TEPEZZA (teprotumumab)

Healthcare Professional Guide:

Safety of teprotumumab: Hearing Impairment, Serious Hyperglycemic Complications and Embryofetal Toxicity

This guide is essential to ensure the safe use of the product and appropriate management of important selected risks and therefore it is advised to be read carefully before prescribing the medicinal product.

The information in this guide is not intended as a replacement for the package insert (PI).

Please read the TEPEZZA Singapore PI in conjunction with this guide.

Contents

Introduction

This guide has been developed for healthcare professionals involved in the care of patients treated with teprotumumab to provide further information about how to minimize or prevent the following risks associated with the use teprotumumab:

- Hearing impairment
- Embryofetal toxicity
- Hyperglycemic complications - Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS)

Educating patients about these factors ensures patients are enabled to make informed decisions regarding their treatment options.

Each patient should receive a patient guide outlining the risks of hearing impairment, embryofetal toxicity and hyperglycemic complications to keep as a reference throughout their treatment.

Hearing Impairment Risk

- Teprotumumab therapy has been associated with hearing impairment, including hearing loss, which in some cases may be permanent.
- In clinical trials, events of hearing loss were reported as deafness, including sensorineural deafness, eustachian tube dysfunction, eustachian tube patulous, hyperacusis, hypoacusis, autophony, tinnitus and tympanic membrane disorder.
- For patients with pre-existing hearing impairment, symptoms may worsen during or after treatment with teprotumumab.

Monitoring and Management of Hearing Impairment Risk

Baseline and Ongoing Assessment for All Patients

- Audiometric assessments should be performed before starting treatment (first infusion), during treatment (around the third or fourth infusion), and after completing teprotumumab treatment.
- Symptoms of hearing impairment should be carefully monitored, and any reported hearing issues should prompt immediate evaluation.
- All patients should be monitored for hearing changes for 6 months following treatment completion, with prolonged follow-up to be considered for patients who develop hearing impairment, at the discretion of the treating physician.
- Discontinuation of teprotumumab should be strongly considered in patients experiencing hearing loss that requires intervention, limits their ability to self-care, or is considered profound.

Patients at Higher Risk for Hearing Impairment

Consider the benefit-risk of treatment for each patient individually, particularly for those with pre-existing hearing impairment. Modifiable risk factors should be addressed prior to and during treatment. Caution and close monitoring of hearing function are recommended for patients with the following risk factors due to increased potential for hearing impairment:

History of hearing issues

Age above 65 years

Significant history of smoking

Systemic hypertension

Diabetes mellitus

Chronic exposure to high-intensity ambient noise

Concomitant use of ototoxic medications, including:

- Platinum-based anticancer agents
- Aminoglycosides
- Vancomycin
- Loop diuretics

Counseling Patients on the Potential Risk of Hearing Impairment Before Initiating Teprotumumab Treatment

Before initiating treatment, physicians should discuss the following with the patient regarding the potential risk of hearing impairment with teprotumumab treatment:

- Inform the patient about signs and symptoms of hearing loss and the importance of reporting any changes to their treating physician as soon as possible.
- Inform the patient that teprotumumab may cause hearing loss which in some cases may be permanent.
- Explain that their hearing will be assessed prior to start of first dose, around third or fourth dose, and after the last dose.
- Explain that their hearing will be assessed for 6 months after the last dose of teprotumumab if necessary.
- Explain that their hearing may be monitored for longer than 6 months if the patient develops changes in hearing.

Embryofetal Toxicity Risk

- Teprotumumab may cause harm to an unborn fetus and is contraindicated during pregnancy.
- Animal studies have shown that teprotumumab may cause fetal harm including decreased fetal growth, reduced fetal size and weight, as well as multiple external and skeletal abnormalities in offspring.
- Women of childbearing potential should use effective contraception prior to initiation, during treatment and for 6 months after the last infusion of teprotumumab.
- It is recommended to perform a pregnancy test for women of childbearing potential to exclude pregnancy before starting treatment with teprotumumab.
- If the patient becomes pregnant during treatment, teprotumumab must be discontinued and the patient informed of the potential risk to the fetus.

