swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Tepezza

International non-proprietary name:	teprotumumab
Pharmaceutical form:	powder for concentrate for solution for infusion
Dosage strength(s):	500 mg
Route(s) of administration:	intravenous
Marketing authorisation holder:	Amgen Switzerland AG
Marketing authorisation no.:	69795
Decision and decision date:	approved on 30 April 2025

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

Table of contents

1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
BIL	Bilirubin
CAS	Clinical Activity Score
CHO	Chinese hamster ovary
CI	Confidence interval
CL/F	Apparent Clearance
C_{max}	Maximum observed plasma/serum concentration of drug
CRCL	Creatinine clearance
CYP	Cytochrome P450
DDI	Drug-drug interaction
DP	Drug Product
EMA	European Medicines Agency
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
GI	Gastrointestinal
GLP	Good Laboratory Practice
GO-QoL	Graves' Ophthalmopathy Quality of Life
HPLC	High-performance liquid chromatography
IBD	inflammatory bowel disease
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
IGF-1	insulin-like growth factor-1
IGF-1R	insulin-like growth factor-1 receptor
IL	Interleukin
INN	International non-proprietary name
ITT	Intention-to-treat
IV	Intravenous
LoQ	List of Questions
mAb	monoclonal antibody
MAH	Marketing authorisation holder
Max	Maximum
MCB	Master Cell Bank
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)

Q3W	every 3 weeks
RANTES	Regulated And Normal T cell Expressed and Secreted
RMP	Risk management plan
SAE	Serious adverse event
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TED	Thyroid Eye Disease
TMDD	Target-mediated drug disposition
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
UGT	UDP-Glucuronosyltransferase
Vc	Volume of distribution in the central compartment
WCB	Working Cell Bank
WFI	Water for injection

2 Background information on the procedure

2.1 Applicant's request(s)

New active substance status
The applicant requested new active substance status for teprotumumab in the above-mentioned medicinal product.

Fast-track authorisation procedure
The applicant requested a fast-track authorisation procedure in accordance with Article 7 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

Tepezza is indicated in adults for the treatment of moderate to severe thyroid eye disease (TED).

2.2.2 Approved indication

Tepezza is indicated in adults for the treatment of moderate to severe active thyroid eye disease (TED) (see "Clinical efficacy").

2.2.3 Requested dosage

The recommended dose of teprotumumab is an intravenous infusion of 10 mg/kg for the first dose followed by an intravenous infusion of 20 mg/kg Q3W for a total of 8 doses. The diluted solution is administered as an intravenous infusion over at least 90 minutes for the first 2 infusions. If well tolerated, subsequent infusions can be administered over 60 minutes.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	24 June 2024
Formal control completed	27 June 2024
List of Questions (LoQ)	30 August 2024
Response to LoQ	28 November 2024
Preliminary decision	28 January 2025
Response to preliminary decision	28 March 2025
Labelling corrections and/or other aspects	16 April 2025
Response to labelling corrections and/or other aspects	25 April 2025
Final decision	30 April 2025
Decision	approval

3 Medical context

Thyroid eye disease (TED), also known as Graves' orbitopathy, is an autoimmune condition often associated with Graves' disease and progresses through an active inflammatory phase and a chronic inactive phase. About 25% of cases are moderate to severe, with proptosis being one of the hallmark symptoms due to inflammation and tissue expansion behind the eye. The active phase typically lasts 1–3 years and can lead to persistent tissue changes, even after inflammation subsides. Glucocorticoids are standard for moderate-to-severe cases, though their long-term benefit is limited and no TED-specific drug was approved in Switzerland at the time of the application.

4 Quality aspects

4.1 Drug substance

Teprotumumab is a fully human immunoglobulin G1 (IgG1) monoclonal antibody (mAb) directed against human insulin-like growth factor-1 receptor (IGF-1R). Teprotumumab is composed of two heterodimers. Each of the heterodimers is composed of a heavy chain of 448 amino acids and a light chain of 215 amino acids. The four polypeptide chains of the antibody molecule are linked together by disulphide bonds and N-linked glycosylation is present on each heavy chain.

Teprotumumab is produced in a Chinese hamster ovary (CHO) cell line. A two-tiered cell banking system of Master Cell Bank (MCB) and Working Cell Bank (WCB) is in place. After thawing of the WCB vial, the cells are grown in suspension culture in a series of seed train bioreactors to generate sufficient cell mass to seed the production bioreactor. The cell culture fluid is harvested, and purification is performed with a series of chromatography steps, ultrafiltration/diafiltration steps, and viral inactivation and viral filtration steps.

The cell culture and purification processes for teprotumumab drug substance are both validated with several consecutive batches, and the data demonstrated a consistent production and an efficient removal of impurities.

Several changes were implemented during development of the manufacturing process for the drug substance, including changes to manufacturing site and production scale. However, comparability studies, including batch release data, extended characterisation data, and stress stability data, demonstrated comparability between the different processes.

The physicochemical and biological properties of the teprotumumab drug substance and its impurities were characterised using state-of-the-art methods.

The specifications for release and stability of the drug substance include relevant tests and acceptance criteria, e.g. for identity, purity and impurities, quantity, and potency. Specifications are based on published limits, stability data, clinical experience and batch analysis data and are in conformance with current compendial or regulatory guidelines.

Batch analysis data for development, clinical, and process validation batches of teprotumumab drug substance were provided. All specific analytical methods are described and are fully validated.

No significant changes were observed during storage of teprotumumab drug substance under the proposed storage conditions.

4.2 Drug product

Teprotumumab drug product (DP), powder for concentrate for solution for infusion, is presented as a single vial of a preservative-free, lyophilised powder packaged in a carton.

The drug product is supplied in a 20 mL, type 1 clear glass vial, closed with an elastomeric stopper and sealed with a flip-off aluminium seal and is stored at 2–8°C. Each vial delivers 500 mg of teprotumumab formulated in 20 mM histidine, 250 mM trehalose and 0.01% w/v polysorbate 20, pH 5.5.

