OZOBAX DS- baclofen solution
Metacel Pharmaceuticals, LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OZOBAX® DS safely and effectively. See full prescribing information for OZOBAX DS.

OZOBAX DS (baclofen) oral solution

Initial U.S. Approval: 1977

INDICATIONS AND USAGE

- OZOBAX DS is a gamma-aminobutyric acid (GABA-ergic) agonist indicated for the treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. (1)
- OZOBAX DS may also be of some value in patients with spinal cord injuries and other spinal cord diseases. (1)

Limitations of Use
OZOBAX DS is not indicated in the treatment of skeletal muscle spasm resulting from rheumatic disorders (1)

DOSAGE AND ADMINISTRATION

- Baclofen oral solution is available in multiple concentrations; include both the total dose in mg and the total dose in volume on prescriptions (2.1)
- Initiate OZOBAX DS with a low dosage, preferably in divided doses, administered orally. Increase gradually based on clinical response and tolerability. (2.2)
- The maximum dosage is 80 mg daily (20 mg four times a day). (2.2)
- When discontinuing, reduce the dosage slowly. (2.3)

DOSAGE FORMS AND STRENGTHS

Oral Solution: 10 mg/5 mL (3)

CONTRAINDICATIONS

- Hypersensitivity to baclofen (4)

WARNINGS AND PRECAUTIONS

- Abrupt discontinuation of baclofen has resulted in serious adverse reactions including death; therefore, reduce the dosage slowly when OZOBAX DS is discontinued. (5.1)
- Neonatal withdrawal symptoms can occur; gradually reduce the dosage and discontinue OZOBAX DS before delivery. (5.2)
- OZOBAX DS 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 OZOBAX DS may be additive to those of alcohol and other CNS depressants. (5.3)
- OZOBAX DS can cause exacerbation of the following: psychotic disorders, schizophrenia, or confusional states; autonomic dysreflexia; epilepsy. Use with caution in patients with these conditions (5.5, 5.6, 5.7)

ADVERSE REACTIONS

- The most common (up to 15% or more) adverse reactions in patients were drowsiness, dizziness, and weakness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Metacel Pharmaceuticals, LLC at 1-833-469-6229 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm (8.1)
- Because baclofen is excreted unchanged through the kidneys it may be necessary to reduce the dosage in patients with impaired renal function. (8.6)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

OZOBAX DS is indicated for the treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity.

OZOBAX DS may also be of some value in patients with spinal cord injuries and other spinal cord diseases.

Limitations of Use
OZOBAX DS is not indicated in the treatment of skeletal muscle spasm resulting from rheumatic disorders.

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosage Information

Baclofen oral solution is available in multiple concentrations; ensure accuracy when prescribing, dispensing and administering baclofen oral solution to avoid dosing errors due to confusion between mg and mL, and with other baclofen oral solutions of different concentrations. When writing prescriptions, include both the total dose in mg and the total dose in volume.

2.2 Recommended Dosage

Initiate OZOBAX DS 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 (2.5 mL) three times a day for three days

10 mg (5 mL) three times a day for three days

15 mg (7.5 mL) three times a day for three days

20 mg (10 mL) 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).

2.3 Discontinuation of OZOBAX DS

When discontinuing OZOBAX DS, reduce the dosage slowly and avoid abrupt withdrawn from the drug to help minimize the risk of adverse reactions *[see Warnings and Precautions (5.1)].*

3 DOSAGE FORMS AND STRENGTHS

Oral Solution: 10 mg/5 mL baclofen as a clear, colorless solution

4 CONTRAINDICATIONS

OZOBAX DS is contraindicated in patients with hypersensitivity to baclofen.

5 WARNINGS AND PRECAUTIONS

5.1 Adverse Reactions from Abrupt Withdrawal of OZOBAX DS

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 OZOBAX DS is discontinued, unless the clinical situation justifies a rapid withdrawal.

5.2 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. If the potential benefit justifies the potential risk to the fetus and OZOBAX DS is continued during pregnancy, gradually reduce the dosage and discontinue OZOBAX DS before delivery. If slow withdrawal is not feasible, advise the parents or caregivers of the exposed neonate of the potential for neonatal withdrawal.

