PRODUCT MONOGRAPH

Pr phl-BACLOFEN

(Baclofen tablets, USP 10 mg & 20 mg)

Muscle Relaxant / Antispastic Agent

PHARMEL INC.
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PRODUCT MONOGRAPH

NAME OF DRUG

^{Pr}phl-BACLOFEN

(Baclofen Tablets, USP 10mg & 20mg)

THERAPEUTIC CLASSIFICATION

Muscle Relaxant and Antispastic Agent

ACTION

The precise mechanisms of action of baclofen are not fully known. It inhibits both monosynaptic and polysynaptic reflexes at the spinal level, probably by hyperpolarization of afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Although baclofen is an analog of the putative inhibitory neurotransmitter gamma-aminobutyric acid (GABA), there is no conclusive evidence that actions on GABA systems are involved in the production of its clinical effects.

Peak plasma concentrations of baclofen are achieved within 2 hours and the plasma half-life is approximately 2-4 hours.

INDICATIONS

phl-BACLOFEN is useful for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis.

phl-BACLOFEN may also be of some value in patients with spinal cord injuries and other spinal cord diseases.

CONTRAINDICATIONS

Hypersensitivity to phl-BACLOFEN or to any of the excipients.

WARNINGS

Abrupt Drug Withdrawal:
Following abrupt withdrawal of baclofen, visual and auditory hallucinations, convulsions (status epilepticus), dyskinesia, confusion, psychotic, manic or paranoid states, anxiety with tachycardia and sweating, insomnia, and worsening of spasticity have occurred. Therefore, except for serious adverse reactions, the dose should be reduced slowly when the drug is discontinued (over a period of approximately 1-2 weeks).

For the intrathecal formulation of baclofen, it has been reported that clinical characteristics of withdrawal may resemble autonomic dysreflexia, malignant hyperthermia, neuroleptic-malignant syndrome, or other conditions associated with a hypermetabolic state or widespread rhabdomyolysis.

Neonatal Withdrawal:
Convulsions have been reported in neonatals after intrauterine exposure to oral baclofen (See WARNINGS - Pregnancy).

Impaired Renal Function:
Because baclofen is primarily excreted unchanged through the kidneys, it should be given with caution in patients with renal insufficiency, and generally with a reduced dose. In patients dependent on dialysis, a particularly low dose of phl-BACLOFEN should be selected i.e. approximately 5 mg daily.

Unscheduled hemodialysis may be considered a treatment option in cases of severe baclofen toxicity as hemodialysis has been reported to effectively remove baclofen from the body, alleviate clinical symptoms of overdose and shorten the recovery time in these patients.

End Stage Renal Failure: phl-BACLOFEN should only be administered to end stage renal failure patients when benefits are considered acceptable, given potential risks. These patients should be closely monitored for prompt diagnosis of early signs and/or symptoms of toxicity (e.g. somnolence, lethargy) (see SYMPTOMS AND TREATMENT OF OVERDOSAGE).

Concomitant medications that may impact renal function: Particular caution is required when combining baclofen to drugs or medicinal products that can significantly impact renal function. Renal function shall be closely monitored and phl-BACLOFEN daily dosage adjusted accordingly to prevent baclofen toxicity (see PRECAUTIONS, Drug interactions).

Stroke:

Baclofen has not significantly benefited patients with stroke. These patients have also shown poor tolerability to the drug.

Pregnancy and Lactation:

Safe use of Baclofen during pregnancy or lactation has not been established. Baclofen crosses the placental barrier and passes into breast milk. High doses are associated with an increased incidence of abdominal hernias in the fetuses of rats and of ossification defects in those of rats and rabbits. Therefore, the drug should be administered to pregnant patients, or women of child-bearing potential only when, in the judgment of the physician, the potential benefits outweigh the possible hazards.

Infants exposed to baclofen through maternal oral dosing during pregnancy are at risk of experiencing baclofen withdrawal at birth; identification of this condition may be confounded due to delayed appearance of withdrawal symptoms in this population. One case of suspected withdrawal reaction (generalized convulsions) has been reported in a week-old infant whose

mother had taken oral baclofen during pregnancy. The convulsions, which were refractory to standard anticonvulsant treatment, ceased within 30 minutes of giving baclofen to the infant.