The product is reconstituted with 10 mL of water for injection (WFI). After reconstitution of the lyophilisate with 10 mL of WFI, the volume of material in the vial is a minimum of 10.5 mL. Prior to administration, the drug product must be diluted in 0.9% (w/v) sodium chloride solution to the required target concentration.

All excipients (L-histidine, L-histidine hydrochloride monohydrate, α-trehalose dihydrate, polysorbate 80, water for injection), are of compendial grade and commonly used for the formulation of biopharmaceuticals. None of the excipients are of animal or human origin.

Several drug product dosage strengths, formulations, presentations, and filling facilities were used during clinical development. However, comparability studies, which included batch release data, extended characterisation data, and stress stability data, demonstrated comparability of the relevant quality attributes between the different processes.

Compatibility studies were conducted to establish the in-use stability of diluted drug product with the intended materials and conditions of use.

The drug product manufacturing process consists of pooling, dilution and mixing, bioburden-reducing filtration of the formulated drug substance, sterile filtration and aseptic filling, lyophilisation, stoppering, crimping, visual inspection, labelling, and secondary packaging.

The drug product manufacturing process is validated with several consecutive batches. The data demonstrated a consistent production.

The specifications for release and stability of the drug product include relevant tests and acceptance criteria, e.g. for identity, purity and impurities, quantity, potency, appearance, pH, osmolality, visible and subvisible particles, bacterial endotoxins, and sterility. The drug product specifications comply with current compendial or regulatory guidelines.

Batch analysis data for several batches of the drug product, including development batches, clinical batches, and process validation batches, were provided. All batch release data comply with the drug product specifications, which were valid at the time of batch release. All specific analytical methods are validated.

The container closure of teprotumumab DP consists of three components: a 20 mL type I borosilicate glass vial, a 20 mm Flurotec-coated chlorobutyl stopper and a crimped aluminium seal, the first two of which are product-contacting. The materials of the type I glass vial and rubber stopper meet compendial requirements.

The vials are stored at 2°C to 8°C. The stability data support a shelf life of 48 months.

4.3 Quality conclusions

Satisfactory and consistent quality of drug substance and drug product has been demonstrated.

Safety of the product with regard to viral and non-viral contaminants is adequately addressed.

5 Nonclinical aspects

Regarding the marketing authorisation application for Tepezza, the Division Nonclinical Assessment conducted an abridged evaluation, which was based on the FDA assessment report dated 12 June 2019 and provided by the applicant.

The pharmaco-toxicological profile has been sufficiently characterised. Drug administration in monkeys was associated with cessation of weight gain, decreased serum alkaline phosphatase, thymic atrophy and embryofetal toxicity. Overall, the submitted nonclinical documentation is considered appropriate to support the authorisation of Tepezza in the proposed indication.

The safety margins are considered to be sufficient. All nonclinical data that are relevant for safety are adequately mentioned in the Information for healthcare professionals, but some modifications or corrections have to be addressed in the section’s pregnancy/lactation and preclinical data.

There is no safety concern regarding impurities and excipients. Based on the ERA, the risk of teprotumumab to the environment is assumed to be low.

In conclusion, from the nonclinical point of view, authorisation can be supported following adequate adaptations to the Information for healthcare professionals.

6 Clinical aspects

6.1 Clinical pharmacology

Pharmacokinetics

ADME

Teprotumumab is administered intravenously.
Based on the trough concentrations over 24 weeks, the steady state was reached after approximately 12 weeks. The accumulation ratio is approximately 2.
Based on the population PK analysis, chronic TED patients showed slightly higher exposures as compared to healthy subjects and active TED patients.

Based on the population PK analyses, the mean estimates for the central and peripheral volumes of distribution of teprotumumab were 2.91 L and 3.67 L, respectively.

No studies regarding the metabolism of teprotumumab have been conducted considering the biological nature of the molecule.
Based on the population PK analysis, the apparent CL/F and elimination half-life in TED patients were estimated at 0.255 L/day and 21.4 days, respectively.
In a previous analysis using data from the Phase 1 study BO19373 in oncology patients, it was shown that teprotumumab displayed linear PK between 3 mg/kg and 20 mg/kg, whereas nonlinear PK was observed at doses <3 mg/kg. These findings suggest saturation of target-mediated drug disposition (TMDD) at higher doses, including the proposed doses.

Special populations / Intrinsic factors

Since renal and hepatic impairment are not expected to have an impact on the PK of mAbs, no dedicated studies in these populations were conducted. The population PK analysis revealed that mild to moderate renal impairment or mild hepatic impairment did not have an impact on the PK of teprotumumab.

Using data from one Phase 1 study, one Phase 2 study, three Phase 3 studies, and one Phase 4 study, a population PK analysis was conducted to identify factors that account for variability of the teprotumumab PK. The dataset included 1168 measurable serum samples from 10 healthy subjects and 176 TED patients. The PK of teprotumumab was well described by a two-compartment model with first-order elimination from the central compartment and redistribution from the peripheral compartment. Only body weight was identified as a statistically significant covariate on both CL and V_c.
Overall, no dose adjustments are required based on any of the investigated covariates, including body weight (43.4 to 169 kg), age (18 to 80 years), sex, ethnicity (Hispanic versus non-Hispanic), race (Asian, Black, White, and Other), smoking status, BIL, AST, ALT, CRCL.

Interactions

No *in vitro* or clinical interaction studies were conducted.
An interaction of teprotumumab with CYPs, UGTs or transporters via its metabolism, chemical properties or mechanism of action is unlikely. Since pro-inflammatory cytokine levels (IL-6, IL-16, and RANTES) in patients with active TED appeared to be unaffected in the Phase 2 study TED01RV, no impact on CYP expression is anticipated.