5.3 Drowsiness and Sedation

Drowsiness and sedation have been reported in up to 63% of patients taking baclofen, the active ingredient in OZOBAX DS *[see Adverse Reactions (6.1)]* . Patients should avoid operation of automobiles or other dangerous machinery and activities made hazardous by decreased alertness when starting OZOBAX DS or increasing the dose until they know how the drug affects them. Advise patients that the central nervous system depressant effects of OZOBAX DS may be additive to those of alcohol and other CNS depressants.

5.4 Poor Tolerability in Stroke Patients

OZOBAX DS 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.

5.5 Exacerbation of Psychotic Disorders, Schizophrenia, or Confusional States

OZOBAX DS should be used with caution in patients suffering from psychotic disorders, schizophrenia, or confusional states. If treated with OZOBAX DS, these patients should be kept under careful surveillance because exacerbations of these conditions have been

observed with oral baclofen administration.

5.6 Exacerbation of Autonomic Dysreflexia

OZOBAX DS should be used with caution in patients with a history of autonomic dysreflexia. The presence of nociceptive stimuli or abrupt withdrawal of OZOBAX DS may cause an autonomic dysreflexic episode.

5.7 Exacerbation of Epilepsy

OZOBAX DS should be used with caution in patients with epilepsy. Deterioration in seizure control has been reported in patients taking baclofen.

5.8 Posture and Balance Effects

OZOBAX DS 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.

5.9 Ovarian Cysts

A dose-related increase in incidence of ovarian cysts was observed in female rats treated chronically with oral baclofen. 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 continued to receive the drug. Ovarian cysts are estimated to occur spontaneously in approximately 1% to 5% of the normal female population.

6 ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Adverse Reactions from Abrupt Withdrawal of OZOBAX DS *[see Warnings and Precautions (5.1)]*
- Neonatal Withdrawal Symptoms *[see Warnings and Precautions (5.2)]*
- Drowsiness and Sedation *[see Warnings and Precautions (5.3)]*
- Poor Tolerability in Stroke Patients *[see Warnings and Precautions (5.4)]*
- Exacerbation of Psychotic Disorders, Schizophrenia, or Confusional States *[see Warnings and Precautions (5.5)]*
- Exacerbation of Autonomic Dysreflexia *[see Warnings and Precautions (5.6)]*
- Exacerbation of Epilepsy *[see Warnings and Precautions (5.7)]*
- Posture and Balance Effects *[see Warnings and Precautions (5.8)]*
- Ovarian Cysts *[see Warnings and Precautions (5.9)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

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.

7 DRUG INTERACTIONS

7.1 CNS Depressants and Alcohol

OZOBAX DS can cause CNS depression, including drowsiness and sedation, which may be additive when used concomitantly with other CNS depressants or alcohol *[see Warnings and Precautions (5.3)].*

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with the use of OZOBAX DS in pregnant women. Oral administration of baclofen to pregnant rats resulted in an increased incidence of fetal structural abnormalities at a dose which was also associated with maternal toxicity. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Clinical Considerations

Fetal/Neonatal adverse reactions

Ozobax DS may increase the risk of late-onset neonatal withdrawal symptoms *[see Warnings and Precautions (5.2)]* .

Data

Animal Data

Baclofen given orally has been shown to increase the incidence of omphaloceles (ventral hernias) in fetuses of rats given approximately 13 times on a mg/kg basis, or 3 times on a mg/m^2 basis, the maximum oral dose recommended for human use; this dose also caused reductions in food intake and weight gain in the dams. This abnormality was not seen in mice or rabbits.

8.2 Lactation

Risk Summary

At recommended oral doses, baclofen is present in human milk. There are no human data on the effects of baclofen on milk production. There are no adequate data on the effects of baclofen on the breastfed infant. Withdrawal symptoms can occur in breastfed infants when maternal administration of OZOBAX DS is stopped, or when breastfeeding is stopped *[see Warnings and Precautions (5.2)]* .

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for OZOBAX DS and any potential adverse effects on the breastfed infant from OZOBAX DS or from the underlying maternal condition.

