20 June 2024
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

Adzynma (rADAMTS13)
Treatment of thrombotic thrombocytopenic purpura
EU/3/08/588

Sponsor: Takeda Manufacturing Austria AG

Note

Assessment report as adopted by the COMP with all information of a commercially confidential nature deleted.

[1] Correction of active substance, 14 October 2025

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1. Product and administrative information

Product	
Designated active substance(s)	Recombinant human ADAMTS-13
Other name(s)	Apadamtase alfa and cinaxadamtase alfa
Common Name	rADAMTS13
Tradename	Adzynma
Orphan condition	Treatment of thrombotic thrombocytopenic purpura
Sponsor's details:	Takeda Manufacturing Austria AG Industriestrasse 67 Donaustadt 1221 Vienna Austria
Orphan medicinal product designation procedural history	
Sponsor/applicant	Baxter AG
COMP opinion	8 October 2008
EC decision	3 December 2008
EC registration number	EU/3/08/588
Post-designation procedural history	
Transfers of sponsorship	Transfer from Takeda Manufacturing Austria AG, Austria, to Baxalta Innovations GmbH, Austria – EC decision of 13 April 2016 Transfer from Baxalta Innovations GmbH, Austria, to Takeda Manufacturing Austria AG, Austria – EC decision of 23 February 2023
Marketing authorisation procedural history	
Rapporteur / Co-rapporteur	Daniela Philadelphy / Patrick Vrijlandt
Applicant	Takeda Manufacturing Austria AG
Application submission	17 April 2023
Procedure start	18 May 2023
Procedure number	EMA/H/C/006198
Invented name	Adzynma
Therapeutic indication	Adzynma is an enzyme replacement therapy (ERT) indicated for the treatment of ADAMTS13 deficiency in children and adult patients with congenital thrombotic thrombocytopenic purpura (cTTP). Adzynma can be used for all age groups. Further information on Adzynma can be found in the European public assessment report (EPAR) on the Agency's website ema.europa.eu/en/medicines/human/EPAR/adzynma
CHMP opinion	30 May 2024

COMP review of orphan medicinal product designation procedural history	
COMP rapporteur(s)	Elisabeth Johanne Rook / Karri Penttila
Sponsor's report submission	29 August 2023 and 15 January 2024
COMP discussion and adoption of list of questions	21-23 May 2024
Response to list of questions	5 June 2024
Oral explanation cancellation	18 June 2024
COMP opinion	20 June 2024

2. Grounds for the COMP opinion

The sponsor, Baxter AG, submitted on 18 July 2008 an application for designation of a medicinal product containing recombinant human ADAMTS-13 as an orphan medicinal product for treatment of thrombotic thrombocytopenic purpura.

Whereas, the Committee for Orphan Medicinal Products (COMP), having examined the application, concluded:

- thrombotic thrombocytopenic purpura (hereinafter referred to as "the condition") was estimated to be affecting approximately 2.2 in 10,000 persons in the Community, at the time the application was made;
- the condition is chronically debilitating and life threatening due to high mortality risk and acute complications;
- although satisfactory methods of treatment of the condition have been authorised in the Community, justifications have been provided that recombinant human ADAMTS-13 may be of significant benefit to those affected by the condition.

The COMP recommends the designation of this medicinal product, containing recombinant human ADAMTS-13, as an orphan medicinal product for the orphan indication: treatment of thrombotic thrombocytopenic purpura.

3. Review of criteria for orphan designation at the time of marketing authorisation

Article 3(1)(a) of Regulation (EC) No 141/2000

Intention to diagnose, prevent or treat a life-threatening or chronically debilitating condition affecting not more than five in 10 thousand people in the Community when the application is made

Condition

Thrombotic thrombocytopenic purpura (TTP) is a blood clotting disorder manifested by microvascular occlusions and consequent thrombocytopenia, haemolytic anaemia, and organ ischemia.

