Clinical Policy Title:	baclofen
Policy Number:	RxA.141
Drug(s) Applied:	Gablofen®, Lioresal® Intrathecal, Ozobax®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Baclofen (Gablofen®, Lioresal® Intrathecal, Ozobax®)* is a gamma-aminobutyric acid (GABA)-ergic agonist and acts as a skeletal muscle relaxant and antispastic. Intracthecal baclofen is indicated for use in the management of severe spasticity of cerebral or spinal cord origin.

Limitations of use:

- Prior to consideration for long term infusion via an implantable pump, patients should first respond positively to a screening dose of intrathecal baclofen.
- 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.

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‡.

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

Limitation of use: Ozobax® is 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 Ozobax® in pediatric patients below the age of 12 have not been established.
***Lioresal® Intrathecal therapy may be considered an alternative to destructive neurosurgical procedures.*

‡*See Medtronic SynchroMed® II Programmable Pump information at:*
http://professional.medtronic.com/pt/neuro/itb/prod/index.htm#.WAUxFuArKhc.

Dosing Information			
Drug Name	**Indication**	**Dosing Regimen**	**Maximum Dose**
baclofen intrathecal (Gablofen®, Lioresal® Intrathecal)	Severe spasticity of cerebral or spinal cord origin	Screening dose: initial bolus of 50 mcg/1 mL (or 25 mcg for very small patient) is given intrathecally by barbotage over a period of at least 1 minute and observe over ensuing 4 to 8 hours. If the initial response is less than desired, a second bolus of 75 mcg/1.5 mL may be given intrathecally 24 hours after the first dose and observe for 4 to 8 hours. If the response is still inadequate, a final bolus of 100 mcg/2 mL may be given intrathecally 24 hours later. Patients who do not respond to the 100mcg dose should not be considered candidates for an implanted pump for chronic infusion. 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 700 mcg/day for spasticity of cerebral origin (for children < 12 years, average dose was 274 mcg/day).	Not available
baclofen oral solution (Ozobax®)	Spasticity resulting from multiple sclerosis	Initiate Ozobax® 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 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 Additional increases may be necessary up to the maximum recommended dosage of 80 mg daily (20 mg four times a day).	80 mg/day

Dosage Forms	
Drug	**Availability**
baclofen intrathecal injection (Gablofen®)	Injection (solution): 50 mcg/1 mL (used for initial screening doses) Injection (vial or syringe): 10,000 mcg/20 mL, 20,000 mcg/20 mL, 40,000 mcg/20 mL
baclofen intrathecal injection (Lioresal® Intrathecal)	Injection ampules: 0.05 mg/mL (used for initial screening doses), 10 mg/20 mL, 10 mg/5 mL, 40 mg/20 mL
baclofen oral solution (Ozobax®)	Oral solution: 5 mg/5 mL

Clinical Policy

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

I. Initial Approval Criteria

A. Requests for Gablofen® or Lioresal® Intrathecal (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, orthopaedist or physical medicine and rehabilitation specialist;
3. Age 4 years or more;
4. If the spasticity is due to TBI, at least one year has passed since the injury;
5. Member was unresponsive or experienced clinically significant adverse effects to oral baclofen therapy;
6. Failure of one of the following conventional therapies (a, b, or c), unless all are contraindicated, or clinically significant adverse effects are experienced:
   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:
         a) Gablofen®: 50 mcg/mL (1 mL syringe);
         b) Lioresal® Intrathecal: 0.05 mg/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:
         a) Any Gablofen® vial/syringe except the 1 mL syringe;
         b) 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
Commercial: Screening: 14 days (up to 3 screening trials) and Maintenance: 3 months
Medicaid: Screening: 14 days (up to 3 screening trials) and Maintenance: 3 months

B. Requests for Ozobax® (must meet all):
1. Diagnosis of severe spasticity of multiple sclerosis or due to spinal cord injury or other spinal cord diseases;
2. Prescribed by or in consultation with a neurologist, orthopedist, or physical medicine and rehabilitation specialist;
3. Age 12 years or more;
4. Member is unable to swallow or has difficulty swallowing oral baclofen tablets;
5. Member was unresponsive or experienced clinically significant adverse effects to oral baclofen therapy;
6. Failure of one of the following conventional therapies (a, b, or c), unless all are contraindicated, or clinically significant adverse effects are experienced:
   a. A benzodiazepine (e.g., diazepam, clonazepam);
   b. Dantrolene;
   c. Tizanidine;
7. Dose does not exceed 80 mg per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Gablofen® and Lioresal® Intrathecal requests only – Member must meet 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;
4. Ozobax® requests only: if request is for a dose increase, new dose does not exceed 80 mg per day.

Approval duration
Commercial: 6 months (Gablofen®, Lioresal® Intrathecal) or 12 months (Ozobax®)
Medicaid: 6 months (Gablofen®, Lioresal® Intrathecal) or 12 months (Ozobax®)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
TBI: traumatic brain injury

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
baclofen oral tablets	5 mg PO TID; increase by 5 mg PO TID every 3 days until optimum effect is achieved	80 mg/day (20mg QID)
benzodiazepines (e.g., diazepam, clonazepam)	Varies	Varies
dantrolene (Dantrium®)	25 mg PO once daily for 7 days, then 25 mg PO TID for 7 days, then, 50 mg PO TID for 7 days, then,100 mg PO TID	400 mg/day
tizanidine (Zanaflex®)	2 mg PO once daily; dose can be repeated at 6- to-8-hour intervals as needed to a maximum of 3 doses/24 hrs. For maintenance, increase the dose by 2mg to 4 mg per dose, in 1-4 day intervals 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):
  - Gablofen®, Lioresal® Intrathecal only:
    - Hypersensitivity to baclofen
    - Do not use via intravenous, intramuscular, subcutaneous, or epidural routes of administration.
  - Ozobax® - hypersensitivity to baclofen.
- Boxed warning(s):
  - Abrupt withdrawal (injection) - Gablofen® and Lioresal® Intrathecal
  - Ozobax® - none reported

APPENDIX D: General Information

- 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.
- Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to programming and monitoring of the infusion system, refill scheduling and procedures, and pump alarms. Patients and caregivers should be advised of the importance of keeping scheduled refill visits and should be educated on the early symptoms of baclofen withdrawal. Special attention should be given to patients at apparent risk (e.g., spinal cord injuries at T-6 or above, communication difficulties, history of withdrawal symptoms from oral or intrathecal baclofen).
- Consult the technical manual of the implantable infusion system for additional post-implant clinician and patient information.

References

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8. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed January 18, 2021.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Reviewed policy criteria - Added criteria under Ozobax® Updated Appendices	04/2020	05/21/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to 'baclofen', Drug(s) Applied was updated to 'Gablofen®, Lioresal® Intrathecal, Ozobax®', Line of business policy applies was updated to All lines of business. 2. Background was updated: Limitation of use was added for Ozobax®. 3. Dosing information: Indications were added. 4. Initial approval criteria IA.4 was updated as for TBI wait at least one year. 5. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 6. Approval durations were updated. 7. Appendix B verbiage was updated to 'Below are suggested therapeutic alternatives..' 8. Appendix C boxed warning was updated at 'Abrupt withdrawal (injection)'. 9. Appendix D was added.	01/18/2021	03/09/2021

10. References were updated.		