



Celebrating 10 Years of Gablofen® Innovation & Advancement

LEARN MORE ABOUT THE
HISTORY AND EVOLUTION
OF BACLOFEN INSIDE.



IMPORTANT RISK INFORMATION

WARNING: 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 (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.

For additional Important Risk Information, including boxed warning, see enclosed Full Prescribing Information.

From oral baclofen to intrathecal administration, and from glass ampules to syringes and vials, the management of severe spasticity has come a long way.

Discover the History of Baclofen and the Evolution of Gablofen®.

Intrathecal Administration of Baclofen Introduced

This resulted in similar, yet manageable side effects and greater efficacy controlling spasticity.

CNS Therapeutics, Inc. Founded by Penn & Foster

Richard Penn, MD, who implanted the first programmable pump in 1982, and John Foster, who was the former Director of Marketing and Strategic Planning at Medtronic, formed a new entity focused on innovating and advancing intrathecal drug delivery.

1984

1971

Oral Baclofen Introduced to Manage Spasticity

Oral baclofen was introduced to manage spasticity yet resulted in side effects and a lack of efficacy controlling spasticity.

1992

Intrathecal Baclofen Approved by the FDA

Intrathecal Baclofen (ITB) commercially approved in the form of glass ampules.

2007

Gablofen Introduced and Approved by the FDA in the SynchroMed II Pump³

CNS Therapeutics launched the first medication innovation in ITB therapy in 18 years called Gablofen® (baclofen injection).

2010

Vials: 500 mcg/mL and 2,000 mcg/mL

2011

Screening Dose: 50 mcg/mL

2011

8500 Pump Refill Concentration Kit



References

1. American Association of Neurological Surgeons (AANS) on Spasticity [Internet]. 2018 [Cited 16 Aug 2018]; Available from: <http://www.aans.org/Patients/Neurosurgical-Conditions-and-Treatments/Spasticity>.
2. Orange Book: Approved drug products with therapeutic equivalence evaluations. U.S. Food and Drug Administration [Internet]. 2018 [Cited 16 Aug 2018]; Available from: https://www.accessdata.fda.gov/scripts/cder/ob/search_product.cfm. Last Accessed April 18, 2018.
3. Piramal Critical Care, Inc. Gablofen® [USPI]. Bethlehem, PA. 2017 [Cited 2018 Aug 16].

With the Addition of the 1,000 mcg/mL Vial, Gablofen Becomes the Only FDA-Approved ITB With 3 Concentrations

CNS Therapeutics, Inc. is acquired by Mallinckrodt/Covidien.



Piramal Critical Care (PCC) Acquired Mallinckrodt's Intrathecal Portfolio

After significant innovation in safety and efficiency, Mallinckrodt's intrathecal product portfolio for spasticity and pain management was acquired by Piramal Critical Care.

2012

2013

2017

2020

Gablofen introduces the first ITB in prefilled syringes in 500 mcg/mL, 1000 mcg/mL and 2000 mcg/mL concentrations

2014 Larger screening trial dose prefilled syringe

The Current State of Gablofen®

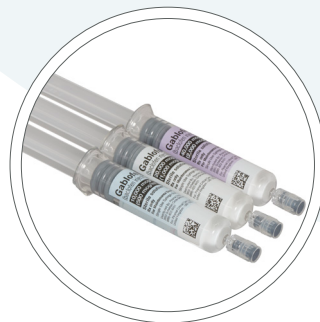
Gablofen® celebrates 10 years on the market, and since the acquisition in 2017, over 275,000 units have been manufactured in the USA and distributed by PCC. Today, ITB is an established and widely accepted option for the management of severe spasticity of cerebral or spinal origin in adult and pediatric patients age 4 years and above¹, and Gablofen® (baclofen injection) is the only FDA-approved intrathecal baclofen in prefilled syringes and factory-sealed vials.^{2,3} Gablofen is now a leader in the market.

You have a choice.
Choose to be innovative.
Request information on
Gablofen® (baclofen injection).

Gablofen.com | 1.800.414.1901

Looking Ahead: The Future of Gablofen®.

Gablofen® has been approved for launch in eight European markets.



INDICATIONS AND USAGE

- Gablofen[®] (baclofen injection) is a gamma-aminobutyric acid (GABA) ergic agonist indicated for use in the management of severe spasticity of cerebral or spinal origin in adult and pediatric patients age 4 years and above.
- Gablofen should be reserved for patients unresponsive to oral baclofen therapy, or those who experience intolerable central nervous system side effects at effective doses.
- Patients should first respond to a screening dose of intrathecal baclofen prior to consideration for long term infusion via an implantable pump.
- Spasticity due to traumatic brain injury: wait at least one year after injury before considering Gablofen therapy.