Two forms of TTP are recognized: congenital (cTTP) and the acquired immune-mediated form (iTTP). Congenital TTP is caused by deficiency of ADAMTS13 (A Disintegrin and Metalloproteinase with Thrombo-Spondin motifs 13), due to mutations of the ADAMTS13 gene. It is also called Upshaw-Schulman syndrome. The acquired immune-mediated form iTTP is caused by the formation of auto-

antibodies targeting the ADAMTS13 enzyme. While the immune-mediated form of TTP is rare, it is relatively more common than cTTP which comprises approximately 5 to 10% of all TTP cases (Alwan et al. 2019).

ADAMTS13 is a protease that normally controls activity of von Willebrand factor (VWF) by cleaving its multimers to smaller units, thereby reducing the platelet binding of VWF and formation of microthrombi. Decreased ADAMTS13 activity leads to an accumulation of ultra large (or unusually large) von Willebrand factor multimers which bind to platelets and induce aggregation. Infections, trauma, pregnancy and birth are triggers for acute TTP events and consistent with the two peaks in initial presentation of cTTP: in newborns/childhood and during pregnancy.

The approved therapeutic indication "Adzynma is indicated for the treatment of ADAMTS13 deficiency in children and adult patients with congenital thrombotic thrombocytopenic purpura (cTTP). Adzynma can be used for all age groups" falls within the scope of the designated orphan condition "Treatment of thrombotic thrombocytopenic purpura''.

Intention to diagnose, prevent or treat

The medical plausibility pending confirmation of a positive benefit risk assessment by the CHMP.

Chronically debilitating and/or life-threatening nature

At the time of initial designation, the COMP agreed that the condition was chronically debilitating and life-threatening. At the time of this review, TTP is presented to remain seriously debilitating and life-threatening disease with a mortality exceeding 90% without treatment of acute TTP episodes, (Alwan et al. 2019; Amorosi and Ultmann 1966; Kremer Hovinga et al. 2017; Scully et al. 2017b). This condition was noted to have extremely low survival rates until the 1990s, when therapeutic plasma exchange (TPE) was established as the standard of care, which improved survival of acute episodes from 10-20% up to 80-90% (Nuñez Zuno JA, Khaddour K. 2023).

The clinical presentation of TTP lies on a spectrum of severity ranging from single or incidental severe acute TTP episodes to chronic, recurring TTP manifestations (Oladapo et al. 2019; Scully et al. 2017b). The consistent markers of TTP remain severe thrombocytopenia (typically <30 × 109/L) and MAHA (microangiopathic haemolytic anaemia) often associated with corresponding symptoms (i.e., skin and mucosal hemorrhage, weakness, and dyspnea). Signs and symptoms of organ ischemia due to microthrombi formation are variable at presentation. Symptoms related to organ ischemia/infarction mostly concern the brain; more than 60% of patients have neurologic symptoms at presentation, with a broad range of manifestations from headache and confusion to stroke, coma, and seizures. Heart ischemia is present in a quarter of patients, ranging from isolated electrocardiographic abnormalities to myocardial infarction. Gastrointestinal ischemia is present in 35% of patients and can result in abdominal pain, nausea, and diarrhea. Renal injury is not uncommon in TTP, hematuria and proteinuria are the most commonly seen renal manifestations (Joly et al. 2017; Sukumar et al. 2021).

Due to the persistent severe ADAMTS13 deficiency, patients with cTTP are at constant risk for developing signs and/or symptoms associated with increased TTP disease activity, especially in the presence of triggering factors such as infections and pregnancy.

The COMP concluded that the condition remains life threatening and chronically debilitating due to the risk of severe neurological impairment, cardiac and renal manifestations.

Number of people affected or at risk

At the time of designation in 2008, the prevalence was agreed to be approximately 2.2 per 10,000.

A systematic literature review was conducted to synthesize the most recent estimates of prevalence and incidence of TTP and its subtypes in Europe. Based on 8 sources identified from January 2010 to May 2023, the sponsor considered the best available published evidence on the diagnosed prevalence of TTP to be 0.13 cases per 10,000 (Mariotte et al., 2016), while the incidence is estimated at 0.008 cases per 10,000 persons per year (Lannon et al., 2016).

