**Dosing**

Dosing of teprotumumab involves 8 infusions delivered over 6 months. The initial dosage involves 10mg/kg body weight, with subsequent infusions dosed at 20mg/kg.

* The dosing of teprotumumab is appropriate for patients with TED; however, the dose frequency may be adjusted in accordance with individual experience. Further evidence regarding teprotumumab dosing is still required.
* Dosing schedules for treatment with teprotumumab can be selected depending on disease severity.
* Early discontinuation of treatment with teprotumumab is not recommended if no symptomatic improvement has occurred at the 4th-6th infusion.
* Treatment dosage should not be decreased among patients experiencing side effects until further data are available; however, the length between treatments may be increased among patients experiencing side effects.
* Re-treatment with teprotumumab can be considered in patients with relapse.
* Treatment with teprotumumab may be discontinued in patients experiencing intolerable side effects (including severe IBD, alopecia, cramps and loss of hearing) or poorly controlled hyperglycemia.

*Rationale*

The dosing for teprotumumab should be followed as per the FDA label dose recommendation1; however, the dose frequency may be adjusted based on individual experience. The time between doses may be increased in patients with TED experiencing side effects as opposed to adjusting the dosage - as lowering the dosage may not produce a significant therapeutic response to the medication.2 Time between doses should not be decreased based on ideal blood levels and pharmacokinetic data but may be increased.

Early discontinuation of teprotumumab is not recommended in patients with TED if no symptomatic improvement has occurred by the 4th–6th infusion as teprotumumab may not yield a therapeutic response until the second half of the treatment cycle. Data demonstrates that significant improvement can occur after the 4th-6th infusion potentially resulting in reduction of TED symptoms such as proptosis and diplopia.3

**Concomitant treatments**

* The following medications for TED do not have to be avoided while using teprotumumab therapy: selenium, biotin, topical steroids for dermatological conditions, inhaled steroids for conditions other than TED, vasoconstrictor eye drops and non-steroid eye drops such as saline or methylcellulose.
* Data are not available, however there are no known contraindications to continue the following treatments while using teprotumumab therapy: steroids, non-steroidal immunosuppressive agents (apart from rituximab or tocilizumab), as well as patients who have received orbital radiation for the treatment of TED.

*Rationale*

There are no current data to suggest teprotumumab is contraindicated when used with any of the above therapies. Patients with TED who demonstrate persistent disease following orbital radiation may be treated with teprotumumab based upon the individual’s risks and benefits.

### Assessment of response

The following indicators represent a good clinical response:

* A reduction in proptosis of ≥ 2mm from baseline by week 24.
* A reduction in eyelid retraction ≥ 2mm from baseline by week 24
* A CAS of 0 or 1 by week 24.
* A reduction of ≥ 2 points in CAS from baseline by week 24.
* A reduction in diplopia of ≥ 1 point.

The following indicators represent a relapse after week 24:

* Increase in proptosis of ≥ 2 mm.
* An increase in CAS ≥2 points since week 24.
* An overall CAS of ≥4 following the week 24 visit taking into consideration the baseline CAS.
* New onset of double vision when other potential conditions such as myasthenia gravis can be ruled out.

Patients exhibiting <1 point of improvement in CAS after 12–18 weeks should complete the remainder of their current therapy and may be considered for another course of therapy (24 weeks) provided they can tolerate another course of teprotumumab.

Discontinuation of therapy can occur if the patient demonstrates no improvement from baseline proptosis and/or diplopia after carrying out two complete courses of teprotumumab.

#### Rationale

The measures presented indicate a good clinical response or relapse after week 24 of teprotumumab treatment; these indicators correlate with clinical studies for teprotumumab.4

The patient should complete the entire course of teprotumumab without early discontinuation as it may take more time for some patients with TED to yield a therapeutic response.

**References**

1. FDA. Teprotumumab FDA label <https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761143s000lbl.pdf>. Published 2020. Accessed 22/02/2021.

2. Xin Y, Xu F, Gao Y, et al. Pharmacokinetics and Exposure-Response Relationship of Teprotumumab, an Insulin-Like Growth Factor-1 Receptor-Blocking Antibody, in Thyroid Eye Disease. *Clin Pharmacokinet.* 2021.

3. Ozzello DJ, Kikkawa DO, Korn BS. Early experience with teprotumumab for chronic thyroid eye disease. *Am J Ophthalmol Case Rep.* 2020;19:100744-100744.

4. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. *New England Journal of Medicine.* 2020;382(4):341-352.