8.4 Pediatric Use

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

8.5 Geriatric Use

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic,

renal, or cardiac function, and of concomitant disease or other drug therapy.

8.6 Renal Impairment

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

10 OVERDOSAGE

10.1 Symptoms of Baclofen Overdose

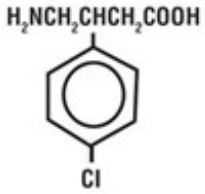
Patients may present in coma or with progressive drowsiness, lightheadedness, dizziness, somnolence, accommodation disorders, respiratory depression, seizures, or hypotonia progressing to loss of consciousness.

10.2 Treatment for Overdose

The treatment of baclofen overdose includes gastric decontamination, maintaining an adequate airway and respirations.

11 DESCRIPTION

OZOBAX DS (baclofen) oral solution is a gamma-aminobutyric acid (GABA-ergic) agonist available as 10 mg/5 mL solution for oral administration. Its chemical name is 4-amino-3-(4-chlorophenyl)-butanoic acid, and its structural formula is:



Molecular formula is $C_{10}H_{12}ClNO_2$.

Molecular Weight is 213.66.

Baclofen USP is a white to off-white, odorless or practically odorless crystalline powder. It is slightly soluble in water, very slightly soluble in methanol, and insoluble in chloroform.

The OZOBAX DS (baclofen) oral solution inactive ingredients are: glycerin, methylparaben, propylparaben, purified water, and sucralose. May also contain sodium hydroxide or hydrochloric acid for pH adjustment.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism 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.

12.2 Pharmacodynamics

Baclofen has been shown to have general CNS depressant properties, as indicated by the production of sedation with tolerance, somnolence, ataxia, and respiratory and cardiovascular depression *[see Warnings and Precautions (5.3), Adverse Reactions (6.1), and Overdosage (10.1)].*

12.3 Pharmacokinetics

A pharmacokinetic study in heathy adult male subjects under fasting conditions at 20 mg dose level demonstrated similar bioavailability for baclofen oral solution (5 mg/5 mL) and oral tablets. The peak plasma concentrations were achieved in about 0.75 hours from oral solution and the apparent elimination half-life is about 5.7 hours. Baclofen is excreted primarily by the kidney in unchanged form, and there is relatively large intersubject variation in absorption and/or elimination.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

No increase in tumors was seen in rats receiving baclofen orally for two years at approximately 30 to 60 times on a mg/kg basis, or 10 to 20 times on a mg/ m^2 basis, the maximum oral dose recommended for human use.

Mutagenesis

Genetic toxicology assays have not been conducted for baclofen.

Impairment of Fertility

Studies to evaluate the effects of baclofen on fertility have not been conducted.

14 CLINICAL STUDIES

The efficacy of OZOBAX DS is based upon a bioavailability study in healthy adults comparing baclofen oral tablets to baclofen oral solution *[see Clinical Pharmacology (12.3)].*

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

OZOBAX DS (baclofen) Oral Solution contains 10 mg/5 mL baclofen. It is a clear, colorless solution and is supplied in bottles of 237 mL (NDC 69528-302-08) and 473 mL

(NDC 69528-302-16).

16.2 Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Dispense in a tight, light-resistant container with a child-resistant closure.

17 PATIENT COUNSELING INFORMATION

Administration Instructions

Instruct patients or caregivers to use an oral dosing syringe to correctly measure the prescribed amount of medication. Inform patients that oral dosing syringes may be obtained from their pharmacy.

Risks Related to Sudden Withdrawal of OZOBAX DS

Advise patients and caregivers not to discontinue use of OZOBAX DS without consulting with their healthcare provider because sudden withdrawal of OZOBAX DS can result in serious complications that include hallucinations, seizures, high fever, confusion, muscle stiffness, multiple organ-system failure, and death *[see Warnings and Precautions (5.1)].* Inform patients that early symptoms of OZOBAX DS withdrawal may include increased spasticity, itching, and tingling of extremities.