The sponsor also estimated the prevalence of immune-TTP in Spain, using an incidence rate of 0.008 per 10,000 (Pascual-Izquierdo et al., 2021) and a disease duration of 60 years, as referenced in the Cablivi maintenance of OD report. This resulted in an estimated prevalence of 0.2 per 10,000.

The sponsor did not provide a specific point prevalence figure as a final estimate. Additional information on the methods and results of this review from the literature can be found in Table 1.

The sponsor also referenced the Orphanet website, which reports a prevalence estimate of 1/77,000 (0.12/10,000) for iTTP based on a French publication from 2016. This information supports the main calculation of prevalence.

Table 1. Summary of systemic review of incidence/prevalence of TTP in Europe

Reference	**Study design, period**	**Methodological quality**	**country**	**Prevalence (per million)**	**Incidence (per million)**
von Krogh, 2016	Retrospective cohort study, 1998 – 2015	good	N	cTTP: 16.7 cases in central Norway 3.1 in toral Norway	iTTP: 0.77 case per year
Mariotte, 2016	Cross-sectional 1999 – 2013	good	FR	TTP: 13	NR
Lannon, 2016	Retrospective cohort 2011 –2014	NA	UK	NR	TTP 0.8 per year
Joly, 2018	Retrospective cohort 2000-2027	good	FR	cTTP 0.86	NR
Miesbach, 2019	Retrospective cohort 2013-2017	good	DE	NR	iTTP 1.47 (95% CI: 1.28-1.57) per year
Pascual-Izquierdo, 2021	Cross-sectional 2015-2017	good	ES	iTTP 21.44 (95% CI: 19.10-23.73)	iTTP 2.67 (95% CI 1.90-3.45) per year
Mancini, 2022	Retrospective cohort 2014-2016	moderate	IT (Tuscany region)	NR	iTTP 0.73 (95% CI: 0.43-1.04 per year

DE=Germany, ES = Spain, FR= France, IT= Italy, N=Norway, NA = not assessable, conference presentation; NR= not reported, UK=United Kingdom,

The sponsor is asked to provide a final point estimate for the prevalence of thrombotic thrombocytopenic purpura in totality (congenital and acquired). Given the ten-fold differences from the original ODD application, the sponsor should also discuss the change in the prevalence estimate from the initial orphan designation to the marketing authorisation. See section 4 below in this report.

Article 3(1)(b) of Regulation (EC) No 141/2000

Existence of no satisfactory methods of diagnosis prevention or treatment of the condition in question, or, if such methods exist, the medicinal product will be of significant benefit to those affected by the condition.

Existing methods

Cablivi is indicated for the treatment of adults and adolescents of 12 years of age and older weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP), in conjunction with plasma exchange (PE) and immunosuppression. The COMP agreed with the sponsor that the therapeutic indication for Cablivi is different from the therapeutic indication for Adzynma for congenital TTP, which is not covered by the indication for Cablivi; therefore, Cablivi is not considered as satisfactory method in the context of establishing the Significant Benefit for Adzynma.

OctaplasLG/octaplas is approved in the EU for therapeutic PE procedures, including those in thrombotic thrombocytopenic purpura (TTP). The sponsor claimed that in clinical practice, however, cTTP patients do not routinely undergo therapeutic PE. Therefore, treatment with octaplasLG/octaplas in the cTTP setting is not generally in accordance with its approved indication. The COMP considers that based on the approved indication, OctaplasLG is considered as satisfactory method therefore the sponsor should justify the significant benefit of OctaplusLG versus Adzynma in more detail.

Factor VIII:VWF concentrates are authorised products for the treatment of Haemophilia A and von Willebrand Disease and are used off-label for prophylaxis or acute on-demand treatment of TTP episodes. Therefore, these are not considered satisfactory methods in the context of establishing significant benefit.

