# Botulinum toxin for constipation

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Policy contains: Botulinum toxin; constipation; dyssynergic defecation; Hirschsprung disease; internal anal sphincter achalasia.

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## Coverage policy

Intrasphincteric botulinum toxin injection for refractory constipation is clinically proven and, therefore, may be medically necessary in cases of either:

- Hirschsprung disease after corrective pull-through surgery (Ambartsumyan, 2023; Kyrklund, 2020; Langer, 2017).
- Internal anal sphincter achalasia before posterior internal anal sphincter myectomy is considered (Halleran, 2019).
- Dyssynergic defecation (Alavi, 2024).

Limitations

Botulinum toxin injection for other chronic defecatory disorders is investigational/not clinically proven and, therefore, not medically necessary.

Alternative covered services

Medical treatments for constipation.

## Background

Chronic constipation is a common condition; approximate prevalence in the general population is about 15%, with higher rates among elderly people. Causes of the condition are multiple. First-line treatments for constipation, which typically resolve most cases, include stool softeners, fiber supplements, osmotic or stimulant laxatives, and the medications secretagogues lubiprostone and linaclotide (Diaz, 2023).

Botulinum toxin is a neurotoxin produced by the bacterium *Clostridium botulinum*. It interferes with neural transmission by blocking the release of acetylcholine, the principal neurotransmitter at the neuromuscular junction, causing muscle paralysis. Botulinum toxins play a significant role in managing medical conditions, including strabismus and focal dystonias, hemifacial spasm, spastic movement disorders, headaches, hypersalivation, hyperhidrosis, and chronic conditions responsive partially to medical treatment (Padda, 2023).

Injection of botulinum toxin into the internal anal sphincter has been proposed as a nonsurgical, local treatment for constipation of various etiologies the most common being Hirschsprung disease and internal anal sphincter achalasia. Hirschsprung disease, also called congenital aganglionic megacolon, is a birth defect found in one in 5,000 live births; infants account for 90% of all diagnosed cases, but young children and adults can also develop the condition. In Hirschsprung disease, the rectoanal inhibitory reflex on rectoanal manometry is absent, and ganglions (nerve cells) are absent in a segment of the bowel, which causes ineffective peristalsis that leads to stool backup, constipation, and partial or total bowel obstruction. Failure to treat the disorder effectively can lead to enterocolitis (National Organization for Rare Disorders, 2017).

Treatment for Hirschsprung disease involves removing the affected portion of the colon or rectum and joining the two healthy ends together, known as a “pull-through” procedure. Following pull-through surgery, patients who continue to struggle may experience fecal incontinence, obstructive symptoms, and recurrent episodes of enterocolitis. Symptomatic treatment may involve enemas, laxatives, and botulinum toxin injections; in some cases, a repeat pull-through procedure may be necessary (Zani, 2017).

Internal anal sphincter achalasia is a clinical condition in which the rectoanal inhibitory reflex is absent on manometry, but, unlike Hirschsprung disease, ganglion cells are present on rectal suction biopsy. One retrospective study (n = 1,072) found children with internal anal sphincter achalasia had earlier onset of symptoms and were more likely to have redundancy or segmental dilation of the colon compared to those with functional constipation, and had later symptom onset compared to those with Hirschsprung disease. The treatment of choice for internal anal sphincter achalasia that does not respond to dietary changes is posterior internal anal sphincter myectomy, but irreversible sphincter injury and fecal incontinence can occur. Botulinum toxin may be an option for treating the disorder (Baaleman, 2021).

## Findings

Guidelines

The American Society of Colon and Rectal Surgeons issued a conditional recommendation based on low-quality evidence for injecting botulinum toxin into the puborectalis and external sphincter muscle to temporarily improve symptoms in patients with outlet dysfunction constipation related to nonrelaxing puborectalis muscle. The Society issued a strong recommendation based on moderate-quality evidence for biofeedback as a first-line treatment in this population (Alavi, 2024).

