in patients with hypertonic bladder sphincters.

BACLOFEN 10/25 BIOTECH should be used with caution in patients in whom spasticity is used to maintain posture or increase functional capacity.

BACLOFEN 10/25 BIOTECH should be used with caution in patients with respiratory impairment, and hepatic impairment.

Some cases of elevated AST, alkaline phosphatase, and glucose levels in the serum have been reported. Appropriate laboratory test should therefore be performed periodically in patients with liver disease or diabetes mellitus.

Patients who have suffered from a stroke, tolerate BACLOFEN 10/25 BIOTECH poorly.

Withdrawal of BACLOFEN 10/25 BIOTECH should be gradual. Sudden withdrawal of BACLOFEN 10/25 BIOTECH after chronic administration may cause muscle rigidity and exaggerated rebound spasticity, severe high fever, altered mental status, and has progressed in rare instances to rhabdomyolysis, multiple organ-system failure and death.

Other withdrawal symptoms are auditory and visual hallucinations, anxiety and tachycardia.

Concomitant treatment of BACLOFEN 10/25 BIOTECH and levodopa in patients with Parkinson's, will result in mental confusion, hallucinations, headaches, nausea and agitation. (*See Interactions*)

BACLOFEN 10/25 BIOTECH contains lactose and should not be administered to patients with rare hereditary problems, or a history of lactose intolerance, Lapp lactose deficiency or glucose-galactose malabsorption.

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

Effects on ability to drive and use machines

Patients should be warned against taking charge of vehicles or machinery or performing potentially hazardous tasks where loss of concentration may lead to accidents.

INTERACTIONS

Alcohol and other central nervous system (CNS) depressants may exacerbate the CNS effects of BACLOFEN 10/25 BIOTECH, especially sedation and should be avoided.

Severe aggravation of hyperkinetic symptoms may occur in patients taking Lithium and should be avoided.

There may be increased muscular weakness if BACLOFEN 10/25 BIOTECH is given to patients taking a tricyclic antidepressant.

There may be an increased hypotensive effect it is given to patients receiving antihypertensive therapy.

NSAID's and other medication that produce renal insufficiency may reduce BACLOFEN 10/25 BIOTECH excretion leading to toxicity.

In patients with Parkinson's disease receiving treatment with BACLOFEN 10/25 BIOTECH and levodopa resulted in mental confusion, hallucinations, headaches, nausea and agitation (*See Warnings and Special Precautions*)

PREGNACY AND LACTATION

BACLOFEN 10/25 BIOTECH should not be administrated during pregnancy and lactation. (see *Contraindications*)

DOSAGE AND DIRECTIONS FOR USE

Treatment should always be initiated with smallest dosage and should be gradually increased. The optimum daily dosage should be individually adapted to the patients' 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 10/25 BIOTECH 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.

BACLOFEN 10/25 BIOTECH should be taken during meals with a little liquid.

The daily dosage should be given in at least 3 divided doses in adults.

Adults

Treatment should as a rule be started with a dosage of 5 mg three times daily, which – for the purpose of cautions dose titration – should subsequently be increased at three-day intervals by 5 mg three times daily until the requisite daily dosage has been attained, see dosage below:

5 mg three times daily for 3 days

10 mg three times daily for 3 days

15 mg three times daily for 3 days

20 mg three times daily for 3 days

In certain patients reacting sensitively to medicines, t may be advisable to begin with a lower daily dosage (5 mg or 10 mg) 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.

Renal Impairment

In patients with impaired renal function or undergoing chronic haemodialysis, a particularly low dosage of BACLOFEN 10/25 BIOTECH should be selected, i.e. approximately 5 mg daily.

Elderly

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 and that the patient be kept under appropriate surveillance.

Children

This presentation is not recommended for children**.**

Withdrawal Effects

Withdrawal of BACLOFEN 10/25 BIOTECH should be gradual. Abrupt discontinuation of the treatment should be avoided (see "*Warnings and Special precautions*")

SIDE EFFECTS

Nervous system disorders

Frequent: Confusion, sedation, somnolence, drowsiness, fatigue, light-headedness, lassitude, exhaustion, dizziness, headache, insomnia, tremor, nystagmus, asthenia.