Neonatal Withdrawal Symptoms

Advise patients to notify their healthcare provider if they are pregnant, plan to become pregnant, or plan to breastfeed *[see Warnings and Precautions (5.2) and Use in Specific Populations (8.2)].*

Increased Risk of Drowsiness with Alcohol and Other CNS Depressants

Advise patients that OZOBAX DS may cause drowsiness, and that they should avoid the operation of automobiles or other dangerous machinery, or activities made hazardous by decreased alertness when starting OZOBAX DS or increasing the dose until they know how the drug affects them *[see Warnings and Precautions (5.3)].* Inform patients and their caregivers that the drowsiness associated with OZOBAX DS use can be worsened by alcohol and other CNS depressants. Advise patients to read all medicine labels carefully, and to tell their healthcare provider about all prescription and nonprescription drugs they may use.

Manufactured by:

Delpharm Montreal, Inc.

3535 Route Trans Canada Highway

Pointe-Claire, QC, Canada H9R 1B4

Manufactured for:
Metacel Pharmaceuticals, LLC
Athens, GA 30601

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PACKAGE LABEL. PRINCIPAL DISPLAY PANEL

NDC 69528-302-08

OZOBAX ® DS

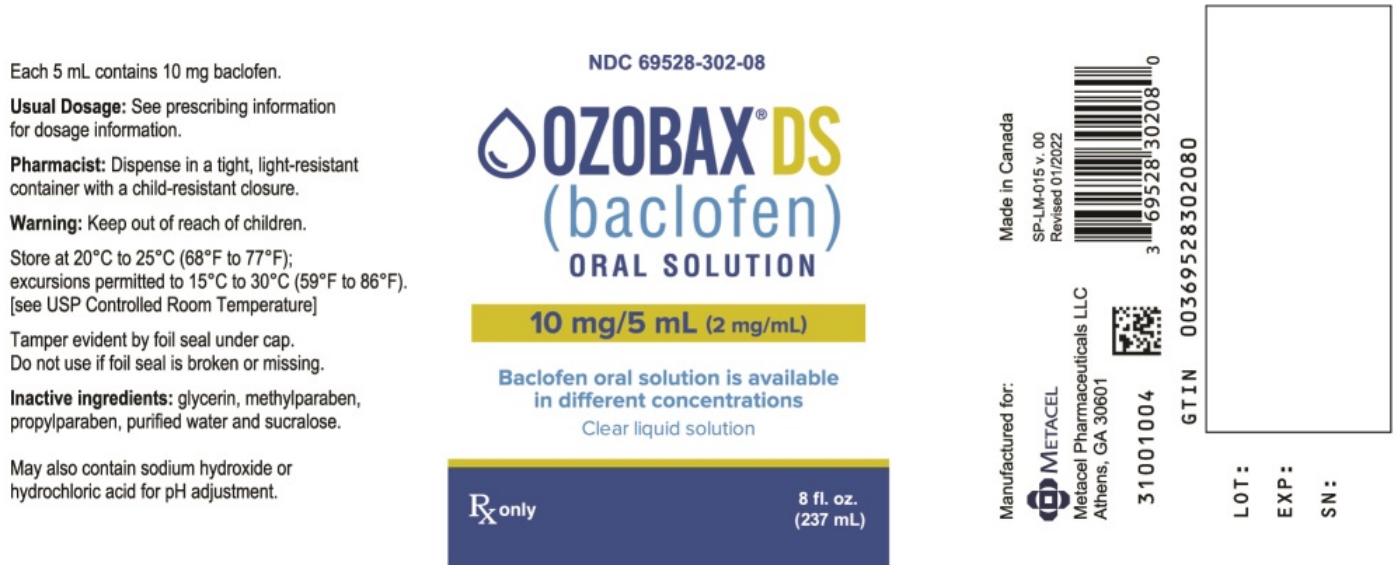
(baclofen)
Oral Solution

10 mg / 5 mL (2 mg/mL)

Baclofen oral solution is available in different concentrations
Clear liqud solution

R_X only

8 fl. oz. (237 mL)