Pharmacodynamics

Mechanism of action and primary pharmacology

Teprotumumab is a fully human IgG1 mAb that binds to the insulin-like growth factor-1 receptor (IGF-1R). By binding with high affinity and selectivity to the extracellular domain of the human IGF-1R, teprotumumab prevents its activation by both natural ligands, insulin-like growth factor-1 (IGF-1) and IGF-2.
In healthy subjects, the IGF-1 serum concentration increase was maintained for at least 70 days post dose, suggesting sustained target engagement.

Secondary pharmacology (safety)

No tQT study was conducted; mAbs generally harbour a low risk of prolonging the QT interval.

Pharmacodynamic interactions with other medicinal products or substances

Pharmacodynamic interactions based on the mechanism of action of teprotumumab are unlikely.

6.2 Dose finding and dose recommendation

No dose-finding study was conducted, but the proposed regimen (10 mg/kg initially, then 20 mg/kg every three weeks for seven doses) showed significant efficacy and good tolerability in TED. Exposure-response analysis suggested a plateau effect, with no link to efficacy or safety. Covariate analysis found no need for dose adjustments based on demographic or clinical factors.

6.3 Efficacy

Four trials have been conducted to evaluate the efficacy and safety of teprotumumab for the treatment of active TED. Those trials include an open-label extension, Phase 3 trial, following the OPTIC trial, enrolling participants who were either non-responders at Week 24 or responders who relapsed during the follow-up period. The entry criteria for the 3 randomised, double-masked, placebo-controlled trials in acute TED were similar. All participants had a clinical diagnosis of Graves' disease with a Clinical Activity Score (CAS) ≥ 4 (≥ 3 in OPTIC-J) on a 7-point scale (with a score of ≥ 3 indicating acute TED) for the more severely affected eye. Measurements such as proptosis, CAS, diplopia and the GO-QoL questionnaire were used in the trials. The primary endpoint (overall responder rate at Week 24 in TED01RV, proptosis responder rate at Week 24 in OPTIC and OPTIC-J) and secondary endpoints (such as diplopia and the GO-QoL questionnaire) compared teprotumumab versus placebo.
The same teprotumumab dose regimen was used in the 3 trials. Participants who met the eligibility criteria were randomly assigned in a 1:1 ratio to receive intravenous infusions Q3W of either teprotumumab (10 mg/kg on Day 1 followed by 20 mg/kg for the remaining 7 infusions) or placebo (8 infusions). In the OPTIC-X trial, all participants received eight infusions of teprotumumab every three weeks (10 mg/kg for the first infusion and 20 mg/kg for the subsequent seven infusions) in an open-label manner.

TED01RV

For the primary efficacy endpoint (the overall responder rate at Week 24= subject with a decrease in overall CAS of ≥2 points **and** a reduction of proptosis of ≥2 mm.), a statistically significantly greater proportion of participants treated with teprotumumab were responders compared to those who received placebo (n=29, 69.0% vs. n=9, 20.0). Statistically significant improvements were observed in the teprotumumab group compared with the placebo group for the GO-QoL overall score, proptosis measurements, CAS, and the GO-QoL visual functioning subscale score.

HZNP-TEP-301 (OPTIC)

The primary efficacy endpoint was the proptosis responder rate (percentage of subjects with a ≥2 mm reduction from baseline in proptosis in the study eye, without deterioration [≥2 mm increase] of proptosis in the fellow eye) at Week 24.
For the primary efficacy endpoint, a statistically significantly greater proportion of participants treated with teprotumumab were proptosis responders compared with participants who received placebo (n=34, 82.9% vs. n=4, 9.5%). Teprotumumab was statistically significantly superior to placebo for all secondary efficacy endpoints.

HZNP-TEP-302 (OPTIC-X)

In this open-label extension study, participants included those from the preceding OPTIC trial who were either proptosis non-responders at Week 24 or initial responders who relapsed during the follow-up period. The primary objective was to evaluate the effect of teprotumumab on the proptosis responder rate. At Week 24, 89.2% of first-course participants (placebo recipients in OPTIC) and 82.9% of teprotumumab recipients from OPTIC were proptosis responders. Additional benefits were observed with a second course of teprotumumab, with 53.8% of second-course participants being proptosis responders at Week 24 relative to study baseline, and 76.9% relative to teprotumumab baseline.

HZNP-TEP-303 (OPTIC-J)

Since this study was conducted in Japan, all participants were of Asian descent. The primary objective was to assess the impact of teprotumumab versus placebo on the proptosis responder rate. Statistically significant and clinically meaningful differences between teprotumumab and placebo were observed for the primary endpoint (n=27, 88.9% vs. n=3, 11.1%), and the main secondary efficacy endpoints.

6.4 Safety

Teprotumumab was evaluated across six trials, involving 246 participants. Adverse events (AEs) were more common in the teprotumumab group. The most frequent treatment-emergent adverse events (TEAEs) included muscle spasms, diarrhoea, hearing impairment, alopecia, and hyperglycaemia. Serious TEAEs were reported more frequently in the teprotumumab group, though most were non-severe. During follow-up, AEs were still more common in the teprotumumab group, but none were treatment-related or severe. Notably, hearing impairment and hyperglycaemia were classified as AEs of special interest, along with a single case of severe inflammatory bowel disease (IBD) exacerbation in a participant with a pre-existing condition. Observational studies suggest that most hearing issues

resolve within 3-6 months, though some persistent cases have been seen in patients with severe pre-existing hearing deficits.

For details, see the sections *Warnings and Precautions* and Adverse *Events* in the Information for healthcare professionals.

6.5 Final clinical benefit risk assessment

Thyroid eye disease (TED) is an autoimmune disorder linked to Graves' disease, with moderate to severe cases accounting for about 25% of instances. Traditionally, glucocorticoids have been the primary treatment for moderate-to-severe TED, despite their side effects and limited placebo-controlled trial data. At the time of submission, no treatments for active TED were authorised in Switzerland, underscoring the significant unmet medical need for effective therapies.

