25 July 2025
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Committee for Orphan Medicinal Products

Orphan Maintenance Assessment Report

of an orphan medicinal product submitted for marketing authorisation application

Romvimza (vimseltinib)
Treatment of tenosynovial giant cell tumour, localised and diffuse type
EU/3/19/2227

Sponsor: Deciphera Pharmaceuticals (Netherlands) B.V.

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	
Designated active substance(s)	2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one
Other name(s)	Romvimza
International Non-Proprietary Name	Vimseltinib
Tradename	-
Orphan condition	Treatment of tenosynovial giant cell tumour, localised and diffuse type
Sponsor's details:	Deciphera Pharmaceuticals (Netherlands) B.V. Atrium Building Floor 4th Strawinskylaan 3051 1077 ZX Amsterdam Noord-Holland Netherlands
Orphan medicinal product designation procedural history	
Sponsor/applicant	Pharma Gateway AB
COMP opinion	7 November 2019
EC decision	16 December 2019
EC registration number	EU/3/19/2227
Post-designation procedural history	
Transfer of sponsorship	Transfer from Pharma Gateway AB to Deciphera Pharmaceuticals (Netherlands) B.V. – EC decision of 3 July 2020
Marketing authorisation procedural history	
Rapporteur / Co-rapporteur	Martin Mengel / Jean-Michel Race
Applicant	Deciphera Pharmaceuticals (Netherlands) B.V.
Application submission	29 June 2024
Procedure start	18 July 2024
Procedure number	EMA/H/C/006363
Invented name	Romvimza
Therapeutic indication	Romvimza is indicated for treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT) associated with clinically relevant physical function deterioration and in whom surgical options have been exhausted or would induce unacceptable morbidity or disability. Further information on Romvimza can be found in the European public assessment report (EPAR) on the Agency's website https://www.ema.europa.eu/en/medicines/human/EPAR/romvimza
CHMP opinion	24 July 2025

COMP review of orphan medicinal product designation procedural history	
COMP rapporteur(s)	Frauke Naumann-Winter / Evangelia Giannaki
Sponsor's report submission	24 February 2025
COMP discussion	10-12 June 2025
COMP opinion (adoption via written procedure)	25 July 2025

2. Grounds for the COMP opinion

The COMP opinion that was the basis for the initial orphan medicinal product in designation in 2019 was based on the following grounds:

The sponsor Pharma Gateway AB submitted on 22 August 2019 an application for designation as an orphan medicinal product to the European Medicines Agency for a medicinal product containing 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one for treatment of tenosynovial giant cell tumour, localised and diffuse type (hereinafter referred to as "the condition"). The application was submitted on the basis of Article 3(1)(a) first paragraph of Regulation (EC) No 141/2000 on orphan medicinal products.

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 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one was considered justified based on preliminary clinical data showing a reduction in tumour volume leading to improvement in joint mobility;
- the condition is chronically debilitating due to loss of function of the affected joints and the development of secondary arthritis;
- the condition was estimated to be affecting approximately 3 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 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 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one as an orphan medicinal product for the orphan condition: treatment of tenosynovial giant cell tumour, localised and diffuse type.

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

Tenosynovial Giant Cell Tumour (TGCT), also known in the literature as Pigmented Villonodular Synovitis (PVNS), is a neoplastic process affecting the synovial joints, tendon sheaths, and bursa membranes.

Both diffuse and localized types of the disease exist: the localized form is characterized by discrete nodular or pedunculated lesions and shows a very low recurrence rate, while the diffuse form shows involvement of the intra-articular soft tissue lining. The more common diffuse form recurs frequently and may result in a chronic disease, hampering normal function of the affected joint (Verspoor 2013). For localized TGCT, recurrences occur in 8–20% of patients and are managed by re-excision. Diffuse-type TGCT tends to recur more often (33–50%) and has a much more aggressive clinical course (Ravi 2011). Microscopically, the two forms are indistinguishable.