Epilepsy:

Extreme caution should be exercised in patients with epilepsy or a history of convulsive disorders. In such patients, the clinical state and electroencephalogram should be monitored at regular intervals during therapy, as deterioration in seizure control and EEG has been reported occasionally in patients taking baclofen.

PRECAUTIONS

Use in Children:

Safe use of baclofen in children under age 12 has not been established and it is, therefore, not recommended for use in children.

Effects on Ability to Drive and Use Machines:

Baclofen may be associated with dizziness, sedation, somnolence and visual disturbance (see section Adverse Reactions) which may impair the patient's reaction. Patients experiencing these adverse reactions should be advised to refrain from driving or using machines. Patients should also be cautioned that the central nervous system effects of baclofen may be additive to those of alcohol and other CNS depressants.

General:

phl-BACLOFEN should be used with caution where spasticity is utilized to sustain upright posture and balance in locomotion, or whenever spasticity is utilized to obtain increased function.

Caution should also be used in treating the following populations: patients with peptic ulceration (or a history of); elderly patients with cerebrovascular disorders; and patients with respiratory or hepatic failure. **Regarding patients with renal failure, see WARNING, Impaired Renal function.**

Urinary disorders:

phl-BACLOFEN should be used with caution in patients with underlying bladder sphincter hypertonia, since acute retention of urine may occur.

Psychiatric and Nervous System Disorders:

Patients with psychiatric disorders such as psychosis, schizophrenia, or confusional states should be treated cautiously with phl-BACLOFEN and kept under close surveillance, since exacerbation of these conditions may occur with baclofen treatment.

Laboratory tests:

The following laboratory tests have been found to be abnormal in a few patients receiving baclofen: SGOT, alkaline phosphatase and blood sugar (all elevated). Therefore, in patients with liver diseases or diabetes mellitus, appropriate laboratory tests should be performed periodically in order to ensure that no drug-induced changes in these underlying diseases have occurred.

Drug Interactions:

The concomitant administration of baclofen and tricyclic antidepressants may potentiate the pharmacological effects of baclofen, resulting in pronounced muscular hypotonia.

The concurrent use of MAO inhibitors and baclofen may result in increased CNS-depressant effects; therefore, caution is advised and the dosage of one or both agents should be adjusted accordingly.

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

In patients with Parkinson's disease receiving treatment with baclofen and levodopa plus carbidopa, there have been several reports of mental confusion, hallucinations and agitation.

Isolated cases of increased blood glucose concentrations have been reported with baclofen; dosage adjustments of antidiabetic agents (oral and insulin) may therefore be necessary with combined phl-BACLOFEN treatment.

Caution should be exercised when administering phl-BACLOFEN and magnesium sulfate (or other neuromuscular blocking agents), since a synergistic effect may theoretically occur.

Drugs or medicinal products that can significantly impact renal function may reduce baclofen excretion leading to toxic effects (see WARNINGS, Impaired Renal Function).

Lactation

Baclofen is excreted in human milk. As a general rule, nursing should not be undertaken while a patient is on a drug.

ADVERSE REACTIONS

Adverse effects most frequently occur at the start of treatment (e.g. sedation, somnolence), particularly if the dosage is increased too rapidly, if large doses are administered, and in the elderly patient. However, these effects are often transient and can be alleviated or eliminated by decreasing the dosage; they are seldom severe enough to warrant withdrawal of the medication. In elderly patients or those patients with cerebrovascular disorder or a history of psychiatric illness, more serious adverse reactions may occur, such as hallucinations and confusion.

The most common adverse reactions associated with baclofen are transient somnolence, sedation, dizziness, weakness and fatigue. Other adverse reactions reported were:

Neuropsychatric:

Headache (<10%), insomnia (<10%), muscular weakness, light-headedness, lassitude, exhaustion, tremor, ataxia, respiratory depression, euphoric mood, depression, confusional state, hallucinations, nightmares, myalgia, nystagmus, and, rarely (≥ 0.01% to < 0.1%), excitement,

paresthesia, tinnitus, slurred speech, coordination disorder, rigidity, dystonia, blurred vision, strabismus, miosis, mydriasis, diplopia, dysarthria, epileptic seizures, lowered convulsion threshold, and, very rarely (< 0.01%), hypothermia.