According to the ISTH (International Society on Thrombosis and Haemostasis) guideline for the treatment of thrombotic thrombocytopenic purpura (2020), PE is the mainstay therapy in acute events (Zheng XL et al., J Thromb Haemost. 2020 Oct;18(10):2496-2502). The guideline suggests either plasma infusion or a watch and wait strategy when a patient with cITP is in remission. For patients with cTTP who are pregnant, the guideline recommends prophylactic treatment with plasma infusion. According to this guideline, the use of Factor VIII:VWF concentrates is no longer recommended due to the lack of evidence from the literature regarding its benefits or harms in the treatment of TTP.

PE removes ultra-large (or unusually large) von Willebrand factor and also replenishes blood levels of ADANTS13. PE has reduced mortality rates of acute episodes from over 90% to 10–20% and a delay in initiation of PE leads to preventable early mortality. Hence, the COMP considered that PE exchange remains a satisfactory method and a demonstration of significant benefit needs to be provided.

In the prophylaxis setting, current standard of care (SoC) treatment of cTTP consist of plasma-based therapies, including FFP (fresh frozen plasma), and SDTP (solvent/detergent treated plasma). Plasma replacement therapy may reduce the frequency and severity of cTTP events (Fujimura et al. 2009; Furlan et al. 1997 Borogovac 2022), and are therefore considered as satisfactory methods.

Significant benefit

The sponsor claimed significant benefit based on improved efficacy and safety.

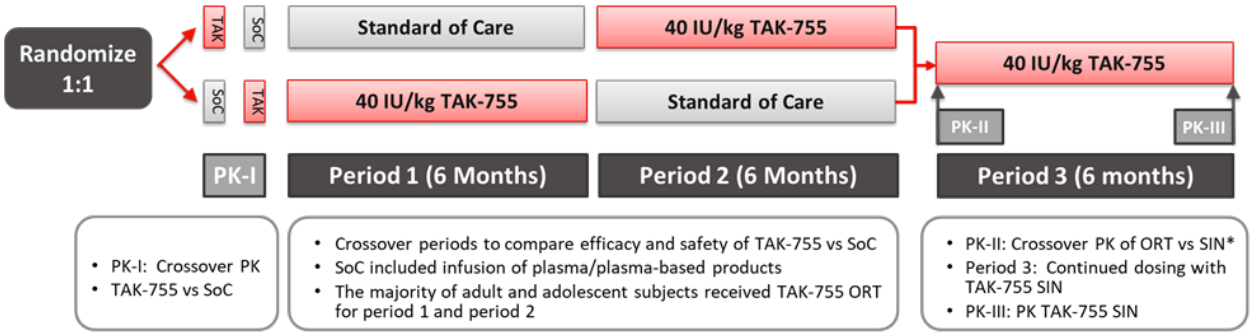
Significant benefit versus plasma based therapies

The clinical efficacy and safety of Adzynma (rADAMTS13) were assessed in two ongoing trials (Study 281102 and Study 3002).

Study 281102 was a global phase 3, prospective, randomized, controlled, open-label, multicentre, two period crossover study, followed by a single arm continuation treatment period. The aim of this pivotal study was evaluating the efficacy and safety of the prophylactic and on demand enzyme replacement therapy (ERT) with Adzynma, compared to plasma-based therapies in patients with severe cTTP (defined as ADAMTS13 activity < 10%).

The study included 46 patients in the prophylaxis cohort who were randomized to receive 6 months of prophylactic treatment with either 40 IU/kg (± 4 IU/kg) of Adzynma (TAK-755) or plasma-based therapies (Period 1) once weekly (for patients who were previously treated with plasma-based therapies once weekly prior to joining the study) or every other week. Patients were then crossed over to the other treatment for 6 months (Period 2). The plasma-based therapy was individually established based on Investigator's choice. After Periods 1 and 2, all patients entered a 6-month single arm treatment period with Adzynma (Period 3). See figure 1 below.

Figure 1. Schedule of the pivotal randomised trial Study 281102



At randomisation the mean (SD) age was 30.5 (16.0) years (range: 3 to 58 years). Of the 46 patients, 4 (8.7%) were < 6 years of age, 4 (8.7%) were ≥ 6 to < 12 years of age, 4 (8.7%) were ≥ 12 to < 18 years of age, and 34 (73.9%) were ≥ 18 years of age. Prior to joining the study, the majority (69.6%) of patients received fresh frozen plasma (FFP) treatment as standard of care (SoC), 21.7% received solvent/detergent (SDTP) plasma, and 6.5% received FVIII- von Willebrand factor (FVIII-VWF) concentrate.