IMPORTANT RISK INFORMATION

WARNING: DO NOT DISCONTINUE ABRUPTLY

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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.

CONTRAINDICATIONS

- Hypersensitivity to baclofen.
- Do not use Gablofen for intravenous, intramuscular, subcutaneous or epidural administration.

WARNINGS AND PRECAUTIONS

- Risk of life-threatening overdose during pump refills. Use extreme caution when filling the Medtronic SynchroMed[®] II Programmable Pump which is equipped with an injection port that allows direct access to the intrathecal catheter. Direct injection into the catheter through the catheter access port may cause a life-threatening overdose.
- Use only with Medtronic SynchroMed[®] II Programmable Pump (or other pumps labeled for intrathecal administration of Gablofen (baclofen injection)).
- Potential for contamination due to non-sterile external surface of prefilled syringe. Although the drug solution and pathway in the Gablofen prefilled syringes are sterile, the external surface of the prefilled syringes (all strengths, including the 50 mcg/mL strength) are non-sterile and have the potential to lead to contamination and consequent adverse reactions. The use of Gablofen prefilled syringe in an aseptic setting (e.g., operating room) to fill sterile intrathecal pumps prior to implantation in patients is not recommended, unless the external surface of the prefilled syringe is treated to ensure sterility. Gablofen supplied in vials may be used with conventional aseptic technique to fill intrathecal pumps prior to implantation.
- Resuscitative equipment and trained staff must be available during screening dose, dose titration, and refills due to the potential life-threatening CNS depression, cardiovascular collapse, and/or respiratory failure.

- Overdose may cause drowsiness, lightheadedness, dizziness, somnolence, respiratory depression, seizures, rostral progression of hypotonia and loss of consciousness progressing to coma.
- Use with caution in patients with psychotic disorders, schizophrenia or confusional states as it may exacerbate condition(s).
- Fatalities have been reported with intrathecal baclofen use.
- Caution should be used in patients with a history of autonomic dysreflexia.
- Presence of infection may increase the risk of surgical complication and complicate dosing of Gablofen.
- May cause drowsiness: use caution in operation of automobiles, dangerous machinery and activity that may be hazardous by decreased alertness. Other CNS depressants and alcohol may add to this effect.
- Potential development of intrathecal mass formation. Clinicians should monitor for signs and symptoms of new neurologic symptoms including the use of imaging diagnostic modalities.
- Oral baclofen use has been associated with a dose-related increase in incidence of ovarian cysts.

ADVERSE REACTIONS

SERIOUS ADVERSE REACTIONS

- Sudden withdrawal of Gablofen can result in serious complications that include high fever, confusion, muscle stiffness, multiple organ-system failure, and death. Inform patients that early symptoms of Gablofen withdrawal may include increased spasticity, itching, and tingling of extremities. If Gablofen withdrawal or a pump malfunction is suspected, patients should be brought immediately to a hospital for assessment and treatment.
- Gablofen overdose may occur suddenly or insidiously, and symptoms may include confusion, drowsiness, lightheadedness, dizziness, slow or shallow breathing, seizures, loss of muscle tone, loss of consciousness, and coma.
- Other serious adverse events may include: potential development of intrathecal mass formation, drainage, infection, meningitis, unmanageable trunk control, CSF leakage, coma and death.

COMMON ADVERSE REACTIONS

- The most common adverse reactions in patients with spasticity of spinal origin were hypotonia (25.3%), somnolence (20.9%), dizziness, nausea/vomiting, hypotension, headache, and convulsions.
- The most common adverse reactions in patients with spasticity of cerebral origin were hypotonia (34.7%), somnolence (18.7%), headache (10.7%), agitation, constipation, leukocytosis, chills, and urinary retention.
- Other common adverse events may include hypoventilation, hypertonia, paresthesia, increased salivation, back pain, pruritus, diarrhea, peripheral edema, asthenia, pain, confusion, speech disorder, amblyopia, accidental injury, and dry mouth.

USE IN SPECIFIC POPULATIONS

- Pregnancy Category C. The effect of baclofen in labor and delivery is unknown.
- Breastfeeding: Baclofen is excreted into breast milk at oral therapeutic doses.
- Pediatric use: Safety and effectiveness in pediatric patients below the age of 4 years have not been established.

To report suspected adverse reactions, call 888.525.8114, contact the FDA at 800.FDA.1088, or <http://www.fda.gov/medwatch>.

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