Overall, the PK profile of teprotumumab generally conforms to that of an mAb. Based on the population PK analysis, no dose adjustment is required based on any of the evaluated covariates including age, body weight, sex, and race.
Four clinical trials have evaluated teprotumumab's efficacy and safety for treating active thyroid eye disease (TED), including Phase 2 and 3 trials conducted in the US, Europe, and Japan, as well as an open-label extension (OPTIC-X). Across these studies, teprotumumab consistently demonstrated statistically significant improvements in key endpoints, such as proptosis and overall responder rates, compared to placebo. Exploratory findings from the open-label extension study showed additional benefits with a second course of teprotumumab. Overall, teprotumumab's efficacy in reducing proptosis, diplopia and improving the quality of life of patients with active TED was demonstrated.

Adverse events (AEs) were more common in the teprotumumab group, with frequent occurrences of muscle spasms, diarrhoea, hearing impairment, alopecia, and hyperglycaemia. Serious AEs were more frequent but mostly non-severe. During follow-up, AEs remained more common in the teprotumumab group, though none were severe or treatment-related. Hearing impairment and hyperglycaemia were noted as AEs of special interest, along with one severe IBD exacerbation

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Tepezza was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected new or serious adverse reactions. See section «Undesirable effects» for advice on the reporting of adverse reactions.

TEPEZZA®

Composition

Active substances

Teprotumumab.
Teprotumumab is a fully human IgG1 monoclonal antibody produced in Chinese Hamster Ovary cells by recombinant DNA technology.

Excipients

L-Histidine, L-histidine hydrochloride monohydrate, Polysorbate 20 (E432), Trehalose dihydrate.

Pharmaceutical form and active substance quantity per unit

Powder for concentrate for solution for infusion.
Sterile, preservative-free white to off-white lyophilised powder.
Each vial contains 500 mg of teprotumumab.

The reconstituted TEPEZZA solution contains 47.6 mg/mL (500 mg / 10.5 mL) of teprotumumab.

Indications/Uses

TEPEZZA is indicated in adults for the treatment of moderate to severe active Thyroid Eye Disease (TED) (see «Clinical efficacy»).

Dosage/Administration

TEPEZZA must be administered by a healthcare professional and under the supervision of a physician with access to appropriate medical support to manage infusion-related reactions.

Posology

TEPEZZA dosing is based on the patient's actual body weight. The recommended dose of TEPEZZA is 10 mg/kg of body weight for the initial dose followed by 20 mg/kg of body weight for 7 additional doses given once every three weeks as an intravenous infusion.

For the first 2 infusions, the diluted solution is administered as an intravenous infusion over at least 90 minutes. If well tolerated, infusions 3 to 8 can be administered over 60 minutes every three weeks. Available data suggest that clinical response is usually achieved within 8 doses of treatment. For patients who have an inadequate response within the first 8-dose of treatment cycle, an additional 8-dose treatment cycle can be considered. There has been no study evaluating the safety and efficacy of TEPEZZA beyond the second course of treatment.

Recommended pre-medication

For patients experiencing immediate hypersensitivity reactions or infusion-related reactions during the first 2 infusions of TEPEZZA, pre-medication with an antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate is recommended (see «Warnings and precautions»).

Special populations

Elderly

No dose adjustment is considered necessary in patients over 65 years old (see «Pharmacokinetics»).

Renal impairment

No clinically significant differences in the pharmacokinetics of TEPEZZA were observed following administration of TEPEZZA to patients with mild to moderate renal impairment (see «Pharmacokinetics»).

No dose adjustment is considered necessary in patients with mild to moderate renal impairment.There is no data in patients with severe renal impairment available.

Hepatic impairment

The effect of moderate to severe hepatic impairment on the pharmacokinetics of TEPEZZA is unknown. However, no clinically significant differences in the pharmacokinetics of TEPEZZA were observed following administration of TEPEZZA to patients with mild hepatic impairment. (see «Pharmacokinetics»).

Paediatric population

The safety and efficacy of TEPEZZA in children <18 years of age has not been established. No data are available.

Method of administration

- TEPEZZA must be administered as an intravenous infusion via an infusion pump.
- Prior to infusion:
  - TEPEZZA must be reconstituted with water for injections
  - The reconstituted TEPEZZA solution must be further diluted in sodium chloride 9 mg/mL (0.9%) solution for infusion, prior to infusion
- TEPEZZA must not be co-administered with other medicinal products through the same infusion line.
- TEPEZZA must not be administered as an intravenous push or bolus.
- For the first 2 infusions, administer the diluted solution intravenously over at least 90 minutes. If well tolerated, the minimum time for subsequent infusions can be reduced to 60 minutes.
- If not well tolerated, the minimum time for subsequent infusions should remain at 90 minutes, the rate of infusion should be reduced and pre-medication is recommended for subsequent infusions.

For instructions on reconstitution and dilution of the medicinal product before administration, see section «Instructions for handling».

Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in «Composition».
- Pregnancy (see «Pregnancy, lactation»).

Warnings and precautions

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Infusion-related reactions

TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA (see «Undesirable effects»). Patients should be advised to contact their healthcare professionals if they experience signs and symptoms of infusion-related reactions including but not limited to transient increases in blood pressure, feeling hot, tachycardia, dyspnoea, headache and muscular pain. Patients should be monitored closely throughout the infusion and for

90 minutes after completion of infusion. Based on the severity of the infusion-related reaction, TEPEZZA infusion should be interrupted or discontinued, and appropriate medical management should be instituted. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate. For patients who experience an anaphylactic reaction, discontinue TEPEZZA immediately and permanently.

Hyperglycaemia
Hyperglycaemia or increased blood glucose may occur in patients treated with TEPEZZA. In double-masked TED clinical trials, 10% of patients (two thirds of whom had pre-existing diabetes or impaired glucose tolerance) experienced hyperglycaemia. Hyperglycaemic events should be managed with medications for glycaemic control, if necessary.