The efficacy of prophylactic treatment with Adzynma in patients with cTTP was evaluated based on the incidence of acute TTP events. This primary endpoint was defined by a drop in platelet count (≥ 50% of baseline or a platelet count < 100 000/µL) and an elevation of lactate dehydrogenase (LDH) (> 2× baseline or > 2×upper limit normal (ULN).

The following endpoints were secondary or exploratory: subacute TTP events as defined by a thrombocytopenia event or a microangiopathic haemolytic anaemia event; organ specific signs and symptoms including but not limited to renal dysfunction events, neurological symptoms events, fever, fatigue/lethargy, and/or abdominal pain, and TTP manifestations such as thrombocytopenia,

microangiopathic haemolytic anaemia, neurological symptoms, renal dysfunction, and abdominal pain; as well as the incidence of supplemental doses prompted by subacute TTP events.

No acute TTP events occurred while subjects received rADAMTS13 prophylaxis, and 1 acute TTP event occurred in 1 subject while receiving SoC prophylaxis. Due to the low occurrence of acute TTP events during the trial, it could not be established whether the primary endpoint was met.

Subacute manifestations were numerically more frequently reported for the control treatments, than for Adzynma (5 versus 1 subject in the randomised study phase).

Treatment with rADAMTS13 prophylaxis in the controlled study periods resulted in generally lower annualized event rates of TTP events and manifestations compared to SoC prophylaxis, except for the renal dysfunction events. See Table 2 below.

Subgroup analyses based on different controls of plasma-based therapies (i.e. SDTP, FPP and FVIII-VWF), showed similar trends of efficacy as observed for the total study population. The Sponsor claims that similar trends of efficacy were observed in subjects receiving the approved product, OctaplasLG, but details were not reported.

The efficacy of the on demand or acute enzyme replacement therapy was evaluated based on the proportion of acute TTP events responding to Adzynma in both the prophylactic and the on-demand cohorts throughout the duration of the study.

An acute TTP event responding to Adzynma was defined as a resolved TTP event when platelet count was ≥ 150 000/µL or platelet count was within 25% of baseline, whichever occurs first, and LDH ≤ 1.5 x baseline or ≤ 1.5 x ULN, without requiring the use of another ADAMTS13-containing agent.

The on-demand cohort included 5 adult patients (≥ 18 years of age) and 1 paediatric patient (< 6 years of age). Patients enrolled in this cohort had a total of 7 acute TTP events. Of these 6 patients, 2 patients were randomized to receive on demand treatment with Adzynma and 4 patients were randomized to receive plasma-based therapies. All 7 acute TTP events resolved after treatment with either Adzynma or plasma-based therapies within five days.

Table 2. Prophylactic cohort efficacy results in cTTP patients (pooled data from periods 1 and 2)

	ADZYNMA **N = 45**	**Plasma-Based Therapies** **N = 46**
Acute TTP events		
Number of subjects with event (number of events)	0 (0)	1 (1)
Subacute TTP events		
Number of subjects with event (number of events)	1 (1)	6 (7)
Number of subjects receiving a supplemental dose prompted by a subacute event	0	4
Number of supplemental doses prompted by a subacute event	0	9
TTP manifestations		
Thrombocytopenia events[a]		
Number of subjects with event	13	23

	ADZYNMA **N = 45**	**Plasma-Based Therapies** **N = 46**
(number of events)	(49)	(91)
Model based annualized event rate,[b] LSM (SE)	0.92 (0.262)	1.72 (0.457)
Microangiopathic haemolytic anaemia events[c]		
Number of subjects with event (number of events)	8 (23)	12 (32)
Model based annualized event rate,[b] LSM (SE)	0.37 (0.136)	0.59 (0.194)
Neurological symptoms events[d]		
Number of subjects with event (number of events)	4 (18)	7 (29)
Model based annualized event rate,[b] LSM (SE)	0.13 (0.068)	0.23 (0.109)
Renal dysfunction events[e]		
Number of subjects with event (number of events)	5 (11)	2 (5)
Model based annualized event rate,[b] LSM (SE)	0.17 (0.090)	0.08 (0.052)
Abdominal pain events		
Number of subjects with event (number of events)	2 (4)	6 (8)
Model based annualized event rate,[b] LSM (SE)	0.09 (0.055)	0.17 (0.086)

