RXADVANCE
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Clinical Policy Title:	Intrathecal Baclofen (Gablofen, Lioresal, Ozobax)
Policy Number:	RxA.141
Drug(s) Applied:	Intrathecal Baclofen(Gablofen®, Lioresal® Intrathecal, Ozobax™)
Original Policy Date:	01/2020
Last Review Date:	04/21/2020
Line of Business Policy Applies to:	Commercial

Background

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

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.

**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	**Drug Name**	**Dosing Regimen**	**Maximum Dose**
	Intrathecal baclofen (Gablofen, Lioresal Intrathecal)	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 100 mcg 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 703 mcg/day for spasticity of cerebral origin (for children < 12 years, average dose was 274 mcg/day).	Not available
	Baclofen oral solution (Ozobax)	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 (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, 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. 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:
Screening – 14 days (up to 3 screening trials)
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, physiatrist, or physical

medicine and rehabilitation specialist;
3. Age ≥ 12 years;
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: 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 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: 6 months (Gablofen, Lioresal) or 12 months (Ozobax)

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
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 until optimum effect is achieved	80 mg/day (20mg QID)
benzodiazepines (e.g., diazepam, clonazepam)	Varies	Varies

dantrolene (Dantrium®)	25 mg PO QD 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 QD; 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 2 to 4 mg per dose, with 1-4 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 only –
    - Hypersensitivity to baclofen
    - do not use via intravenous, intramuscular, subcutaneous, or epidural routes of administration;
  - Ozobax – hypersensitivity to baclofen.
- Boxed warning(s):
  - Gablofen and Lioresal

  - 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. 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 (eg, 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

  - Ozobax – none reported.

References

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6. Dantrolene. Micromedex Solutions. Truven Health Analytics, Inc. Ann Arbor, MI; 2020, March 17. Accessed with subscription at: http://www.micromedexsolutions.com. Accessed April 21, 2020.
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8.

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	