NDC 69528-302-16

OZOBAX ® DS

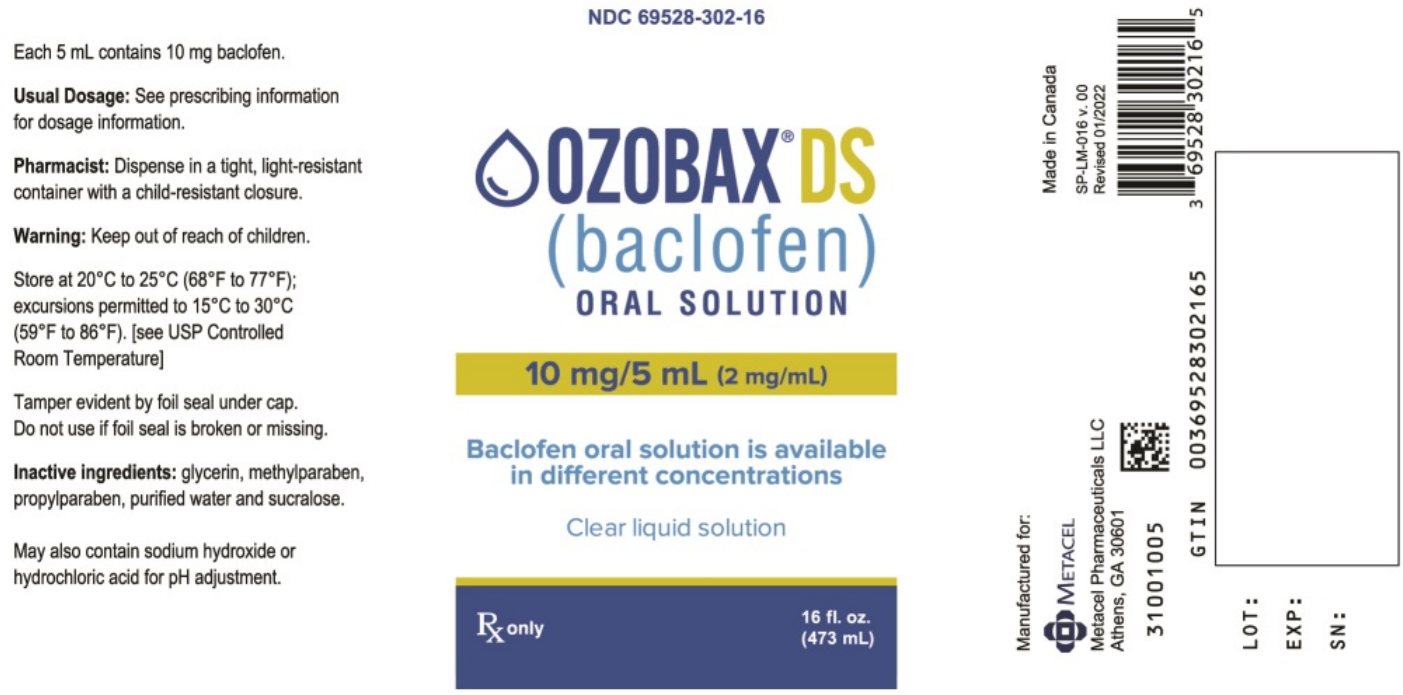
(baclofen)
Oral Solution

10 mg / 5 mL (2 mg/mL)

Baclofen oral solution is available in different concentrations
Clear liqud solution

R_X only

16 fl. oz. (473 mL)



OZOBAX DS

baclofen solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:69528-302
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
BACLOFEN (UNII: H789N3FKE8) (BACLOFEN - UNII:H789N3FKE8)	BACLOFEN	10 mg in 5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
GLYCERIN (UNII: PDC6A3C0OX)	
METHYLPARABEN (UNII: A2I8C7HI9T)	
PROPYLPARABEN (UNII: Z8IX2SC1OH)	
SUCRALOSE (UNII: 96K6UQ3ZD4)	
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:69528-302-08	237 mL in 1 BOTTLE; Type 0: Not a Combination Product	10/12/2023	
2	NDC:69528-302-16	473 mL in 1 BOTTLE; Type 0: Not a Combination Product	10/12/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA208193	10/12/2023	

Labeler - Metacel Pharmaceuticals, LLC (079475312)

Registrant - Metacel Pharmaceuticals, LLC (079475312)

Revised: 10/2023 Metacel Pharmaceuticals, LLC