Less frequent: Paraesthesia, dysarthria, dysgeusia, convulsions, slurred speech, paradoxical increase in spasticity, hypothermia, coma, encephalopathy, incoordination, dystonia, seizures.

Frequency not known: Aseptic meningitis, encephalopathy.

Psychiatric disorders

Frequent: Mental confusion, euphoria, hallucination, nightmares.

Less frequent: Depression.

Frequency not known: Catatonic reaction, mania, mood disorder, amnesia.

Respiratory, thoracic and mediastinal disorders

Frequent: Respiratory depression.

Frequency not known: Acute bronchospasm, bronchial hyper responsiveness, dyspnoea and chest tightness, decreased cough reflex, nasal congestion.

Musculoskeletal disorders

Frequent: Myalgia, muscular weakness and pain, ataxia.

Rare: Muscle rigidity.

Certain patients have shown increased spasticity as a paradoxical reaction to the medication. An undesirable degree of muscular hypotonia – making it more difficult for patient to walk or fend for themselves – may occur and may be relieved by re-adjusting the dosage.

Eye disorders

Frequent: Accommodation disorders, visual disturbances.

Less frequent: Nystagmus, strabismus, diplopia, mydriasis.

Ear and labyrinth disorders

Less frequent: Tinnitus.

Cardiac disorders

Frequent: Decrease cardiac output, cardiac depression.

Less frequent: Chest pain, palpitations, syncope.

Frequency not known: Bradycardia.

Vascular disorders

Less frequent: Hypotension, ankle oedema.

Frequency not known: Increased sweating.

Gastrointestinal disorders

Frequent: Nausea, gastrointestinal disturbances, retching, vomiting, constipation or diarrhoea, dryness of mouth, taste alterations, xerostomia.

Less frequent: Abdominal pain, dryness of mouth.

Hepato-biliary disorders

Less frequent: Abnormal hepatic function, elevated liver enzymes.

Skin and subcutaneous tissue disorders

Frequent: Hyperhidrosis, rash.

Frequency unknown: Allergic skin reactions, pruritus, urticaria.

Renal and urinary disorders

Frequent: Urinary disturbances, pollakiuria.

Less frequent: Urinary retention, dysuria, haematuria.

Frequency not known: Enuresis, urinary incontinence.

Endocrine disorders

Frequency not known: Blood sugar changes, weight gain or anorexia.

Reproductive system and breast disorders

Less frequent: Erectile dysfunction, impotence.

KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT

Signs and symptoms of an overdosage are predominantly coma, respiratory depression, seizures and impairment of consciousness have been reported following significant over dosage.

Convulsions occur mainly in patents with a history of epilepsy.

Deterioration in the condition may occur if various substances acting on the central nervous system have been taken at the same time.

No specific antidote is known. Elimination of baclofen from the gastro-intestinal tract (induction of vomiting, gastric lavage; comatose or convulsing patients should be intubated prior to gastric lavage).

Treatment is symptomatic and supportive.

IDENTIFICATION

10 mg: 7.5 mm round, biconvex, white tablet with score mark on one side.

25 mg: 8 mm Flat bevelled edge white tablet with score mark on one side and plain on other side.

PRESENTATION

Baclofen 10 Biotech and Baclofen 25 Biotech tablets are available in the following packaging options:

- White polypropylene securitainer with clip on LDPE white opaque lid and cotton wool (non-absorbent). Pack sizes: 30's and 100's
- Amber glass bottle with black, hard plastic screw on cap and polycell inner seal and cotton wool (non-absorbent). Pack sizes: 30's and 100's
- White HDPE opaque container (50 mL) with a white opaque coloured cap with induction sealing wad. Pack sizes: 30's and 100's
- Silver aluminium and clear, transparent PVC/PVdC blister packs. Each blister containing 10 tablets. Pack sizes: 3 x 10's
- White, opaque, plain polyethylene zip-lock pouch, open from bottom side, with a zip lock and perforation on the top side. Pack sizes: 28's

STORAGE INSTRUCTION

Store at or below 25 ˚C in a dry place.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

BACLOFEN 10 BIOTECH - W/2.10/0236

BACLOFEN 25 BIOTECH – W/2.10/0237

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