# PDL DRUG REVIEW

**Proprietary Name: Trulance®**
**Common Name: plecanatide**
**PDL Category: GI, Constipation-IBS-OIC**

| Comparable Products | Preferred Drug List Status |
|---|---|
| Amitiza | Non-Preferred with Conditions |
| Linzess | Non-Preferred with Conditions |

## Summary


**Pharmacology/Usage:** Plecanatide, the active ingredient of Trulance®, is a guanylate cyclase-C (GC-C) agonist. Both plecanatide and its active metabolite bind to GC-C and act locally on the luminal surface of the intestinal epithelium. Activation of GC-C results in an increase in both intracellular and extracellular concentrations of cyclic guanosine monophosphate (cGMP). Increases in intracellular cGMP stimulates secretion of chloride and bicarbonate into the intestinal lumen, mainly through activation of the cystic fibrosis transmembrane conductance regulator (CFRT) ion channel, which results in increased intestinal fluid and accelerated transit.

**Indications:** In adults for the treatment of chronic idiopathic constipation (CIC)

There is no pregnancy category for this product; however, the risk summary indicates plecanatide and its active metabolites are negligibly absorbed systemically after oral administration and maternal use is not expected to result in fetal exposure to the drug. The available data on use in pregnant women are not sufficient to inform any drug-associated risks for major birth defects and miscarriage. The safety and efficacy of use in the pediatric population have not been established. Use is contraindicated in pediatric patients less than 6 years of age and use should be avoided in patients 6 years to less than 18 years of age.

**Dosage Forms:** Tablets: 3mg

**Recommended Dosage:** Take 3mg PO QD with or without food. If swallowing difficulties, tablets can be crushed and administered orally in applesauce or with water or administered via a nasogastric or gastric feeding tube. Trulance® crushed tablets in other soft foods or in other liquids has not been tested.

Information was not found regarding use in hepatic or renal impairment.

**Drug Interactions:** There were no drug interactions listed with this product.

**Common Adverse Drug Reactions:** *Listed % incidence for adverse drug reactions= reported % incidence for drug (Trulance®) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or that the active drug was less than its comparator.* The most frequently reported adverse events included diarrhea (4%). Severe diarrhea was also reported (0.3%), which was reported to occur within the first 3 days of treatment. If severe diarrhea occurs, it is recommended to suspend dosing and rehydrate the patient.

Trulance® has a box warning regarding the risk of serious dehydration in pediatric patients. Use is contraindicated in pediatric patients less than 6 years of age, and use should be avoided in pediatric patients 6 years to less than 18 years of age. The warning adds that the safety and efficacy have not been established in patients less than 18 years of age.

**Contraindications:** Patients <6 years of age due to risk of serious dehydration; Patients with known or suspected mechanical gastrointestinal obstruction

**Manufacturer:** Synergy Pharmaceuticals, Inc

**Analysis:** The safety and efficacy of Trulance® were established in two double-blind, placebo-controlled, randomized, multicenter studies that included adult patients (N=1775) with symptoms of CIC. To be eligible for the studies, patients were required to meet modified Rome III criteria for ≥3 months prior to the screening visit, with symptom onset for at least 6 months prior to diagnosis. Rome III criteria were modified to require that patients report less than 3 defecations per week, rarely have a loose stool without the use of laxatives, not use manual maneuvers to facilitate defecations, and not meet criteria for IBS-C. In addition, at least 2 of the following symptoms had to be reported, which included straining during at least 25% of defecations, lumpy or hard stool in at least 25% of defecations, sensation of incomplete evacuations for at least 25% of defecations, or sensation of anorectal obstruction/blockage for at least 25% of defecations. If met those criteria above, additional criteria were also needed to be met during the last 2 weeks of the screening period.

The efficacy was assessed using a responder analysis and change-from-baseline in complete spontaneous bowel movements (CSBM) and spontaneous bowel movement (SBM) endpoints. A CSBM was defined as a SBM associated with a sense of complete evacuation. A SBM is a bowel movement occurring in the absence of laxative use. A responder was defined as a patient who had ≥3 CSBMs in a given week and an increase of ≥1 CSBM from baseline in the same week for at least 9 weeks out of the 12-week treatment period and at least 3 of the last 4 weeks of the study. Results of the efficacy responder rates can be found in the table below, which was adapted from the prescribing information.

| | Trial 1 | | Trial 2 | |
|---|---|---|---|---|
| | Trulance® (N=453) | Placebo (N=452) | Trulance® (N=430) | Placebo (N=440) |
| Responder | 21% | 10% | 21% | 13% |
| Treatment difference, p-value | 11%; p<0.005 | | 8%; p<0.005 | |

In both studies, improvements in the frequency of CSBMs per week were seen as early as week 1, with improvement maintained through week 12. The difference between Trulance® and placebo in the mean change of CSBMs per week frequency from baseline to week 12 was about 1.1 CSBMs/week. Over the 12 weeks of treatment, improvements were seen in stool frequency and/or stool consistency, and/or in the amount of straining with bowel movements in the Trulance® group as compared with placebo.

A third treatment arm of Trulance® 6mg daily was used in both studies, but it did not demonstrate additional treatment benefit and had a greater incidence of adverse reactions as compared with Trulance® 3mg daily. Thus, Trulance® 6mg daily is not recommended.

**Place in Therapy:** Trulance® is an oral agent indicated for the treatment of chronic idiopathic constipation. It was found to be significantly effective as compared with placebo for the primary endpoint of meeting criteria for being a responder to treatment. Comparator trials with other active ingredients were not found. This offers physicians additional treatment options for this condition.

There is no evidence at this time to support that Trulance® is safer or more effective than the currently available, more cost effective medications. It is therefore recommended that Trulance® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

**PDL Placement:**
☐ **Preferred**
☒ **Non-Preferred with Conditions**

## References

[1] Trulance [package insert]. New York, NY: Synergy Pharmaceuticals; 2017.


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