Cardiovascular:
Hypotension (<10%), cardiac output decreased, rare instances (≥ 0.01% to < 0.1%) of dyspnea, palpitation, chest pain, syncope.

Gastrointestinal:
Nausea (approx. 10%), constipation (<10%), gastrointestinal disturbance**,** retching, vomiting, diarrhea, dry mouth, and, rarely (≥ 0.01% to < 0.1%), anorexia, dysgeusia, abdominal pain, and positive test for occult blood in stool.

Genitourinary:
Pollakiuria (<10%), enuresis, dysuria, and, rarely (≥ 0.01% to < 0.1%), inability to ejaculate, nocturia, hematuria, urinary retention and erectile dysfunction.

Other:
Instances of rash, pruritus, urticaria, ankle edema, hyperhidrosis, weight gain, nasal congestion, accommodation disorders, visual disturbances, and, rarely (≥ 0.01% to < 0.1%), hepatic function abnormal.

Certain patients have shown increased muscle spasticity as a paradoxical reaction to the medication.

Muscular hypotonia of a degree sufficient to make walking or movement difficult may occur, but is usually relieved by readjusting the dosage. For this purpose, the daytime dose may be reduced and the evening dose increased.

Some of the CNS and genitourinary symptoms reported may be related to the underlying disease rather than to drug therapy.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Signs and Symptoms:

Symptoms of overdosage are predominantly those of central nervous system depression and include drowsiness, impairment of consciousness, respiratory depression, coma, seizures, confusion, hallucinations, agitation, EEG changes (burst suppression pattern and triphasic waves), accomodation disorders, absent pupillary refexes, muscular hypotonia, myoclonia, hyporeflexia or areflexia, hypotension or hypertension, bradycardia, tachycardia or cardiac arrhythmias, hypothermia, peripheral vasodilatation, nausea, vomiting, diarrhea, increased salivation, elevated LDH, AST, alkaline phosphatase and blood glucose values.

The signs and symptoms may be further aggravated by co-administration of a variety of other agents including alcohol, diazepam, and tricyclic antidepressants.

Treatment:

There is no specific antidote. Supportive measures and symptomatic treatment should be given for complications such as hypotension, hypertension, convulsions, gastrointestinal disturbances, and respiratory or cardiovascular depression.

After ingestion of a potentially toxic amount, activated charcoal should be considered, especially during the early period after ingestion. 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. A high urinary output should be maintained since phl-BACLOFEN (baclofen) is excreted mainly by the kidneys. For this purpose, generous quantities of fluid should be administered, possibly together with a diuretic. Hemodialysis (sometimes unscheduled) is indicated in severe poisoning associated with renal

failure (see WARNINGS, Impaired Renal Function). In the event of convulsions, administer diazepam i.v. with caution.

For management of a suspected drug overdose, contact your regional Poison Control Center Immediately.

DOSAGE AND ADMINISTRATION

The determination of optimal dosage of phl-BACLOFEN (baclofen) requires individual titration. Start therapy at a low dosage and increase gradually until optimum effect is achieved (usually between 40 mg -80 mg daily).

Treatment should be started with a dosage of 15 mg daily, preferably in divided doses.
The following dosage titration schedule is suggested:

5 mg t.i.d. for 3 days

10 mg t.i.d. for 3 days

15 mg t.i.d. for 3 days

20 mg t.i.d. for 3 days

Thereafter additional increases may be necessary but the total daily dose should not exceed a maximum of 80 mg daily (20 mg q.i.d.).

The lowest dose compatible with an optimal response is recommended. If benefits are not evident after a reasonable trial period, patients should be slowly withdrawn from the drug (See WARNINGS).

Impaired Renal Function:

Because baclofen is primarily excreted unchanged through the kidneys, it should be given with caution in patients with renal insufficiency, and generally with a reduced dose. In patients

dependent on dialysis, a particularly low dose of phl-BACLOFEN should be selected i.e. approximately 5 mg daily (see WARNINGS, Impaired Renal Function).

AVAILABILITY OF DOSAGE FORMS

phl-BACLOFEN tablet:

10 mg: White, oval shaped tablets debossed with a score on one side of the tablet and "BAC 10" on the other side. Available in bottles of 100 and 500.

20 mg: White, oval shaped tablet debossed with a score on one side of the tablet and "BAC 20" on the other side. Available in bottles of 100.

