24 June 2021
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

Enspryng (satralizumab, humanised anti-IL-6 receptor monoclonal antibody)
Treatment of neuromyelitis optica spectrum disorders
EU/3/16/1680

Sponsor: Roche Registration GmbH

Note

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

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1. Product and administrative information

Product	
Active substances(s) at the time of orphan designation	Humanised anti-IL-6 receptor monoclonal antibody
Other name(s)	-
International Non-Proprietary Name	Satralizumab
Tradename	-
Orphan condition	Treatment of neuromyelitis optica spectrum disorders
Sponsor's details:	Roche Registration GmbH Emil-Barell-Strasse 1 Grenzach 79639 Grenzach-Wyhlen Baden-Wuerttemberg Germany
Orphan medicinal product designation procedural history	
Sponsor/applicant	Chugai Pharma Europe Ltd
COMP opinion date	19 May 2016
EC decision date	27 June 2016
EC registration number	EU/3/16/1680
Post-designation procedural history	
Transfer of sponsorship	- Transfer from Chugai Pharma Europe Ltd to Chugai Pharma France – EC decision of 11 January 2019 - 2nd Transfer from Chugai Pharma France to Roche Registration GmbH – EC decision of 14 August 2019
Marketing authorisation procedural history	
Rapporteur / Co-rapporteur	K. Dunder / M. C. Prieto Yerro
Applicant	Roche Registration GmbH
Application submission date	20 August 2019
Procedure start date	12 September 2019
Procedure number	EMA/H/C/004788
Invented name	Enspryng
Approved therapeutic indication	Enspryng is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive. Further information on Enspryng can be found in the European public assessment report (EPAR) on the Agency's website https://www.ema.europa.eu/en/medicines/human/EPAR/Enspryng
CHMP opinion date	22 April 2021
COMP review of orphan medicinal product designation procedural history	
COMP rapporteur(s)	T. Leest / A. Magrelli
Sponsor's report submission date	29 November 2019

COMP discussion	13-15 April 2021
COMP opinion date (via written procedure)	26 April 2021

2. Grounds for the COMP opinion

Orphan medicinal product designation

The COMP opinion that was the basis for the initial orphan medicinal product in 2016 designation was based on the following grounds:

The sponsor Chugai Pharma Europe Ltd submitted on 29 January 2016 an application for designation as an orphan medicinal product to the European Medicines Agency for a medicinal product containing humanised anti-IL-6 receptor monoclonal antibody for treatment of neuromyelitis optica. The application was submitted on the basis of Article 3(1)(a) first paragraph of Regulation (EC) No 141/2000 on orphan medicinal products.

For the purpose of orphan designation, the Committee for Orphan Medicinal Products (COMP) considered that the condition originally proposed by the sponsor should be renamed as "neuromyelitis optica spectrum disorders" (hereinafter referred to as "the condition") based on the International Panel for Neuromyelitis Optica Diagnosis (Neurology 2015; 85:1-13).

Having examined the application, the COMP considered that the sponsor has established the following:

- the intention to treat the condition with the medicinal product containing humanised anti-IL-6 receptor monoclonal antibody was considered justified based on the reduction of plasmablast population in cells isolated from patients affected by the condition, in combination with clinical data with a comparable antibody, which improved the annualised relapse rate and the Expanded Disability Status Scale score in patients affected by the condition;
- the condition is chronically debilitating and life-threatening due to neurological impairment such as paraplegia, sensory loss, bladder dysfunction, peripheral pain, and increased 5-year mortality;
- the condition was estimated to be affecting approximately 0.4 in 10,000 persons in the European Union, at the time the application was made.

Thus, the requirements under Article 3(1)(a) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled.

The sponsor has also established that there exists no satisfactory method of treatment that has been authorised in the European Union for patients affected by the condition.

Thus, the requirement under Article 3(1)(b) of Regulation (EC) No 141/2000 on orphan medicinal products is fulfilled.

The COMP concludes that the requirements laid down in Article (3)(1) (a) and (b) of Regulation (EC) No 141/2000 on orphan medicinal products are fulfilled. The COMP therefore recommends the designation of this medicinal product, containing humanised anti-IL-6 receptor monoclonal antibody as an orphan medicinal product for the orphan indication: treatment of neuromyelitis optica spectrum disorders.

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

The proposed condition represents a group of severe autoimmune inflammatory demyelinating disorders that are typically characterized by optic neuritis and transverse myelitis. The 2015 consensus defines describes 5 core clinical characteristics: optic neuritis, acute myelitis, postrema syndrome, narcolepsy or acute diencephalic clinical syndrome with typical MRI findings, symptomatic cerebral syndrome with MRI findings. In general, at least 2 core characteristics (for the NMOSD without autoantibodies) or 1 core characteristic and presence of autoantibodies are required (Wingerchuk, Neurology 2015; 85:1-13).

