RxAdvance

NEW DRUG APPROVAL

Brand Name	Lyvispah™
Generic Name	baclofen
Drug Manufacturer	Saol Therapeutics Inc

New Drug Approval

FDA approval date: November 22, 2021

Review designation: Standard

Type of review: Type 3 - New Dosage Form; New Drug Application (NDA) 215422

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Spasticity is a motor disorder marked by a velocity-dependent increase in muscle tone or tonic stretch reflexes associated with hypertonia. Colloquially, it is often referred to as “tightness” or “stiffness.” Spasticity can present variably in a clinical setting, sometimes with a subtle neurological manifestation and, other times, with severely increased muscle tone leading to immobility of joints. Spasticity can lead to many complications, including but not limited to, interference with daily function, hygiene, comfort, and nursing care as well as contractures, increasing the risk of pressure ulcers and subsequent infections. Also, spasticity poses an increased risk of subluxation and/or dislocation as well as heterotopic ossification. In some cases, manifestations are subtle, and in others, muscle tone is increased to the point that joints become immobilized. This activity describes the evaluation and management of spasticity and highlights the role of team-based interprofessional care for affected patients. Many clinical scenarios can lead to spasticity, such as stroke, cerebral palsy (CP), anoxia, traumatic brain injury (TBI), spinal cord injury (SCI), multiple sclerosis (MS), and other neurodegenerative diseases.

Epidemiology- Of the diseases mentioned, spasticity affects approximately 35% of those with stroke, more than 90% with CP, about 50% of TBI patients, 40% of SCI patients, and between 37% and 78% of MS patients.

Efficacy

The efficacy of Lyvispah™ is based upon a bioavailability study in healthy adults comparing baclofen oral tablets to Lyvispah™. Pharmacokinetic studies in heathy adult subjects under fasting conditions at 20 mg dose level demonstrated similar bioavailability for baclofen oral granules and oral tablets.

Safety

ADVERSE EVENTS

The most common adverse reaction is transient drowsiness. In one controlled study of 175 patients, transient drowsiness was observed in 63% of those receiving baclofen compared to 36% of those in the placebo group. Other common adverse reactions (up to 15%) are dizziness and weakness.

Adverse reactions with a frequency of ≥1% are listed in Table 1.

Table 1. Common (≥1%) Adverse Reactions in Patients Treated with baclofen for Spasticity

Adverse reaction	Percent
Drowsiness	10-63%
Dizziness	5-15%
Weakness	5-15%
Nausea	4-12%
Confusion	1-11%
Hypotension	0-9%
Headache	4-8%
Insomnia	2-7%
Constipation	2-6%
Urinary Frequency	2-6%
Fatigue	2-4%

The following adverse reactions not included in Table 1, classified by body system, were also reported:
Neuropsychiatric: euphoria, excitement, depression, hallucinations, paresthesia, muscle pain, tinnitus, slurred speech, coordination disorder, tremor, rigidity, dystonia, ataxia, blurred vision, nystagmus, strabismus, miosis, mydriasis, diplopia, dysarthria, epileptic seizure.
Cardiovascular: dyspnea, palpitation, chest pain, syncope.
Gastrointestinal: dry mouth, anorexia, taste disorder, abdominal pain, vomiting, diarrhea, and positive test for occult blood in stool.
Genitourinary: enuresis, urinary retention, dysuria, impotence, inability to ejaculate, nocturia, hematuria.
Other: rash, pruritus, ankle edema, excessive perspiration, weight gain, nasal congestion.

The following laboratory tests have been found to be abnormal in patients receiving baclofen: increased SGOT, elevated alkaline phosphatase, and elevation of blood sugar.

WARNINGS & PRECAUTIONS

Adverse Reactions from Abrupt Withdrawal of Lyvispah™-
Abrupt discontinuation of baclofen, regardless of the cause, has resulted in adverse reactions that include hallucinations, seizures, high fever, altered mental status, exaggerated rebound spasticity, and muscle rigidity, that in rare cases has advanced to rhabdomyolysis, multiple organ-system failure, and death. Therefore, reduce the dosage slowly when Lyvispah™ is discontinued, unless the clinical situation justifies a rapid withdrawal.

Neonatal Withdrawal Symptoms-
Withdrawal symptoms in neonates whose mothers were treated with oral baclofen throughout pregnancy have been reported starting hours to days after delivery. The symptoms of withdrawal in these infants have included increased muscle tone, tremor, jitteriness, and seizure.

Drowsiness and Sedation-

Drowsiness and sedation have been reported in up to 63% of patients taking baclofen, the active ingredient in Lyvispah™. Patients should avoid operation of automobiles or other dangerous machinery and activities made hazardous by decreased alertness when starting Lyvispah™ or increasing the dosage until they know how the drug affects them. Advise patients that the central nervous system depressant effects of Lyvispah™ may be an additive to those of alcohol and other CNS depressants.

Poor Tolerability in Stroke Patients-
Lyvispah™ should be used with caution in patients who have had a stroke. Baclofen has not significantly benefited patients with stroke. These patients have also shown poor tolerability to the drug.

Exacerbation of Psychotic Disorders, Schizophrenia, or Confusional States-
Lyvispah™ should be used with caution in patients suffering from psychotic disorders, schizophrenia, or confusional states. If treated with Lyvispah™, these patients should be kept under careful surveillance because exacerbations of these conditions have been observed with oral baclofen administration.

Exacerbation of Autonomic Dysreflexia-
Lyvispah™ should be used with caution in patients with a history of autonomic dysreflexia. The presence of nociceptive stimuli or abrupt withdrawal of Lyvispah™ may cause an autonomic dysreflexic episode.

Exacerbation of Epilepsy-
Lyvispah™ should be used with caution in patients with epilepsy. Deterioration in seizure control has been reported in patients taking baclofen.

Posture and Balance Effects-
Lyvispah™ should be used with caution in patients where spasticity is utilized to sustain upright posture and balance in locomotion or whenever spasticity is utilized to obtain increased function.

Ovarian Cysts-
Ovarian cysts have been found by palpation in about 4% of the multiple sclerosis patients who were treated with oral baclofen for up to one year. In most cases, these cysts disappeared spontaneously while patients continue to receive the drug.

CONTRAINDICATIONS

Hypersensitivity to baclofen.

Clinical Pharmacology

MECHANISMS OF ACTION

The precise mechanism of action of baclofen is not fully understood. Baclofen inhibits both monosynaptic and polysynaptic reflexes at the spinal level, possibly by decreasing excitatory neurotransmitter release from afferent terminals, although actions at supraspinal sites may also occur and contribute to its clinical effect. Baclofen is a structural analog of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) and may exert its effects by stimulation of the GABA-B receptor subtype.

Dose & Administration

ADULTS

Initiate Lyvispah™ with a low dosage, preferably in divided doses, administered orally. The following gradually increasing dosage regimen is suggested, but should be adjusted based on clinical response and tolerability:

- 5 mg three times a day for three days.
- 10 mg three times a day for three days.
- 15 mg three times a day for three days.
- 20 mg three times a day for three days.
- Additional increases may be necessary up to the maximum recommended dosage of 80 mg daily (20 mg four times a day).

PEDIATRICS

N/A

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

None

HEPATIC IMPAIRMENT

None

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Oral granules: 5 mg, 10 mg, or 20 mg baclofen in a packet.