PHARMACEUTICAL INFORMATION

Proper Name: Baclofen

Chemical Names:

(i) 4-Amino-3-(p-chlorophenyl) butyric acid

(ii) ß-(Aminomethyl)-4-chlorobenzenepropionic acid

(iii) ß-(Aminomethyl)-p-chlorohydrocinnamic acid

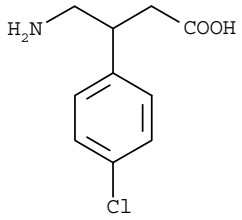
(iv) τ-Amino-ß-(p-chlorophenyl)butyric acid

(v) ß-(4-Chlorophenyl) GABA

Molecular Weight: 213.66 g/mol

Molecular Formula: $C_{10}H_{12}ClNO_2$

Structural Formula:



Description:

Baclofen is a white to off-white, virtually odourless, crystalline powder with a slightly bitter taste.

The melting range (192°C-193°C) of baclofen can vary due to lactam formation with a concomitant loss of water.

Baclofen is slightly soluble in water, poorly soluble in organic solvents.

The pKa values in water ($5.0x10^{-3}$ moles/1) at 20°C are as follows:

pKa1 = 3.87 + 0.1 (carboxyl group)

pKa2 = 9.62 + 0.1 (amino group)

Stability and Storage Recommendations

Store between 15°C and30°C

Protect from heat and humidity.

phl-BACLOFEN must be kept out of the reach and sight of children.

CLINICAL TRIALS

COMPARATIVE BIOAVAILABILITY STUDY

A bioavailability study was performed to compare the plasma levels produced after a single oral dose administration of two different formulations of baclofen 20 mg to 24 healthy volunteers in order to test their bioequivalency.

The results of the investigation show that the pharmacokinetic profile of the Pharmel Inc. baclofen formulation is almost superimposable to the one of the reference formulation, thus proving its bioequivalency.

Baclofen (1x 20 mg) From measured data Geometric Mean Arithmetic Mean (CV %)				
Parameter	**Test***	**Reference†**	**% Ratio of Geometric Means**	**Confidence Interval (90 %)**
AUC_T (ng•h/mL)	1727.36 1750.80 (16.9)	1643.22 1662.59 (15.4)	105.12	99.02-111.60
AUC_α (ng•h./mL)	1932.48 1955.94 (16.0)	1864.46 1888.63 (16.4)	103.65	97.58-110.10
C_{MAX} (ng/mL)	348.73 354.99 (18.9)	329.64 334.98 (18.0)	105.79	98.95-113.10
T_{MAX}§ (h)	1.57 (0.70)	1.22 (0.75)		
$T_{½el}$□ (h)	4.24 (1.09)	4.47 (1.23)		

* phl-BACLOFEN 20 mg tablets, Pharmel Inc

† Lioresal (baclofen) 20 mg tablets, Ciba-Geigy. (purchased in Canada)

§ Expressed as the arithmetic mean (CV%)

□ Expressed as the arithmetic mean (CV%) only.

PHARMACOLOGY

Baclofen exerted a pronounced muscle-relaxant effect in the non-anesthetized mouse, rabbit, cat, and dog. Doses of up to 10 mg/kg p.o. did not affect coordination in mice. Intravenous doses of 1 or 2 mg/kg decreased polysynaptic (flexor) spinal reflexes in anesthetized rabbits or cats respectively by 50%. A similar reduction was found in decerebrated or spinal cats. The monosynaptic (extensor) spinal reflex was reduced 50% by a dose of 0.5 mg/kg i.v. in spinalized, decerebrate, or anesthetized cats. Baclofen had no direct effect on the alpha-motor nerve fibres, neuromuscular transmission, or contraction of extrafusal muscle fibres in anesthetized cats. An intravenous dose of 0.8 mg/kg diminished the tonic activity of gamma motoneurons in decerebrate cats by 50%. Baclofen diminished or abolished decerebrate rigidity in cats in doses of 1-3 mg/kg. It had no effect on the de-efferented muscle spindle or the slowly-adapting pulmonary stretch receptors in anesthetized cats.
Baclofen had anticonvulsive effects against thiosemicarbazide and pentetrazole-induced convulsions in mice but had no effect against electroshock or strychnine-induced convulsions.