Assess patients for elevated blood glucose and symptoms of hyperglycaemia prior to infusion and continue to monitor while on treatment with TEPEZZA. Ensure patients with hyperglycaemia or pre-existing diabetes are under appropriate glycaemic control before and while receiving TEPEZZA (see «Undesirable effects»).

Hearing impairment
TEPEZZA may cause severe hearing impairment including hearing loss, which in some cases may be permanent. Events associated with hearing impairment including hearing loss (reported as deafness, including sensorineural deafness, eustachian tube dysfunction, eustachian tube patulous, hyperacusis, hypoacusis, autophony and tinnitus and tympanic membrane disorder), have been observed in clinical trials with TEPEZZA (see «Undesirable effects»).

Patients' hearing should be assessed before, during and after treatment with TEPEZZA.
For patients with pre-existing hearing impairment, a worsening of hearing impairment symptoms during or after the completion of the treatment with TEPEZZA cannot be excluded. The benefit-risk of treatment should be considered in these patients.

The benefit-risk of continuing treatment with TEPEZZA should be considered in patients who experience severe hearing impairment during the treatment. Patients should be advised to stop smoking and avoid high intensity noises during treatment with TEPEZZA. Additionally, blood pressure and blood glucose should be appropriately controlled before and while receiving TEPEZZA.

Patients should be advised to report symptoms of altered hearing promptly to their healthcare professional.

Worsening of pre-existing inflammatory bowel disease (IBD)
TEPEZZA may cause an exacerbation of pre-existing inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA (see «Undesirable effects»).

Interactions

No formal medicinal product interaction studies have been performed.

Since TEPEZZA is cleared from the circulation by proteolytic catabolism, no metabolic medicinal product interactions are expected.

Pregnancy, lactation

Women of childbearing potential/contraception
Women of childbearing potential should use effective contraception (methods that result in less than 1% pregnancy rates) prior to initiation, during treatment and for 6 months after the last administration of TEPEZZA.

Pregnancy
There are no adequate data from the use of teprotumumab in pregnant women. No human developmental and reproductive studies were conducted with teprotumumab.

Studies in animals have shown reprotoxicity (see «Preclinical data»).

Based on mechanism of action inhibiting IGF-1R and reprotoxicity in animals, TEPEZZA may cause congenital malformations such as foetal growth retardation and developmental anomalies when administered during pregnancy (see «Preclinical data»). Therefore, TEPEZZA is contraindicated during pregnancy (see «Contraindications»).

If a patient becomes pregnant while taking TEPEZZA, therapy should be discontinued, and the patient advised of the potential risk to the foetus.

Breast-feeding
It is unknown whether teprotumumab is excreted in human milk. Teprotumumab caused reproductive toxicity in animals (see «Preclinical Data»). Thus, as a precautionary measure, Tepezza should not be used during breastfeeding.

Fertility
The effects of TEPEZZA in humans are unknown. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see «Preclinical data»).

Effects on ability to drive and use machines

TEPEZZA can have a minor influence on the ability to drive and use machines because fatigue and headaches have been reported with the use of TEPEZZA (see «Undesirable effects»).

Undesirable effects

Summary of the safety profile
The most common adverse reactions observed in clinical trials are; muscle spasms, diarrhoea, hearing impairment, alopecia, hyperglycaemia, fatigue, nausea, headache, dry skin, dysgeusia, COVID-19, ear discomfort and nail disorder.

The most common serious adverse reactions are; diarrhoea, inflammatory bowel disease, infusion-related reaction.

Tabulated list of adverse reactions
The adverse reaction frequencies from clinical trials are based on all-cause adverse event frequencies, where a proportion of the events for an adverse reaction may have other causes than the medicinal product, such as the disease, other medicines or unrelated causes.

Adverse reactions reported in clinical trials and derived from spontaneous reporting are listed below in table 1. The adverse reactions are listed by MedDRA System Organ Class and by frequency. The frequencies of adverse reactions is based on 4 placebo-controlled studies with 285 patients. Patients were exposed to teprotumumab for a median of 148 days.

Frequencies are defined according to the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1’000 to <1/100); rare (≥1/10’000 to <1/1’000); very rare (<1/10’000); not known (cannot be estimated from the available data).

Table 1. Adverse reactions

MedDRA system organ class	Very common (> 1/10)	Common (> 1/100 to < 1/10)	Uncommon (> 1/1 000 to < 1/100)	Rare (> 1/10 000 to < 1/1 000)	Not known/cannot be estimated from available data
Infections and infestations		COVID-19			
Metabolism and nutrition disorders	Hyperglycaemia (13%)		Diabetic ketoacidosis		Hyperosmolar hyperglycaemic state[3]
Nervous system disorders	Headache (11%)	Dysgeusia			
Ear and labyrinth disorders	Hearing impairment[1] (14%)	Ear discomfort			
Gastrointestinal disorders	Diarrhoea (15%), Nausea (11%)		Inflammatory bowel disease		
Skin and subcutaneous tissue disorders	Alopecia (13%)	Dry skin, nail disorder			
Musculoskeletal and connective tissue disorders	Muscle spasms (28%)				
Reproductive system and breast disorders	Menstrual disorders[2] (13%)				
General disorders and administration site conditions	Fatigue (13%)				
Investigations		Weight decreased			
Injury, poisoning and procedural complications		Infusion-related reaction			

[1] Hearing impairment includes hearing loss (deafness, including sensorineural deafness, eustachian tube dysfunction, eustachian tube patulous, hyperacusis, hypoacusis, autophony, tinnitus, and tympanic membrane disorder).

[2] Menstrual disorders includes amenorrhea, hypomenorrhea, dysmenorrhea, irregular menstruation, heavy menstrual bleeding.

[3] Observed in the postmarketing setting – frequency cannot be estimated from the available data.