For patients with Hirschsprung disease who present with persistent defecation problems postoperatively, the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition suggests some children with elevated intra-anal pressures may benefit from botulinum toxin injection into the anal sphincter (Ambartsumyan, 2023).

A guideline from the European Reference Network for rare inherited and congenital digestive disorders issued a conditional recommendation for intrasphincteric botulinum toxin injections for patients with recurrent or persistent symptoms of outlet obstruction or Hirschsprung-associated enterocolitis. The recommendation was based on evidence that botulinum toxin reduced the incidence of Hirschsprung-associated enterocolitis and/or outlet obstruction in 62% to 89% of patients after the first botulinum toxin injection. Injections may need to be repeated after three to six months. Most episodes usually occur within the first few years after pull-through, with reduced tendency over time (Kyrklund, 2020).

The Hirschsprung Disease Interest Group of the American Pediatric Surgical Association issued a consensus-based practice guideline on treatment of children with Hirschsprung disease, suggesting 60 to 100 unit administration of botulinum toxin diluted in 1.0 mL of saline, given circumferentially at the level of the dentate line where the internal anal sphincter is located. The guideline advises repeating the procedure every three to six months, as many times as necessary until clinical improvement is observed. These injections generally are unnecessary after age five (Langer, 2017).

Evidence review

The evidence base from the systematic reviews described below consists of small, retrospective studies of highly selected referral populations of children with chronic constipation. The most common etiology studied was Hirschsprung disease. The evidence suggests botulinum toxin can be safely administered to treat persistent symptoms following pull-through or for treating internal anal sphincter achalasia prior to posterior internal anal sphincter myectomy. Adverse effects are mild or transient.

However, efficacy was defined inconsistently, leading to wide variations in results. The type of botulinum toxin, average dose, and average age at first injection has not been standardized. The retrospective nature of these studies limits the ability to identify patient factors predictive of response, and, therefore, those mostly likely to benefit from treatment.

Botulinum toxin use in current practice also varies; its adoption into practice has been based on early low-quality case series suggesting some efficacy as a nonsurgical treatment alternative. In one multisite study (n = 494), redo surgery and undergoing pull-through at an older age were associated with greater botulinum toxin use; Hispanic patients received fewer injections (Rice-Townsend, 2022). Guidelines for childhood defecatory disorders are lacking, and further study is needed on timing of injections and potential disparities in care.

After a 2015 literature review, botulinum toxin injection for pelvic floor dysfunction in elderly persons with constipation was not recommended, based on available evidence (Vazquez Roque, 2015).

Other evidence on efficacy of botulinum toxin for constipation from the professional medical literature includes:

*Constipation*

A systematic review of 45 low-quality studies (n = 1,157) of children with idiopathic constipation of various pathologies analyzed the effectiveness of several treatments, including antegrade continence enema operations and colon resection (both of which were generally successful), and anal dilatation (which was not). Botulinum toxin injection proved as effective as internal sphincter myectomy after an average follow-up of one-and-a-half years (Siminas, 2015).

A Cochrane review of biofeedback therapy for constipation in adults included a study (n = 48) that showed botulinum toxin injections had better short-term results than biofeedback, but the enhanced results proved uncertain one year after treatment (Woodward, 2014).

A retrospective study addressed a group of 164 children with severe constipation unresponsive to medical management. Response was defined in term of decreased pain or increased defecation. Each study participant had a sphincter botulinum toxin injection, and 142 had anorectal manometry; 98 (70%) improved, and 57%

improved long-term, that is, greater than six months. Comparing children with normal versus abnormal rectoanal inhibitory reflexes, there was no statistically significant difference in the proportion of responders (*P* = .41). Fecal incontinence prior to injection was a predictor of poor response (*P* = .02) (Zar-Kessler, 2018).