An intravenous dose of 3-6 mg/kg exerted a hypnotic effect in the unanesthetized dog.

Large doses impaired respiration in mice, rabbits, and dogs. Doses of 1 mg/kg i.v. produced a fall in the blood pressure of anesthetized rabbits or cats, but 3 mg/kg i.v. had no effect on the blood pressure, heart rate, ECG, or respiration of unanesthetized dogs.

In man a single oral dose of 10 mg of baclofen is rapidly and almost completely absorbed whereas absorption of 20 mg and 40 mg doses is less complete. Animal studies indicate rapid distribution throughout the body except to the CNS where concentrations are lower than average. The decay in CNS concentration is, however, slower than the decay from other tissues.

About 85% of a single oral dose is excreted unchanged in the urine. The remaining 15% is mainly deaminated to ß-p-chlorophenyl)-τ-hydroxybutyric acid within 24 hours. Baclofen is about 30% bound to serum proteins.

TOXICOLOGY

Acute Toxicity:

SPECIES	ROUTE	LD_{50} (mg/kg)
Mouse	i.v.	26 ± 6
Mouse	p.o.	75 ± 22
Rat	i.v.	112 ± 14
Rat	p.o.	150 ± 18
Rat	s.c.	137 ± 17

The toxic symptoms in mice and rats included ataxia, clonic-tonic convulsions and respiratory paralysis.

Species	Sex M	Sex F	No. of Groups	No. of Animals per Group	Dose mg/kg/day	Route	Duration of Study	Toxic Effects
Rat	20	20	4	5M 5F	0,5, 10; 20-80 (weekly increases of 10 mg/kg/day)	p.o.	30 D	Slight adrenal enlargement
Rat	10	10	5	2M 2F	Baclofen + diazepam: 0 + 0, 4 + 2, 20 + 10, 0 + 10, 20 + 0	p.o.	30 D	None
Dog	8	8	4	2M 2F	0, 1, 2, 4-8 (doubled in last week)	p.o.	30 D	Emesis at all dose levels, anorexia, salivation, ataxia, sedation, weight loss.
Rat	80	80	4	20M 20F	0,5, 20-160, 40-500	p.o.	1 Y	Weight loss, mild alopecia, urinary incontinence at intermediate and high doses. Elevated mean neutrophil/lymphocyte ratios and SGPT at intermediate and high doses.
Rat	280	280	1 3	Control 100M 100F Test: 60M 60F	0,5, 25-50, 50-100	p.o.	1 Y	Reduced weight gain. Dose-related urinary frequency. Dose-related increase in incidence of ovarian cysts.
Dog	12	12	4	3M 3F	0, 2-4, 3-6, 4-12	p.o.	1 Y	Transient emesis, sedation, convulsions and cardiovascular collapse (single animal), possible slight adrenal enlargement, hind limb weakness or paralysis.

TERATOLOGY AND REPRODUCTION STUDIES

Rat: Doses of 4.4-5 mg/kg/day and 17.7-21.3 mg/kg/day were administered orally to two groups of female rats during pre-mating, mating, gestation, and lactation. The only significant effect was a reduction in litter size and survivability of offspring (possibly due to agalactia) in the high-dose group. In another rat study, doses of 5 and 10 mg/kg/day were administered by gavage during the last trimester of pregnancy and throughout the lactation period. Five of 31

dams in the high-dose group showed severe weight loss from days 15-21 of gestation as well as agalactia and the entire litter of each of these dams died by day 2 post-partum.

Rat and Mouse: Doses of 5 mg/kg/day and 20 mg/kg/day were administered by gavage to two groups of pregnant rats on days 6-15 of gestation. The only significant finding was the presence of abdominal hernias in 4/160 fetuses in the high-dose group. In a second similar study, 1/229 control fetuses and 6/293 fetuses from dams receiving 20 mg/kg/day had abdominal hernias. Comparable lesions did not occur in a similar mouse study.

The average number of stillbirths or viable newborns did not differ significantly between control and medicated groups. The average weight of neonates from the high-dose group was significantly reduced.

Rabbit: Doses of 1, 5, and 10 mg/kg/day were administered by gavage to groups of rabbits from the 6th to 18th day of gestation. There was an increased incidence of unossified phalangeal nuclei of forelimbs and hind-limbs in the fetuses from the high-dose group.

