RXADVANCE
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NEW DRUG APPROVAL

Brand Name	Tepezza™
Generic Name	teprotumumab-trbw
Drug Manufacturer	Horizon Therapeutics

New Drug Approval

FDA Approval Date: January 21, 2020
Review Designation: Orphan
Review Type: Biologics License Application 761143

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Thyroid eye disease is a condition in which the eye muscles, eyelids, tear glands and fatty tissues behind the eye become inflamed. This can cause the eyes and eyelids to become red, swollen and uncomfortable and the eyes can be pushed forward ('staring' or 'bulging' eyes).

TED – also known as Graves' Orbitopathy or Ophthalmopathy – is an autoimmune condition. It occurs when the body's immune system attacks the tissue surrounding the eye causing inflammation in the tissues around and behind the eye. In most patients, the same autoimmune condition that causes TED also affects the thyroid gland, resulting in Graves' disease. Graves' disease most commonly causes thyroid overactivity (hyperthyroidism) but can also rarely cause thyroid underactivity (hypothyroidism). TED can occur in people when their thyroid is overactive, underactive or functioning normally. It can also occur after treatment for Graves' disease. People with TED need to be looked after by an eye specialist (ophthalmologist) and a thyroid specialist (endocrinologist).

TED has a higher prevalence in women than men. Both men and women demonstrate a bimodal pattern of age of diagnosis. The median age is 43 years for all patients, with a range from 8 to 88 years old. Patients diagnosed over 50 -year have worse prognosis overall.

Efficacy

The safety of TEPEZZA was evaluated in two randomized, double-masked, placebo-controlled clinical studies (Study 1 [NCT:01868997] and Study 2 [NCT:03298867]) consisting of 170 patients with Thyroid Eye Disease (84 received TEPEZZA and 86 received placebo). Patients were treated with TEPEZZA (10 mg/kg for first infusion and 20 mg/kg for the remaining 7 infusions) or placebo given as an intravenous infusion every 3 weeks for a total of 8 infusions. The majority of patients completed 8 infusions (89% of TEPEZZA patients and 93% of placebo patients). The most common adverse reactions (≥5%) that occurred at greater incidence in the TEPEZZA group than in the control group during the treatment period of Studies 1 and 2.

Safety

ADVERSE EVENTS

- >10%:
  - Dermatologic: Alopecia (13%)
  - Gastrointestinal: Nausea (17%), diarrhea (12%)
  - Nervous system: Fatigue (12%)
  - Neuromuscular & skeletal: Muscle spasm (25%)

- 1% to 10%:
  - Dermatologic: Xeroderma (8%)
  - Endocrine & metabolic: Hyperglycemia (10%)
  - Gastrointestinal: Dysgeusia (8%)
  - Nervous system: Headache (8%)
  - Otic: Auditory impairment (10%)
  - Miscellaneous: Infusion related reaction (4%)

WARNINGS & PRECAUTIONS

- **Infusion reactions**: If an infusion reaction occurs, interrupt or slow the rate of infusion and use appropriate medical management.
- **Exacerbation of Preexisting Inflammatory Bowel Disease (IBD) :** Monitor patients with preexisting IBD for flare of disease; discontinue TEPEZZA if IBD worsens.
- **Hyperglycemia:** Monitor glucose levels in all patients; treat hyperglycemia with glycemic control medications.

CONTRAINDICATIONS

None

Clinical Pharmacology

MECHANISMS OF ACTION

Teprotumumab-trbw's mechanism of action in patients with Thyroid Eye Disease has not been fully characterized. Teprotumumab-trbw binds to IGF-1R and blocks its activation and signaling.

Dose & Administration

ADULTS

IV: 10 mg/kg as a single dose, followed by 20 mg/kg every 3 weeks for 7 additional doses

PEDIATRICS

Safety and effectiveness have not been established in pediatric patients.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

There are no dosage adjustments provided in the manufacturer's labeling; however, there are no significant differences in the pharmacokinetics of teprotumumab in patients with CrCl ≥30 mL/minute.

HEPATIC IMPAIRMENT

There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

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500 mg lyophilized powder in a single-dose vial for reconstitution.