Abbreviated Drug Review

Trade Name (generic)	
Trulance™ (plecanatide)	Indication not funded

Indications

Plecanatide is indicated in adults for the treatment of chronic idiopathic constipation (CIC)

Dosage

3 mg tablet taken orally once daily, with or without food

Background

Plecanatide is a guanylate cyclase-C (GC-C) receptor agonist that acts on the luminal surface of the intestinal epithelium. GC-C receptor activation results in increased cGMP, which stimulates chloride and bicarbonate secretion into the intestinal lumen. This leads to increased intestinal fluid and accelerated intestinal transit.[1]

Efficacy

FDA approval of plecanatide was based on two identically designed, 12-week, double-blind, placebo-controlled, randomized, multicenter, phase 3 clinical trials in 1775 adult patients with CIC who were randomized 1:1 to either placebo or plecanatide 3 mg once daily.[1] The study populations had a mean age of 45 years (range 18 to 80 years) and were 80% female, 72% white, and 24% black. Included were subjects who met modified Rome III functional constipation diagnostic criteria for ≥3 months before screening, with symptom onset for ≥6 months before diagnosis. Modified Rome III criteria required that patients report <3 defecations/week, rarely have a loose stool without laxative use, not manually facilitate defecations, and not meet criteria for irritable bowel syndrome with constipation. Also, patients were required to report at least two of the following symptoms for ≥25% of defecations: straining, lumpy or hard stool, sensation of incomplete evacuations, or sensation of anorectal obstruction/blockage. Consistency of stools was rated with a validated, pictorial, 7 point Bristol Stool Form Scale (BSFS). A score of 1 indicated hard lumps ranging up to 7, which was a watery stool. Patients also had to demonstrate the following during the two-week pre-treatment assessment period: <3 spontaneous (i.e., without laxative use) bowel movements associated with a sense of complete evacuation (CSBM) per week; BSFS of 6 or 7 in <25% of spontaneous bowel movements; and BSFS of 1 or 2 in ≥25% of defecations or a straining value recorded on ≥25% of days when a BM was reported or ≥25% of BMs resulting in a sense of incomplete evacuation. Plecanatide demonstrated efficacy over placebo for response rate (primary endpoint), with a responder defined as a patient who had ≥3 CSBMs in the same week for ≥9 weeks out of the 12-week treatment period and ≥3 of the last 4 weeks of the study:

	Plecanatide 3 mg	Placebo	Difference (95% CI, p-value)	NNT
Response rate study 1	21% (n=453)	10% (n=452)	11% (6.1 to 15.4, p<0.005)	10
Response rate study 2	21% (n=430)	13% (n=440)	8% (2.6 to 12.4, p<0.005)	13

The difference in the mean change in CSBMs/week frequency (from baseline to week 12) between plecanatide group and placebo group was about a 1.1 CSBMs/week.

Safety

Black box warning: Risk of serious dehydration in pediatric patients; contraindicated in patients less than 6 years of age; avoid use in patients 6 to 17 years old; and safety and effectiveness not established in patients less than 18 years of age
Common adverse reactions: Diarrhea
Contraindications: Patients who are <6 years of age, due to the risk of serious dehydration, and patients who have known or suspected mechanical gastrointestinal obstruction
Warnings and precautions: Severe diarrhea may occur. Also, same as black box warning above.

Evidence Gaps/Limitations

No studies found to support evidence for use in the treatment of Oregon Health Plan (OHP) funded conditions or co-morbidities.

Recommendation

Restrict use for OHP-funded conditions through Prior Authorization. Add plecanatide to “Drugs for Constipation” PA criteria.

References

1.Trulance (plecanatide) tablets [prescribing information]. New York, NY. Synergy Pharmaceuticals, Inc.; January 2017.

Author: S. Willard

Date: July 2017