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PART III: CONSUMER INFORMATION

[Pr]phl-BACLOFEN
Baclofen Tablets, USP

This leaflet is part III of a three-part "Product Monograph" published when phl-BACLOFEN was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about phl-BACLOFEN. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
phl-BACLOFEN is one of a group of medicines called muscle relaxants.

phl-BACLOFEN is used to reduce and relieve the excessive tension (spasms) in your muscles occurring in various conditions such as multiple sclerosis and diseases or injuries of the spinal cord.

What it does:
Due to the relaxation of muscle and the consequent relief from pain, phl-BACLOFEN improves your ability to move, makes it easier for you to manage your daily activities and facilitates physiotherapy.

If you have any questions about how phl-BACLOFEN works or why this medicine has been prescribed for you, ask your doctor.

When it should not be used:
Do not take phl-BACLOFEN:

- If you are allergic (hypersensitive) to baclofen or any of the other ingredients listed in "**What the nonmedicinal ingredients are**".

If this applies to you, tell your doctor without taking phl-BACLOFEN.

If you think you may be allergic, ask your doctor for advice.

What the medicinal ingredient is:
The active substance of phl-BACLOFEN is baclofen.

What the non-medicinal ingredients are:
The non-medicinal ingredients are: colloidal silicon dioxide, dibasic calcium phosphate, lactose, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate.

What dosage forms it comes in:
Tablets: 10 mg and 20 mg.

WARNINGS AND PRECAUTIONS

BEFORE you use phl-BACLOFEN talk to your doctor or pharmacist if you:
• Have kidney disease. Your doctor will decide whether or not phl-BACLOFEN is the appropriate treatment for you;

- Are suffering from epilepsy (seizures);
- Have acute pain in your stomach (ulcer) or intestines, breathing problems, liver disease, or a disturbance of circulation in your brain;
- Are taking medicines for arthritis or pain (see section:"**Interactions with this medication**");
- Have difficulty urinating;
- Have certain mental illnesses accompanied by confusion or depression;
- Are diabetic.

Older people or people with a disturbance of circulation in the brain

If you are in one of these groups, you may experience more side effects. Therefore, your doctor will keep you under appropriate surveillance and may adapt the dose of phl-BACLOFEN you take.

Children and adolescents
Safe use of phl-BACLOFEN in children under age 12 has not been established and it is therefore not recommended for use in children.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.

You should not use phl-BACLOFEN during pregnancy unless your doctor advises you to do so. Tell your doctor if you are pregnant, planning to become pregnant, or breast-feeding. He or she will discuss with you the potential risk of taking phl-BACLOFEN during pregnancy or if you are breast-feeding. Use of phl-BACLOFEN during pregnancy may result in the newborn experiencing withdrawal from the drug sometime after delivery; in one case, the main symptom in the newborn was generalized convulsions.

Driving and using machines
In some people, phl-BACLOFEN may be associated with dizziness, sleepiness or visual disturbance. If this happens to you, do not drive a car, use a machine, or do other things that need your full attention.

Further safety measures
Before having any kind of surgery (including by the dentist), or emergency treatment, tell the doctor in charge of you that you are taking phl-BACLOFEN.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with phl-BACLOFEN include:
- Alcohol;
- Sedative drugs;
- Medicines used to treat depression;
- Medicines used to treat high blood pressure;
- Medicines used to treat Parkinson's disease;
- Medicines for arthritis or pain.

Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

You should not drink alcohol during your treatment with phl-BACLOFEN.

PROPER USE OF THIS MEDICATION

Usual dose:
Follow your doctor's instructions carefully. Do not exceed the recommended dose.

How much phl-BACLOFEN to take
Treatment usually start with 15 mg daily, preferably taken in divided doses. The dose is then gradually increased until the best results are obtained; this may be between 40 mg to 80 mg per day, taken in divided doses.

The dose prescribed by your doctor may be different from that written here. If this is the case, follow the doctor's instructions.

Your doctor will tell you exactly how many tablets of phl-BACLOFEN to take.

Depending on how you respond to the treatment, your doctor may suggest a higher or lower dose.

When to take phl-BACLOFEN
Taking phl-BACLOFEN at the same time each day will help you remember when to take your medicine.

