Clinical Policy: Baclofen (Fleqsuvy, Gablofen, Lioresal, Lyvispah, Ozobax/Ozobax DS)

Reference Number: CP.PHAR.149
Effective Date: 12.01.15
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Baclofen (Fleqsuvy®, Gablofen®, Lioresal® Intrathecal, Lyvispah™, Ozobax®, Ozobax® DS) is a muscle relaxant and antispastic. Baclofen's pharmacological class is a gamma-aminobutyric acid (GABA)-ergic agonist.

FDA Approved Indication(s)

Gablofen and Lioresal Intrathecal** are indicated for use in the management of severe spasticity of cerebral or spinal cord origin.*

- Patients should first respond to a screening dose of intrathecal baclofen prior to consideration for long term infusion via an implantable pump.
- For spasticity of spinal cord origin, chronic infusion of Gablofen/Lioresal Intrathecal via an implantable pump should be reserved for patients unresponsive to oral baclofen therapy, or those who experience intolerable central nervous system side effects at effective doses.
- Patients with spasticity due to traumatic brain injury (TBI) should wait at least one year after the injury before consideration of long-term intrathecal baclofen therapy.

Fleqsuvy, Lvyispah and Ozobax/Ozobax DS are indicated for the treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. Fleqsuvy, Lyvispah and Ozobax may also be of some value in patient with spinal cord injuries and other spinal cord diseases.

Limitation(s) of use: Fleqsuvy, Lyvispah and Ozobax/Ozobax DS are not indicated in the treatment of skeletal muscle spasm resulting from rheumatic disorders.

**Gablofen is indicated in adults and pediatric patients age 4 years and above; safety and effectiveness of Lioresal Intrathecal in pediatric patients below the age of 4 have not been established. Safety and effectiveness of Fleqsuvy, Lyvispah and Ozobax/Ozobax DS in pediatric patients below the age of 12 have not been established.*
***Lioresal Intrathecal therapy may be considered an alternative to destructive neurosurgical procedures.*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Fleqsuvy, Gablofen, Lioresal, Lyvispah, and Ozobax/Ozobax DS are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Requests for Gablofen or Lioresal (must meet all):

1. Diagnosis of severe spasticity of cerebral or spinal cord origin (e.g., due to spinal cord injury, multiple sclerosis, hypoxic-ischemic encephalopathy, cerebral palsy, TBI);
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
3. Age ≥ 4 years;
4. If the spasticity is due to TBI, > 1 year has passed since the injury;
5. Documentation supports inability to use oral baclofen therapy;
6. Failure of one of the following conventional therapies (a, b, or c), unless clinically significant adverse effects are experienced or all are contraindicated:
   a. A benzodiazepine (e.g., diazepam, clonazepam);
   b. Dantrolene;
   c. Tizanidine;
7. Baclofen will be used in one of the following ways (a or b):
   a. Screening trial (i and ii):
      i. Prescribed formulation is one of the following (1 or 2):
         1) Gablofen: 50 mcg/mL (1 mL syringe);
         2) Lioresal Intrathecal: 50 mcg/mL (1 mL ampule);
      ii. Dose does not exceed 100 mcg;
   b. Maintenance therapy (i and ii):
      i. Prescribed formulation is one of the following (1 or 2):
         1) Any Gablofen vial/syringe except the 1 mL syringe;
         2) Any Lioresal Intrathecal ampule except the 1 mL ampule;
      ii. Member responded positively to an intrathecal baclofen screening dose (bolus of ≤ 100 mcg) as evidenced by decrease in muscle tone/frequency or spasm severity.

Approval duration:
Screening – 14 days (up to 3 screening trials)
Maintenance – 3 months

B. Requests for Fleqsuvy, Lyvispah or Ozobax/Ozobax DS (must meet all):

1. Diagnosis of severe spasticity of multiple sclerosis or due to spinal cord injury or spinal cord diseases;
2. Prescribed by or in consultation with a neurologist, orthopedist, physiatrist, or physical medicine and rehabilitation specialist;
3. Age ≥ 12 years;
4. Member must use generic baclofen oral solution, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of one of the following conventional therapies (a, b, or c), unless clinically significant adverse effects are experienced or all are contraindicated:
   a. A benzodiazepine (e.g., diazepam, clonazepam);
   b. Dantrolene;
   c. Tizanidine;
6. Dose does not exceed 80 mg per day.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. For Fleqsuvy, Lyvispah or Ozobax/Ozobax DS , member must use generic baclofen oral solution, unless contraindicated or clinically significant adverse effects are experienced;
4. Gablofen and Lioresal requests only: Member meets all of the following (a, b, and c):
   a. Documented adherence with scheduled refill visits;
   b. Baclofen is requested for continuance of maintenance therapy;
   c. Prescribed formulation is one of the following (i or ii):
      i. Any Gablofen vial/syringe except the 1 mL syringe;
      ii. Any Lioresal Intrathecal ampule except the 1 mL ampule;
5. Fleqsuvy, Lyvispah and Ozobax/Ozobax DS requests only: If request is for a dose increase, new dose does not exceed 80 mg per day.