Description of selected adverse reactions

Infusion-related reactions

Infusion-related reactions were usually mild or moderate in intensity and can be successfully managed with antihistamines and/or corticosteroids, if needed. No infusion-related reactions in TED trials were reported as anaphylactic reactions. See sections «Dosage/Administration» and «Warnings and precautions» for action to be taken in case of infusion-related reactions.

Inflammatory bowel disease (IBD)

In study 1, two teprotumumab-treated participants with a history of IBD reported serious treatment-emergent adverse events (TEAEs) that led to discontinuation of study drug. No events of new-onset IBD have been observed in the TED trials, see sections «Dosage/Administration» and «Warnings and precautions».

Hyperglycaemia

In clinical studies, hyperglycaemia (5.3%) and events associated with hyperglycaemia including blood glucose increased (3.3%), diabetes mellitus (2.6%), glucose tolerance impaired (1.3%), glycosylated haemoglobin increased (2.0%) were mild or moderate in severity and managed as needed with medications used for glycaemic control. One event of diabetic ketoacidosis (0.7%) was reported in clinical studies for a patient who received a single dose of teprotumumab. Post marketing cases of hyperosmolar hyperglycaemic state have been reported. The events of diabetes mellitus, diabetic ketoacidosis, and hyperosmolar hyperglycaemic state all occurred in patients with pre existing diabetes or pre diabetes, and other co morbidities. Participants with diabetes or pre diabetes at baseline may experience increased hyperglycaemic excursion, as insulin and IGF 1 receptors are homologous and share downstream signalling pathways. Recommendations for management of hyperglycaemia are provided in section «Warnings and precautions».

Hearing impairment

In clinical trials, 21 (13.8%) participants in the teprotumumab group and 3 (2.3%) participants in the placebo group experienced hearing impairment. Hearing impairment includes hearing loss [hypoacusis (5.3%), tinnitus (3.3%), deafness (1.3%), neurosensory hypoacusis (1.3%) and deafness unilateral (0.7%), eustachian tube dysfunction (1.3%), eustachian tube patulous (1.3%), autophony (1.3%), hyperacusis (0.7%) and tympanic membrane disorder (0.7%)]. One patient (0.7%) with pre existing hearing impairment reported an event of neurosensory hypoacusis, which led to the discontinuation of teprotumumab. Additionally, one patient (0.7%) with pre existing hearing

impairment reported a serious event of conductive deafness, also resulting in the discontinuation of teprotumumab. 10 of the 21 participants in the teprotumumab group reported that their hearing impairment resolved; the mean duration of the events was 108.6 days (range 1 to 204, median 141 days). Mean time to first hearing impairment event after the first dose was 77.9 days (range: 3 to 153 days) among teprotumumab-treated participants. The average number of teprotumumab infusions received prior to event onset was 4.2. For clinical management of hearing impairment, see «Warnings and precautions».

Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease.
In randomised placebo-controlled studies (OPTIC and OPTIC-J) with teprotumumab in active TED patients, 3.0% (2 of 67) patients who received teprotumumab treatment had detectable levels of anti-drug antibodies (ADA) with low titer values at post-baseline visits. There was no apparent impact of ADA on efficacy, safety, or pharmacokinetics.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

There is no known antidote for teprotumumab overdose. Treatment consists of discontinuation of the medicinal product and supportive therapy.

Properties/Effects

ATC-Code

L04AG13

Mechanism of action

Teprotumumab mechanism of action in patients with TED has not been fully characterised. Teprotumumab binds to insulin-like growth factor-1 receptor (IGF-1R) and blocks its activation and signalling.

Clinical efficacy

TED01RV was a randomized, double-masked, placebo-controlled study in patients with acute TED. Patients were given intravenous infusions (10 mg/kg for first infusion and 20 mg/kg for the remaining 7 infusions) every 3 weeks for a total of 8 infusions. Patients with active thyroid eye disease had a median time since diagnosis of TED of 5.76 months, mean proptosis for the study eye of 23 mm, and median clinical activity score CAS for the study eye at baseline of 5.

A total of 43 patients were randomized to TEPEZZA and 45 patients were randomized to placebo. The median age was 52.9 years (range 20.4 to 77.0), 73.6% were female and 66.7% were non-smoker. 86.2% were white, 9.2% were black, 9.2% were Asian, and 1.1% were native Hawaiian or other Pacific Islander.

The primary endpoint in phase II study TED01RV was the overall responder rate, defined as the percentage of participants with ≥ 2-point reduction in CAS and ≥ 2 mm reduction in proptosis measurement from baseline in the study eye, provided there is no corresponding deterioration (≥ 2-point increase in CAS or ≥ 2 mm increase in proptosis in the fellow eye) at week 24.
Efficacy results of study TED01RV are summarised in table 2.

Table 2. Overview of efficacy parameters in study TED01RV at week 24 (ITT population)

	Teprotumumab (N =42)	Placebo (N =45)	Treatment Difference (95% CI)	p-value
Primary endpoint				
Overall responder rate, %	69.0	20.0	48.9 (30.2, 67.6)	< 0.001[a]
Secondary endpoints[b]				
Proptosis in study(mm), LS Mean	-2.95	-0.30	-2.65 (-3.38, -1.92)	< 0.001
CAS in study eye, LS Mean	-4.04	-2.49	-1.55 (-2.17, -0.94)	< 0.001

CAS = Clinical Activity Score; CI = confidence interval; ITT = intent-to-treat; LS = Least Squares

Note: Results shown are those for the study eye for overall responder rate and change from baseline in proptosis.

[a] P-value was obtained from a logistic regression model with treatment and smoking status as covariate. Odds ratio of teprotumumab over placebo was 8.86 (95% CI [3.29, 23.83]).