LSM = least squares mean; SE = standard error; TTP = thrombotic thrombocytopenic purpura.
[a] Drop in platelet count ≥ 25% of baseline or a platelet count < 150 x 10^9/L.
[b] From a negative binominal mixed-effects model.
[c] Elevation of LDH > 1.5 × baseline or > 1.5 x ULN.
[d] Nervous system disorders (e.g., headache, confusion, memory issues, irritability, paraesthesia, dysarthria, dysphonia, visual disturbances, focal or general motor symptoms including seizures).
[e] An increase in serum creatinine > 1.5 × baseline.

Regarding the safety claim, the sponsor argued that plasma products carry the risk of transfusion-transmitted infections and central venous catheter thrombosis, which is unlikely for Adzynma. Adzynma may exhibit less hypersensitivity reactions than plasma-based therapies. Prior to plasma infusions, multiple prophylactic medications like steroids and antihistamines are routinely required which have their own associated adverse effects (Zheng et al. 2020). Patients have in particular described intense irritability and emotional distress from glucocorticoids.

In the pivotal trial, the incidence rate of adverse events (AEs) was significantly lower for TAK-755 than for the SoC (incidence rates 19 versus 133 per 100 patients' years). None of the serious AEs under TAK-755 treatment was considered to be treatment related.

The sponsor also claimed a major contribution to patient care (MCPC). Adzynma (IV home-administration) provides a significant decrease in infusion volume and duration compared to current therapies. The use of Adzynma reduces the burden of extensive inpatient hospital time associated with current plasma-based intravenous infusions. A large volume of plasma (often 10 to 15 ml/kg) is required to achieve the Adzynma replacement with plasma, and long infusions times (2-4 hours).

COMP discussion

The COMP concluded that the significant benefit over plasma-based therapies could be agreed based on totality of evidence for efficacy advantage, based on the strong pharmacological rationale,

supported by the pharmacodynamic and clinical outcomes from several secondary endpoints (thrombocytopenia and MAHA).

Regarding the arguments for the improved safety and the MCPC, the COMP concluded that the data are too limited regarding the number of patients and study duration, to justify the significant benefit.

Significant benefit versus OctaplasLG

The sponsor should discuss in more detail the significant benefit versus OctaplasLG which is authorised in several EU member states.

Comments on sponsor's responses to the COMP list of issues

In the written response, the sponsor presented their responses to the COMP's list of questions: The sponsor should propose one final figure estimate for the prevalence. The sponsor should further discuss the change in the prevalence estimate from the designation to the marketing authorisation. The sponsor should discuss in more detail the significant benefit versus OctaplasLG which is authorised in several EU member states.

For the question on the prevalence the sponsor explained that the differences from the initial estimates in 2008 arise from newer data sources and improved epidemiological understanding. The sponsor proposed a figure of 0.13 per 10,000 persons as the final estimate, aligning with Mariotte et al. 2016, based on a French National database for thrombotic microangiopathy. The sponsor considers that this reference represents the best available direct measure of diagnosed prevalence of TTP. The sponsor explained that the high estimate of the prevalence at the time of the original orphan designation in 2008, was due to limited sources available in the literature, and that the estimate was mainly driven by one outlier value stemming from a publication with data from Oklahoma, USA (Terrell et al., 2005). However, when the current stricter definition of ADAMTS13 deficiency, defined as <5% ADAMTS13 activity, is applied in the Terrel et al (2005) reference, the prevalence would be more in line with the figure extracted from the French National database (0.35/10,000 and 0.13/10,000 respectively).