Approval duration: 6 months (Gablofen, Lioresal) or 12 months (Fleqsuvy, Lyvispah, Ozobax/Ozobax DS)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
GABA: gamma-aminobutyric acid
TBI: traumatic brain injury

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
baclofen oral tablets	5 mg PO TID; increase slowly every 3 days by 5 mg PO TID up to 40 to 80 mg/day given in 3 to 4 divided doses	150 mg/day
benzodiazepines (e.g., diazepam, clonazepam)	Varies	Varies
dantrolene (Dantrium®)	25 mg PO QD; a gradual dose titration of 25 mg PO QD for 7 days, 25 mg PO TID for 7 days, 50 mg PO TID for 7 days, and 100 mg PO TID QD is recommended.	400 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Tizanidine (Zanaflex®)	2 mg PO QD; dose can be repeated at 6 to 8 hour intervals as needed to a maximum of 3 doses/24 hrs. Gradually increase the dose by 2 to 4 mg at each dose, with 1-4 days in between dose increases until satisfactory reduction in muscle tone is achieved.	36 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to baclofen
  - Gablofen and Lioresal only – do not use via intravenous, intramuscular, subcutaneous, or epidural routes of administration
- Boxed warning(s):
  - Gablofen and Lioresal only – do not discontinue abruptly
    - Abrupt discontinuation of intrathecal baclofen, regardless of the cause, has resulted in sequelae that include 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.
  - Fleqsuvy, Lyvispah and Ozobax/Ozobax DS – none reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Intrathecal baclofen (Gablofen, Lioresal Intrathecal)	Gablofen and Lioresal Intrathecal are intended for use by the intrathecal route as follows: • In single bolus test doses (via spinal catheter or lumbar puncture); • For chronic use, only in implantable pumps approved by the FDA specifically for the administration of Gablofen/Lioresal Intrathecal into the intrathecal space, including the Medtronic SynchroMed® II Programmable Pump‡. Screening phase: initial: 50 mcg (or 25 mcg for very small patient) intrathecally by barbotage over a period of at least 1 minute, and observed over 4 to 8 hours. If the initial response is less than desired, a second bolus of 75 mcg intrathecally may be given 24 hours after the first dose, and again observe for 4 to 8 hours. If the response is still inadequate, a final bolus of 100 mcg intrathecally may be given 24 hours later. Patients who do not respond to the 100 mcg dose should not be considered candidates for an implanted pump for chronic infusion.	Not available

Drug Name	Dosing Regimen	Maximum Dose
	Maintenance therapy: Titrate patients individually; lowest dose with an optimal response should be used, generally 300 mcg/day to 800 mcg/day for spasticity of spinal cord origin (for children < 12 years, average dose was 274 mcg/day) and 90 mcg/day to 703 mcg/day for spasticity of cerebral origin (for children < 12 years, average dose was 274 mcg/day). ‡*See Medtronic SynchroMed® II Programmable Pump information at* http://professional.medtronic.com/pt/neuro/itb/prod/index.htm#.WAUxFuArKhc.	
Baclofen oral granules (Lyvispah)	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).	80 mg/day
Baclofen oral solution (Ozobax, Ozobax DS)	Initiate Ozobax/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: Ozobax: • 5 mL (5 mg) three times a day for three days • 10 mL (10 mg) three times a day for three days • 15 mL (15 mg) three times a day for three days • 20 mL (20 mg) three times a day for three days Ozobax DS: • 5 mL (2.5 mg) three times a day for three days • 10 mL (5 mg) three times a day for three days • 15 mL (7.5 mg) three times a day for three days • 20 mL (10 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).	80 mg/day
Baclofen oral suspension (Fleqsuvy)	Initiate Fleqsuvy 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: • 1 mL (5 mg) three times a day for three days • 2 mL (10 mg) three times a day for three days	80 mg/day

Drug Name	Dosing Regimen	Maximum Dose
	• 3 mL (15 mg) three times a day for three days • 4 mL (20 mg) three times a day for three days Additional increases may be necessary up to the maximum recommended dosage of 80 mg daily [4 mL (20 mg) four times a day].	

