NEW DRUG APPROVAL

Brand Name	Fleqsuvy™
Generic Name	baclofen oral suspension
Drug Manufacturer	Azurity Pharmaceuticals, Inc.

New Drug Approval

FDA approval date: February 4, 2022

Review designation: Standard

Type of review: Type 3 - New Dosage Form; New Drug Application (NDA): 215602

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Spasticity is one of the most disabling and difficult-to-treat symptoms shown by patients with multiple sclerosis, who often show a suboptimal and unsatisfactory response to classic treatment and new available nonpharmacological alternatives. Due to the progressive nature of this condition, the early management should be essential to improve long-term outcomes.

Spasticity is one of the most prevalent symptoms in multiple sclerosis (MS). Spasm as “a disorder of sensory motor control caused by an upper motor neuron lesion that manifests as intermittent or sustained activation of muscles” This definition considers the role of viscoelastic properties of soft tissue to limb stiffness and proprioceptive and cutaneous neural pathways.

Multiple sclerosis (MS) is a chronic, debilitating, inflammatory disease of the central nervous system. There is no cure for the disease, and management of it includes the use of disease-modifying therapies and symptomatic agents to reduce and/or prevent relapses and disease progression. MS affects approximately 400,000 persons in the United States (1), with an estimated prevalence of 1 in 1,000 individuals in North America and is one of the most common causes of disability in young adults. The symptoms of MS are numerous and include weakness, paresthesias, visual changes, fatigue, cognitive dysfunction, ataxia, and spasticity. Patients with MS report that their spasticity has a significant detrimental effect on their lives. A survey of 1,554 self-reporting people with MS residing in the United Kingdom demonstrated that 82% experience spasticity and 54% classified the impact of spasticity as “high” or “moderate” (2). Greater than 80% of patients with MS report some degree of spasticity, with one third of these modifying or eliminating daily activities as a result.

Spinal cord injury (SCI) Disease

SCI is damage to the spinal cord, the bundle of nerves running from the base of the brain (brainstem) to the upper part of the lumbar spine. SCI disrupts communication between the brain and the rest of the body below the level of the injury and depending on the severity resulting in the inability to move limbs, loss of sensation, bowel and bladder function. Depending on the underlying mechanism of injury, SCI can be divided into traumatic and non-traumatic causes. It can be further classified by the level of injury: tetraplegia involving all four limbs or paraplegia involving legs only; and the severity of injury: complete vs incomplete, with incomplete tetraplegia being most common.
According to the National Spinal Cord Injury Association, as many as 450,000 people in the United States are living with a spinal cord injury (SCI). Other organizations conservatively estimate this figure to be about 250,000.

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Every year, an estimated 17,000 new SCIs occur in the U.S. Most of these are caused by trauma to the vertebral column, thereby affecting the spinal cord's ability to send and receive messages from the brain to the body's systems that control sensory, motor and autonomic function below the level of injury.

According to the Centers for Diseases Control and Prevention (CDC), SCI costs the nation an estimated $9.7 billion each year.

Efficacy

Not available

Safety

ADVERSE EVENTS

The most common (up to 15% or more) adverse reactions in patients were drowsiness, dizziness, and weakness.

WARNINGS & PRECAUTIONS

- Abrupt discontinuation of baclofen has resulted in serious adverse reactions including death; therefore, reduce the dosage slowly when Fleqsuvy™ is discontinued.
- Neonatal withdrawal symptoms can occur; gradually reduce the dosage and discontinue Fleqsuvy™ before delivery.
- Fleqsuvy™ can cause drowsiness and sedation. Patients should avoid the operation of automobiles or other dangerous machinery until they know how the drug affects them. Advise patients that the central nervous system effects of Fleqsuvy™ may be additive to those of alcohol and other CNS depressants.
- Fleqsuvy™ can cause exacerbation of the following: psychotic disorders, schizophrenia, or confusional states; autonomic dysreflexia; epilepsy. Use with caution in patients with these conditions.

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 GABAB receptor subtype.

Dose & Administration

ADULTS

Fleqsuvy™ is a concentrated formulation. Verify the dose of the product prior to dispensing.

- Initiate Fleqsuvy™ with a low dosage, preferably in divided doses, administered orally. Increase gradually based on clinical response and tolerability.
- The maximum dosage is 80 mg daily (20 mg four times a day).
- When discontinuing, reduce the dosage slowly.

PEDIATRICS

Safety and effectiveness in pediatric patients below the age of 12 have not been established.

GERIATRICS

Refer to adult dosing; use with caution. If benefits are not observed, withdraw the drug slowly.

RENAL IMPAIRMENT

Because baclofen is primarily excreted unchanged through the kidneys, Fleqsuvy™ should be given with caution to patients with renal impairment, and it may be necessary to reduce the dosage.

- CrCl more than 80 mL/minute: No dosage adjustment necessary.
- CrCl 50 to 80 mL/minute: Reduce PO dosage by one-third.
- CrCl 30 to 50 mL/minute: Reduce PO dosage by one-half.
- CrCl less than 30 mL/minute and not on dialysis: Reduce PO dosage by two-thirds.

HEPATIC IMPAIRMENT

No dosage adjustment necessary.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Oral Suspension: 25 mg per 5 mL (5 mg/mL)