Counseling Patients on the Embryofetal Toxicity Risks Before Initiating Teprotumumab Treatment

Before initiating treatment, physicians should discuss the following with the patient regarding the embryofetal toxicity risks with teprotumumab treatment:

- Inform the patient that teprotumumab can cause harm to the unborn fetus.
- Confirm whether the patient is pregnant or planning pregnancy.
- Reinforce the need for effective contraception prior to initiation, during treatment and for 6 months after the last dose of teprotumumab.
- Advise patients to notify their treating physician immediately if they become pregnant during treatment.

Hyperglycemic Complications - Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic State (HHS)

- Teprotumumab therapy has been associated with hyperglycemia, including rare but serious events of hyperglycemic complications such as DKA and HHS.

For patients with pre-existing diabetes or impaired glucose tolerance, glycemic control may worsen during or after treatment with teprotumumab.

- In patients with persistent hyperglycemia or symptoms suggestive of DKA/HHS, obtain prompt laboratory evaluation (glucose, ketones, electrolytes, renal function, acid–base status) and institute appropriate management according to current DKA/HHS guidelines.
- Withhold further infusions of teprotumumab until metabolic stability is achieved.

Monitoring and Management of Hyperglycemic Complications - DKA and HHS

Baseline and Ongoing Assessment for All Patients

- Detailed history of diabetes, pre-diabetes, gestational diabetes and other metabolic risk factors should be collected.
- Baseline fasting plasma glucose and/or HbA1c should be performed before starting treatment (first infusion), during treatment (around the third or fourth infusion), and for 6 months after completing teprotumumab treatment.
- For patients with diabetes or pre-diabetes, ensure an individualized glycemic management plan (including potential adjustment of insulin and/or oral agents) is in place before starting therapy.
- Monitoring of capillary blood glucose or continuous glucose monitoring data is recommended before each infusion and periodically between infusions, with increased frequency during intercurrent illness.

Patients at Higher Risk for Hyperglycemic Complications - DKA and HHS

Close monitoring of blood glucose levels and consideration of endocrinology co-management is advised for patients with:

a. Pre-existing type 1 or type 2 diabetes, particularly if sub-optimally controlled (e.g. elevated HbA1c, prior DKA/HHS)
b. Pre-diabetes or impaired glucose tolerance
c. Older age and/or frailty
d. Obesity and metabolic syndrome
e. Concomitant use of systemic glucocorticoids or other agents that may worsen glycemic control
f. Chronic kidney disease or other significant comorbidities (e.g. cardiovascular disease)
g. Limited access to diabetes care or challenges with self-management (e.g. cognitive impairment, health literacy, psychosocial barriers)

Counseling Patients on Potential Hyperglycemic Complications - DKA and HHS - Before Initiating Teprotumumab Treatment

Before initiating treatment, physicians should discuss the following with the patient regarding the potential hyperglycemic complication risks, including DKA and HHS, with teprotumumab treatment:

- Inform patients that teprotumumab can worsen glycemic control and may precipitate serious hyperglycemic complications, including DKA and HHS, particularly in those with diabetes or pre-diabetes.
- Reinforce the importance of regular blood glucose monitoring and adherence to diabetes medications when indicated.
- Review signs and symptoms of DKA/HHS (eg, marked thirst, polyuria, nausea, vomiting, abdominal pain, dyspnoea, extreme fatigue, confusion, reduced level of consciousness) and instruct patients to seek immediate medical attention if these occur.
- Advise patients to promptly contact their diabetes care team or treating physician if home blood glucose readings are persistently elevated or if they are unable to maintain adequate oral intake due to intercurrent illness.

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Notes

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