Regarding the significant benefit, the sponsor claimed that in the pivotal Study 281102, plasma therapies like FFP/SDTP (Investigator's' choice) were used as active controls. Out of a total of 48 subjects, 33 received exclusively FFP and 12 received SDTP, including OctaplasLG, as their plasma-based therapy for the SoC sequence. It was not possible to confirm the exact proportion of OctaplasLG users among the SDTP treated patients, though it is understood that a number of the study sites use OctaplasLG as their SDTP. The Sponsor claimed that the treatment effects of OctaplasLG could be extrapolated from the total group of subjects that received SDTP and/or FFP as active control in the pivotal trial, based on similar ADAMTS13 content and enzyme activity among the used SDTP/FFP products.

Data provided by the manufacturer of OctaplasLG state that the ADAMTS13 contents of OctaplasLG and FFP are similar. The reported values for mean (range) ADAMTS13 content are 0.91 IU/ml (0.75 – 1.30) for OctaplasLG vs. 1.24 IU/ml (1.07 – 1.44) for FFP. Therefore, OctaplasLG and FFP have generally similar ADAMTS13 content, with a trend towards lower ADAMTS13 content in OctaplasLG. The ADAMTS13 content measured in FFP and SDTP study bags prior to administration were generally similar in Study 281102, yielding a median administered dose of approximately 11 IU/kg. In comparison, Adzynma consistently delivered 40 IU/kg rADAMTS13 per dose (Scully et al., 2024). Furthermore, in Study 281102, PK-PD-data demonstrated that the plasma ADAMTS13 activity was approximately 5-fold higher, with lower variability, for Adzynma compared to either SDTP or FFP therapies.

COMP discussions

The COMP agreed with the figure proposed by the sponsor, however chose to use the figure 0.3 per 10,000 persons, taking into consideration the reported incidence rates from other literature references from Europe that were provided in the systemic review of the sponsor (2010-2023, see Table 1 above). When taking into consideration a conservative disease duration of 60 years for cTTP, and a 40-year disease duration for the iTTP (which is mainly diagnosed in patients in their forties or fifties), and assuming that 90% of all TTP cases consist of iTTP and 10% of cTTP, the point prevalence of TTP was estimated to be approximately 0.3/10,000 in the European Union.

Furthermore the claim of significant benefit based on a clinically relevant advantage for Adzynma over the plasma-based therapies can be considered established based on the data provided.

COMP conclusions

The COMP concluded that the data presented are considered sufficient to support maintenance of the orphan designation of Adzynma for the treatment of ADAMTS13 deficiency in children and adult patients with congenital thrombotic thrombocytopenic purpura and cancelled the oral explanation.

4. COMP position adopted on date

The COMP concluded that:

- the proposed therapeutic indication falls entirely within the scope of the orphan condition of the designated Orphan Medicinal Product.
- the prevalence of thrombotic thrombocytopenic purpura (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be 0.3 in 10,000 persons in the European Union, at the time of the review of the designation criteria;
- the condition is life threatening and chronically debilitating due to the risk of thrombocytopenia and microangiopathic haemolytic anaemia, and ischaemic organ damage with neurological, cardiac and renal manifestations;
- although satisfactory methods for the treatment of the condition have been authorised in the European Union, the claim that Adzynma is of significant benefit to those affected by the orphan condition is established. The sponsor provided clinical data which showed a reduction of thrombocytopenia and indicated a lower incidence of acute thrombotic thrombocytopenic purpura events compared to plasma-based therapies.

The COMP, having considered the information submitted by the sponsor and on the basis of Article 5(12)(b) of Regulation (EC) No 141/2000, is of the opinion that:

- the criteria for designation as set out in the first paragraph of Article 3(1)(a) are satisfied;
- the criteria for designation as set out in Article 3(1)(b) are satisfied.

The Committee for Orphan Medicinal Products has recommended that Adzynma, recombinant human ADAMTS-13, rADAMTS13 for treatment of thrombotic thrombocytopenic purpura (EU/3/08/588) is not removed from the Community Register of Orphan Medicinal Products.