VI. Product Availability

Drug	Availability
Baclofen intrathecal injection (Gablofen)	Injection: 50 mcg/1 mL, 10,000 mcg/20 mL (500 mcg/mL), 20,000 mcg/20 mL (1,000 mcg/mL) , 40,000 mcg/20 mL (2,000 mcg/mL)
Baclofen intrathecal injection (Lioresal Intrathecal)	Injection ampules: 0.05 mg/mL (50 mcg/mL), 10 mg/20 mL (500 mcg/mL), 10 mg/5 mL (2,000 mcg/mL), 40 mg/20 mL (2,000 mcg/mL)
Baclofen oral granules (Lyvispah)	Oral granules packets: 5 mg, 10 mg, 20 mg
Baclofen oral solution (Ozobax, Ozobax DS)	Oral solution: 5 mg/5 mL (1 mg/mL), 10 mg/5 mL (2 mg/mL)
Baclofen oral suspension (Fleqsuvy)	Oral suspension: 25 mg/5 mL (5 mg/mL)

VII. References

1. Gablofen Prescribing Information. Bethlehem, PA: Piramal Critical Care, Inc.; October 2020. Available at http://www.gablofen.com/. Accessed July 15, 2024.
2. Lioresal Intrathecal Prescribing Information. Minneapolis, MN: Medtronic, Inc.; August 2022. Available at https://lioresal.com/wp-content/uploads/2023/01/Lioresal-PI_08-2022-00.pdf. Accessed July 15, 2024.
3. Ozobax Prescribing Information. Athens, GA: Metacel Pharmaceuticals, LLC; May 2020. Available at https://ozobax.com/hcp/. Accessed July 15, 2024
4. Ozobax DS Prescribing Information. Athens, GA: Metacel Pharmaceuticals, LLC; September 2023. Available at: https://ozobaxds.com/wp-content/uploads/2023/10/Ozobax-DS-baclofen-Oral-Solution-10-mg-5-mL-Prescribing-Information-v00-rev0923.pdf. Accessed August 14, 2024.
5. Lyvispah Prescribing Information. Athens, GA: Metacel Pharmaceuticals, LLC; April 2023. Available at https://www.lyvispah.com. Accessed July 15, 2024.
6. Fleqsuvy Prescribing Information. Wilmington, MA: Azurity Pharmaceuticals, Inc.; February 2023. Available at: https://fleqsuvy.com/. Accessed July 15, 2024.
7. SynchroMed II Programmable Infusion Pump. Medtronic, Inc., Minneapolis, MN. Available at http://professional.medtronic.com/pt/neuro/itb/prod/#.WAZHK-ArKhc. Accessed August 13, 2024.

8. Chang E, Ghosh Nilasha, Yanni D, et al. A review of spasticity treatments: pharmacological and interventional approaches. Crit Rev Phys Rehabil Med. 2013; 25(1-2)11:22. doi:10.1615/CritRevPhysRehabilMed.2013007945.
9. Gold R and Oreja-Guevara C. Advances in the management of multiple sclerosis spasticity: multiple sclerosis spasticity guidelines. Expert Rev Neurother. 2013; 13(12s): 55-59.
10. Delgado MR, Hirtz D, Aisen A, et al. Practice parameter: Pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review). Neurology January 2010 (reaffirmed on July 16, 2022); 74(4): 336-343.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0475	Injection, baclofen, 10 mg
J0476	Injection, baclofen, 50 mcg for intrathecal trial

Reviews, Revisions, and Approvals	Date	P&T Approval Date
For Ozobax requests, modified trial of oral formulation to state 'Medical justification supports inability to use compounded baclofen oral solution (using crushed tablets) or baclofen crushed or split tablets administered with food (e.g., applesauce)' per March SDC and prior clinical guidance.	03.03.20	
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.21.20	11.20
4Q 2021 annual review: no significant changes; Gablofen/Lioresal requirement for oral baclofen was revised to "Documentation supports inability to use…" language; Ozobax requirement for compounded oral solution was revised to "Member must use…" language; HIM.PHAR.21 changed to HIM.PA.154; references reviewed and updated.	06.26.21	11.21
RT4: added newly FDA approved Lyvispah oral granules.	12.14.21	
RT4: added newly FDA approved Fleqsuvy oral suspension.	03.01.22	
4Q 2022 annual review: no significant changes; updated product availability, contraindications and boxed warnings per PI; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	07.28.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	06.30.23	11.23
4Q 2024 annual review: added Ozobax DS formulation to policy; for requests for Fleqsuvy, Lyvispah or Ozobax/Ozobax DS,	07.15.24	11.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
removed requirement for compounded baclofen oral solution or baclofen crushed or split tablets and added requirement for generic baclofen oral solution per SDC; references reviewed and updated.		

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.