A systematic review and meta-analysis examined 14 studies including four randomized controlled trials and 10 observational studies, (n = 272) evaluated the effectiveness of botulinum toxin injection for treating dyssynergic defecation, a common cause of constipation. Approximately 66.1% of patients experienced short-term symptom improvement after Botulinum toxin injection, which decreased to 38.2% in the long term (beyond 12 months). Repeated injections led to symptom improvement in 93.9% of patients. The review also noted improvements in objective parameters such as the balloon expulsion test, anal surface electromyography, and digital rectal examination. Higher doses of Botulinum toxin were associated with greater long-term symptom improvement and reduced voluntary contraction anal pressure but also with higher rates of fecal incontinence and symptom recurrence. The evidence suggests that Botulinum toxin injection may be considered for patients with dyssynergic defecation, particularly for short-term symptom relief. However, more high-quality randomized controlled trials with standardized injection protocols are needed to confirm its effectiveness and safety (Chu, 2023).

*Hirschsprung disease*

A systematic review/meta-analysis of Hirschsprung disease included 14 studies (n = 278) of patients who received botulinum toxin injections to improve fecal passage and internal anal sphincter relaxation. Injections effectively treated obstructive symptoms in 66% of patients (*P* < .004). A significantly higher response rate was observed within one month after injections versus over one month after (*P* < .001). Adverse events, mostly mild, occurred in 17% of the patients. Type of botulinum toxin, average dose, average age at first injection, and proportion of patients with associated syndromes were not predictive of response (Roorda, 2019).

A systematic review/meta-analysis of 29 studies compared treatments for Hirschsprung disease. In nine of 29 (n = 166), botulinum toxin injections had a 77.3% short-term response rate, but just a 43.0% long-term rate. These results showed lower effectiveness than posterior myotomy/myectomy (79% resolution of obstructive symptoms); post-operative rectal irrigations (obstructive symptoms and enterocolitis, *P* = .001); and topical nitric oxide (100% of patients improved) (Soh, 2018).

*Internal anal sphincter achalasia*

A meta-analysis of 16 studies (n = 395) that were published from 1973 to 2009 analyzed patients with internal anal sphincter achalasia. Botulinum toxin injections were given to 42% of the patients. Compared with the 58% given posterior internal anal sphincter myectomy, those given botulinum toxin had significantly worse outcomes (higher rates of transient fecal incontinence (*P* < .01), subsequent surgical procedures (*P* < .0001), and non-response (*P* = .04), plus lower rates of regular bowel movements (*P* = .04), short-term improvements (*P* = .04) and long-term improvements (*P* < .0001) (Friedmacher, 2012).

*Other indications*

Other studies have reviewed effects of botulinum toxin injections for various gastrointestinal disorders, with little or no conclusive evidence about efficacy and safety for specific disorders. A large institutional study of 881 infants and children under age 20 with anorectal and colonic disorders analyzed safety of the 1,332 botulinum toxin injections into the anal sphincter. Complications occurred after 0.7% of injections, leading authors to conclude the procedure was safe for children with Hirschsprung disease, severe functional constipation, and internal anal sphincter achalasia. However, the precise dosing and age at which complications are more likely to arise could not be determined and require further research (Halleran, 2019).

In 2022, we deleted several references and added four retrospective surgical series of patients who received botulinum toxin injection following pull-though surgery. The new studies provide conflicting evidence of efficacy

with inconsistent effects on the incidence of Hirschsprung-associated enterocolitis, other obstructive symptoms, or reoperation (Ahmad, 2022; Rentea, 2021; Roorda, 2021; Svetanoff, 2022). No policy changes are warranted.

In 2023, we added no newly published relevant literature to the policy. No policy changes are warranted.

In 2025, we updated the references and added dyssynergic defecation as a new indication based on a new American Society of Colon and Rectal Surgeons' guideline recommendation.

## References

On May 12, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were "constipation/surgery" (MeSH), "constipation/therapy" (MeSH), "botulinum toxins, type a/therapeutic use" (MeSH), "achalasia," "botulinum toxin," "constipation," and "Hirschsprung disease." We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.


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## Policy updates

7/2020: initial review date and clinical policy effective date: 8/2020

7/2021: Policy references updated.

7/2022: Policy references updated.

7/2023: Policy references updated.

7/2024: Policy references updated.

7/2025: Policy references updated. Coverage modified.