The proposed therapeutic indication "Enspryng is indicated as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years of age who are anti-aquaporin-4 IgG (AQP4-IgG) seropositive" falls entirely within the scope of the designated orphan condition "treatment of neuromyelitis optica spectrum disorders".

Intention to diagnose, prevent or treat

The medical plausibility was considered justified on the basis of the positive benefit/risk assessment of the CHMP.

Chronically debilitating and/or life-threatening nature

The COMP has previously noted that the condition is chronically debilitating due to neurological impairment such as paraplegia, sensory loss, bladder dysfunction, and central visual loss accompanied by ocular pain and life-threatening with the 5-year mortality reported as high as 30%. The sponsor has not noted any changes in the seriousness of the disease since designation. The seriousness of NMOSD is acknowledged.

Number of people affected or at risk

The sponsor conducted a literature review and identified three European studies, which they use supported by several non-EU reference publications.

The three European studies were the following:

- Bizzoco et al (2009) reviewed 850 patients diagnosed with demyelinating disorders in north east Tuscany between 1998 and 2006 using current diagnostic techniques. This paper does not give a population-based prevalence but the "prevalence" of NMOSD amongst this group of patients was 1.5%, of which 56% had NMO.
- Asgari et al (2011) reviewed 477 patients with multiple sclerosis (MS), acute transverse myelitis (TM) or optic neuritis (ON) diagnosed between 1998 and 2008 in southern Denmark according to

contemporary diagnostic criteria. They identified a total of 42 NMO/NMOSD patients (36 NMO, 6 NMOSD, 62% of whom were anti-AQP4 antibody positive) and calculated a population-based prevalence estimate of 0.44 per 10,000 individuals.

- Cossburn et al (2012) surveyed medical records of 717,572 patients from south Wales and identified 14 cases of NMO/NMOSD (11 NMO, 3 NMOSD) using contemporary diagnostic criteria, giving a population-based prevalence estimate of 0.196 per 10,000 patients.

Further studies referring to extra-European populations were also reviewed but are not going to be further commented herein. Previously the COMP considered the population-based retrospective case series study referred above, in a Caucasian population in the Region of Southern Denmark, as a conservative estimate (Asgari et al, 2011 0.44/10,000).

An approximately 0.4 conclusion was considered acceptable for the time of the review.

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.

There is one product that has been identified as authorised in the treatment of the proposed orphan condition. In particular, Soliris is indicated (among others) in adults for the treatment of "Neuromyelitis optica spectrum disorder (NMOSD) in patients who are anti-aquaporin-4 (AQP4) antibody-positive with a relapsing course of the disease".

For the purpose of establishing whether this product is relevant for the significant benefit exercise, the therapeutic indication of Enspryng was juxtaposed to the one of Soliris. Enspryng is indicated, as discussed above: "as a monotherapy or in combination with immunosuppressive therapy (IST) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adult and adolescent patients from 12 years who are antiaquaporin 4 (AQP4) seropositive".

Having regard to the two indications, the COMP noted that whereas Soliris is indeed authorised in NMOSD, no authorised products exist for the entirety of the population for which Enspryng is indicated. In particular, no authorised products exist for the adolescent AQP4 positive patients and for AQP4 positive patients without a prior relapsing course of the disease. The authorised indication of Enspryng is thus broader than the indication of Soliris, as it includes additional patient populations for whom Soliris is not authorised.

The COMP concluded that Soliris would not be qualified as a satisfactory treatment for the purpose of the examination of the significant benefit of Enspryng, as Soliris does not cover the entire patient population for which Enspryng is intended.

4. COMP list of issues

Not applicable.

5. COMP position adopted on 26 April 2021

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 neuromyelitis optica spectrum disorders (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be 0.4 in 10,000 persons in the European Union, at the time of the review of the orphan designation criteria;
- the condition is chronically debilitating due to neurological impairment such as paraplegia, sensory loss, bladder dysfunction, and central visual loss accompanied by ocular pain and life-threatening with the 5-year mortality reported as high as 30%;
- at present no satisfactory method has been authorised in the European Union for the treatment of the entirety of patients covered by the therapeutic indication of Enspryng.

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 Enspryng, satralizumab, humanised anti-IL-6 receptor monoclonal antibody for treatment of neuromyelitis optica spectrum disorders (EU/3/16/1680) is not removed from the Community Register of Orphan Medicinal Products.