How to take phl-BACLOFEN
Be sure to take this medicine regularly, and exactly as your doctor tells you. This will help you to get the best results and reduce the risk of side effects.

How long to take phl-BACLOFEN
Continue taking phl-BACLOFEN as your doctor tells you. If you have questions about how long to take phl-BACLOFEN talk to your doctor or your pharmacist.

Do not suddenly stop taking phl-BACLOFEN without first checking with your doctor. He or she will tell you when and how you can stop taking this medicine; stopping suddenly can make your condition worse.

If you stop your treatment suddenly, you may experience: nervousness, feeling confused, hallucinations, abnormal thinking or behaviour, convulsions, uncontrollable twitching, jerking or writhing movements, fast heart beat, high body temperature. The excessive tension (spasms) in your muscles may also become worse.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are not symptoms.

If you have accidentally taken many more tablets than your doctor has prescribed, seek immediate emergency medical treatment, even though you do not feel sick.

The main symptoms of overdose are drowsiness, breathing difficulties, trouble of consciousness and being unconscious (coma).

Other symptoms may include: feeling confused, hallucinations, agitation, convulsions, blurred vision, unusual muscle weakness, sudden contraction of the muscles, poor or absent reflexes, high or low blood pressure, slow, fast or irregular heart beat, low body temperature, nausea, vomiting, diarrhea or salivating a lot.

Missed Dose:
If you have forgotten to take one dose as scheduled, take it as soon as you remember. However, if it is almost time for your next dose, do not take the missed one at the same time as the scheduled one, otherwise you will be doubling the dose. Just go back to your regular dosing timetable. If you have forgotten to take several doses you should contact your doctor.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, phl-BACLOFEN can have some side effects, although not everybody gets them. These are often mild and are usually at the start of treatment; they normally wear off after a few days.

Very common side effects
These side effects may affect more than 1 in 10 patients.

- Drowsiness, sleepiness;
- Nausea.

If any of these affects you severely, **tell your doctor.**

Common side effects
These side effects may affect between 1 and 10 in every 100 patients.

- Feeling faint, tiredness, exhaustion, dizziness, headache, inability to sleep, weakness in arms and legs, pain in muscles, uncontrollable eye movement, dry mouth;
- Disturbance of the digestive tract, retching, vomiting, constipation, diarrhea;
- Sweating a lot;
- Passing more urine than normal, bedwetting.

If any of these affects you severely, **tell your doctor.**

Rare side effects
These side effects may affect between 1 and 10 in every 10,000 patients.

- Tingling or numbness of the hands and/or feet, difficulty in speaking, taste disturbance;
- Abdominal pain;
- Sudden decrease in urine;
- Inability to get or to maintain an erection (impotence).

If any of these affects you severely, **tell your doctor.**

If you notice any other side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek immediate emergency medical treatment
		Only if severe	In all cases	
Common	Breathing problems		√	
	Feeling of confusion		√	
	Feeling of extreme happiness		√	
	Sad mood (depression)		√	
	Loss of coordination affecting balance and walking, limb and eye movements and/or speech (signs of ataxia)		√	
	Trembling		√	
	Hallucinations		√	
	Nightmares		√	
	Blurred vision/visual disturbance		√	
	Shortness of breath at rest or with activity, swelling in the legs and tiredness (signs of decreased cardiac output)		√	
	Low blood pressure (hypotension).		√	
	Skin rash and hives		√	
	Difficulty passing urine, pain when passing urine or a sudden decrease in urine.		√	
Rare	Abdominal pain, yellowing of the skin or eyes and tiredness (signs of liver disturbance)			√
	Convulsions			√
Very rare	Low body temperature		√	

This is not a complete list of side effects. For any unexpected effects while taking phl-BACLOFEN, contact your doctor or pharmacist.

HOW TO STORE IT

- Store between 15°C and30°C
- Protect from heat and humidity.
- Do not use after the expiry date shown on the bottle.
- Keep out of the reach and sight of children

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect .

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Please consult your doctor or pharmacist with any questions or concerns you may have regarding your individual condition

This document plus the full product monograph, prepared for health professionals, can be obtained by contacting the sponsor, Pharmel Inc. at, 1-888-550-6060.

This leaflet was prepared by
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