[b] For secondary endpoints, analysis results were obtained from a mixed model for repeated measures (MMRM) with an unstructured covariance matrix using treatment, smoking status, baseline value, visit, treatment by visit,

and visit by baseline value interaction as fixed effects. A change from baseline of zero was imputed at the first baseline visit for patients with no post-baseline assessment.

After 48-weeks off-treatment, 14 of 29 proptosis responders (48.3%) in the teprotumumab group maintained responder status, and 11 of 29 (37.9%) experienced a relapse. Relapse was defined as increase in proptosis of ≥ 2 mm from week 24 in the study eye.

OPTIC was a randomized, double-masked, placebo-controlled study in patients with acute TED. Patients were given intravenous infusions (10 mg/kg for the first infusion and 20 mg/kg for the remaining 7 infusions) every 3 weeks for a total of 8 infusions. Patients with active thyroid eye disease had a median time since diagnosis of TED of 6.78 months, median proptosis for the study eye of 23 mm, and median clinical activity score CAS for the study eye at baseline of 5.0.

A total of 41 patients were randomized to TEPEZZA and 42 were randomized to placebo. The median age was 52.0 years (range 20 to 79), 72.3% were female and 79.5% were non-smoker. 86.7% were white, 7.2% were black, 3.6% were Asian, and 2.4% were categorized as other.

The primary endpoint, in the phase III OPTIC study was the proptosis responder rate at week 24 (defined as the proportion of patients with a ≥ 2 mm reduction in proptosis from baseline in the study eye, without deterioration (≥ 2 mm increase) in proptosis in the fellow eye).
Efficacy results of the OPTIC study is summarised in table 3.

Table 3. Overview of efficacy parameters in study OPTIC at week 24 (ITT population)

	Teprotumumab (N = 42)	Placebo (N = 41)	Treatment Difference (95% CI)	p-value
Primary endpoint				
Proptosis responder rate, %	82.9	9.5	73.5 (58.9, 88.0)	< 0.001[a]
Secondary endpoints				
Overall responder rate, %	78.0	7.1	70.8 (55.9, 85.8)	< 0.001[a]
CAS responder rate, %	58.5	21.4	36.0 (17.4, 54.7)	< 0.001[a]
Change from baseline in proptosis (mm) through week 24, LS mean	-2.82	-0.54	-2.28 (-2.77, -1.80)	< 0.001[b]
Diplopia responder rate, %[c]	67.9	28.6	39.3 (15.6, 63.0)	< 0.001[a]

CAS = Clinical Activity Score; CI = confidence interval; ITT = intent-to-treat; LS = Least Squares

Note: Results shown are those for the study eye for proptosis responder rate, overall responder rate, CAS responder rate, and diplopia responder rate.
Overall responder rate = Overall responders are defined as achieving ≥ 2 points reduction in CAS and ≥ 2 mm reduction in proptosis from baseline, provided there was no corresponding deterioration (≥ 2 points/mm increase) in CAS or proptosis in the fellow eye at week 24.
CAS responder rate = CAS responders are defined as achieving a reduction to a CAS of 0 or 1 at week 24.
Diplopia responder rate = Diplopia responders are defined as achieving ≥ 1 grade reduction in diplopia in the study eye without worsening by at least one grade in the fellow eye at week 24.
[a] Cochran–Mantel–Haenszel (CMH) test stratified by tobacco use status (smoker vs non-smoker).
[b] Results obtained from mixed model repeated measurements (MMRM) analysis with an unstructured covariance matrix including baseline value, tobacco use status, treatment group, visit, visit by treatment, and visit by baseline value interactions. A change from baseline of 0 was imputed at the first post baseline visit for any patient without a post-baseline value at all.
[c] Evaluated based on only those who presented diplopia at baseline.

Of 34 proptosis responders, 10 (29.4%) relapsed during the 48-week off-treatment follow-up. Among the 21 who had assessments at week 48, 19 (90.5%) maintained their responder status.

OPTIC-J was a randomized, double-masked, placebo-controlled study in Japanese patients (100% Asian) with acute TED (27 randomized to TEPEZZA, 27 to placebo). TEPEZZA demonstrated statistically significant and clinically meaningful improvements for the primary efficacy endpoint (proptosis responder rate at week 24 defined as a ≥ 2-mm reduction from baseline in proptosis in the study eye without deterioration [≥ 2-mm increase] of proptosis in the fellow eye).

Pharmacokinetics

Absorption

The pharmacokinetics of teprotumumab was described by a two-compartment population pharmacokinetic (PK) model based on data from 10 healthy subjects (dose of 1 500 mg) single IV and 176 patients with TED (first infusion at 10 mg/kg followed by 7 repeated doses of 20 mg/kg Q3W). Following the recommended dose regimen (first infusion at 10 mg/kg followed by 7 repeated doses of 20 mg/kg Q3W), the mean (±SD) estimates for AUC_{ss}, peak $C_{max,ss}$ and $C_{min,ss}$ concentrations of teprotumumab were 139 (±27) mg*hr/mL, 675 (±147) µg/mL, and 159 (±38) µg/mL, respectively. Teprotumumab showed linear PK between doses of 3 mg/kg and 20 mg/kg.

Distribution

Following the recommended teprotumumab dosing regimen, the population PK estimated mean (± standard deviation) for total volume of distribution of teprotumumab was 6.76 (±1.17) L.

Metabolism

Metabolism of teprotumumab has not been fully characterised. However, teprotumumab is expected to undergo metabolism via proteolysis.

Elimination

Following the recommended teprotumumab dosing regimen, the population PK estimated mean (± standard deviation) based on post hoc individual parameter estimates of 176 participants with TED for the clearance of teprotumumab was 0.27 (±0.07) L/day and for the elimination half-life was 22 (±4) days.

Kinetics in specific patient groups

No clinically significant differences in the pharmacokinetics of teprotumumab were observed following administration of teprotumumab based on patient's age (18-80 years), gender, race/ethnicity (White, Asian and Black), weight (43-169 kg), mild to moderate renal impairment (creatinine clearance 30 to 89 mL/min estimated by Cockcroft-Gault Equation), bilirubin levels (2.60-24.5 mcmol/L), aspartate aminotransferase (AST) levels (8-73 U/L), or alanine aminotransferase (ALT) levels (7-174 U/L). No clinically significant differences in the pharmacokinetics of TEPEZZA were observed following administration of TEPEZZA to patients with mild hepatic impairment.

Preclinical data

Non-clinical data reveal no special hazard for adult humans based on the repeated dose toxicity studies.
Adverse effects were observed in preclinical studies only at exposures that were considered to be sufficiently above the maximum exposure in humans, suggesting that these are of little relevance to clinical use.

Mutagenesis and carcinogenesis
There have been no studies to assess the carcinogenic or mutagenic potential of teprotumumab.

Reproductive toxicity
No reproductive organ toxicity or histopathology findings were observed in any repeat dose toxicity studies for male or female cynomolgus monkeys.

In an embryofoetal development study, seven pregnant cynomolgus monkeys were dosed intravenously at one dose level of teprotumumab, 75 mg/kg (2.8-fold the maximum recommended human dose based on AUC) once weekly from gestation day 20 through the end of gestation. The incidence of abortion was higher for the teprotumumab-treated group (2 out of 7 foetuses, 28.6%) compared to the control group (1/6, 16.7%). Teprotumumab caused decreased foetal growth during pregnancy, decreased foetal size and weight at caesarean section, decreased placental weight and size, and decreased amniotic fluid volume. Multiple external and skeletal abnormalities were observed in each exposed foetus, including: misshapen cranium, closely set eyes, micrognathia, pointing and narrowing of the nose, and ossification abnormalities of skull bones, sternebrae, carpals, tarsals and teeth. The test dose, 75 mg/kg/week of teprotumumab, was the maternal no observed adverse effect level.

Based on the mechanism of action of teprotumumab which is the inhibition of IGF-1R signalling, exposure to teprotumumab may cause harm to the foetus.

Other information

Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section «Instructions for handling».

No incompatibilities between teprotumumab and polyethylene (PE), polyvinyl chloride (PVC), polyurethane (PUR) or polyolefin (PO) bags and intravenous administration sets have been observed.

Shelf life

Do not use this medicine after the expiry date «EXP» stated on the pack.

Shelf life after reconstitution and dilution

The product does not contain any preservative. Diluted infusion solution should be used immediately.

Chemical and physical in-use stability of the reconstituted solution in the vial has been demonstrated for ≤4 hours at room temperature (20–25°C) or ≤48 hours at 2 to 8°C storage condition.
The combined storage duration of the reconstituted solution in the vial and the diluted solution in the infusion bag containing 0.9% sodium chloride for injection is a total of 4 hours at room temperature (20°–25°C) or up to 48 hours at 2°–8°C while protected from light.

For microbiological reasons, the ready-to-use preparation should be used immediately after dilution/reconstitution. If this is not possible, use-up periods and storage conditions are the responsibility of the user and should not exceed 24 hours at 2-8°C, unless dilution/reconstitution was carried out under controlled and validated aseptic conditions.

If refrigerated prior to administration, allow the diluted solution to reach room temperature prior to infusion.

Special precautions for storage

Store in a refrigerator (2°C-8°C).
Do not freeze.
Keep the vial in the outer carton in order to protect from light.
For storage conditions after reconstitution and dilution of the medicinal product, see section «Shelf life after reconstitution and dilution».
Keep out of the reach of children.

Instructions for handling

TEPEZZA should be prepared by a healthcare professional using aseptic technique to ensure the sterility of the prepared solution.

After reconstitution, teprotumumab is a nearly colourless or slightly brown, clear to opalescent solution which is free of foreign particulate matter. The reconstituted solution should be inspected for particular matter and discolouration prior to administration. Discard the solution if particulate matter is present or discolouration is observed. Refer to section «Shelf life» for stability after reconstitution.

Preparation of the medicinal product before administration
Step 1: Calculate the dose (mg) and determine the number of vials needed for the 10 or 20 mg/kg dosage based on patient weight. Each TEPEZZA vial contains 500 mg of the teprotumumab antibody.

Step 2: Using appropriate aseptic technique, reconstitute each TEPEZZA vial with 10 mL of sterile water for injection. Ensure that the stream of diluent is not directed onto the lyophilised powder, which has a cake-like appearance. Do not shake, but gently swirl the solution by rotating the vial until the lyophilised powder is dissolved. The reconstituted solution has a total volume of 10.5 mL. Withdraw 10.5 mL of reconstituted solution to obtain 500 mg. After reconstitution, the final concentration is 47.6 mg/mL.

Step 3: The reconstituted TEPEZZA solution must be further diluted in sodium chloride 9 mg/mL (0.9%) solution for infusion, prior to infusion. To prepare the diluted solution, use 100 mL infusion bags for a dose less than 1’800 mg, and 250 mL infusion bags for a dose equal of greater than 1’800 mg. To maintain a constant volume in the infusion bag, a sterile syringe and needle should be used to remove the calculated volume equivalent to the amount of the reconstituted TEPEZZA solution to be placed into the infusion bag. Discard the volume of sodium chloride 9 mg/mL (0.9%) solution for infusion withdrawn.

Step 4: Withdraw the required volume from the reconstituted TEPEZZA vial(s) based on the patient’s weight (in kg) and transfer into an intravenous bag containing sodium chloride 9 mg/mL (0.9%) solution for infusion. Mix diluted solution by gentle inversion. Do not shake. If refrigerated prior to administration, allow the diluted solution to reach room temperature prior to infusion.

Care should be taken to ensure the sterility of the prepared solution.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Authorisation number

69795 (Swissmedic)

Packs

Each carton contains 1 vial. [A]

Marketing authorisation holder

Amgen Switzerland AG, Risch; Domicile: 6343 Rotkreuz

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