While TGCT can be present at all ages, it most typically affects young adults. These tumours are driven by the overexpression of colony stimulating factor-1 (CSF1). CSF1 is expressed by a minority of tumour cells, which, in turn attract non-neoplastic inflammatory cells that express CSF1 receptor (CSF1R) through a paracrine effect. It is usually caused by a chromosomal translocation involving CSF1. CSF1R activation leads to the recruitment of CSF1R-expressing cells of the mononuclear phagocyte lineage that constitute the tumour mass.

The approved therapeutic indication "ROMVIMZA is indicated for treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT) associated with clinically relevant physical function deterioration and in whom surgical options have been exhausted or would induce unacceptable morbidity or disability."

Intention to diagnose, prevent or treat

The medical plausibility has not yet been confirmed by the positive benefit/risk assessment of the CHMP, see EPAR.

Chronically debilitating and/or life-threatening nature

Despite the non-life-threatening character of TGCT, patients are often severely affected due to the long course of the disease. Currently, surgery remains the treatment of choice. Localized TGCT is managed by marginal excision. Recurrences occur in 8–20% of patients and are managed by re-excision. Diffuse Type TGCT tends to recur more often (33–50%) and has a much more aggressive clinical course. Patients are often symptomatic and require multiple surgical procedures during their lifetime. Multiple surgeries (occasional amputation) lead to advanced or relapsed TGCT with perioperative morbidity and secondary arthritis.

Number of people affected or at risk

The sponsor has referred to their initial prevalence from 2019 and indicated that at the time the estimate proposed was 3 in 10,000. At the time they conducted a literature search.

A similar search that was conducted on 11 October 2024 with restriction of publication year to 2019 or later.

Only one new publication with relevance for TGCT prevalence was identified. This publication (in German language only) analysed data from 7,595 arthritis patients included in the arthritis register maintained by the German Society for Rheumatology and Clinical Immunology. Of these patients, 45 were diagnosed with localized TGCT, equivalent to 0.6% of all cases in the registry. As the registry might not include all cases in Germany, the prevalence in the entire population cannot be determined (Liebisch et al, 2024).

The sponsor proposes that the prevalence continues to be 3 in 10,000. The estimate aims at compromising the very different possible disease course of localized and diffuse types of TGCT and focusses on active and recurrent disease. The COMP accepted this prevalence estimate.

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

In the absence of detailed treatment guidelines from EMSO or NCCN, an international consensus meeting was held involving international multidisciplinary sarcoma experts in collaboration with patient representatives in order to define best clinical practice and to generate treatment recommendations (Stacchiotti et al. 2023).

To date, surgical resection is the treatment of choice for both subtypes but can be associated with high recurrence rates and multiple additional surgeries, in particular for diffuse-type TGCT. It is challenging to balance the effects of increased morbidity of multiple or invasive surgeries, alternative therapeutic options, and daily symptoms of the tumour. A more aggressive resection or other multimodality treatments might adversely affect joint function, quality of life, and development of osteoarthrosis. These adverse consequences would justify a less invasive approach, using systemic therapy, provided the therapies are associated with tumour shrinkage and, most importantly, symptomatic improvements.

There are no authorised medicines in Europe for the condition. Clinically, TGCTs can have a range of behaviours, from favourable to locally aggressive, and can consequently have a major effect on daily life.

In the past decade, targeted therapy has been added to the armamentarium. Non-selective colony stimulating factor-1 (CSF-1) inhibitor therapies with nilotinib or imatinib have been used off-label, and newer, more potent selective CSF-1 inhibitors such as emactuzumab, and cabiralizumab were or are under investigation (Stacchiotti et al 2023).

Significant benefit

Not applicable.

4. COMP position adopted on 25 July 2025

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 tenosynovial giant cell tumour, localised and diffuse type (hereinafter referred to as "the condition") was estimated to remain below 5 in 10,000 and was concluded to be 3 in 10,000 persons in the European Union, at the time of the review of the designation criteria;
- the condition can be chronically debilitating due to impaired function of affected joints, either due to local destruction by the disease or by repeated surgery and may be associated with pain and stiffness.
- 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 Romvimza.

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 Romvimza, 2-(isopropylamino)-3-methyl-5-(6-methyl-5-((2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yl)oxy)pyridin-2-yl)pyrimidin-4(3H)-one, vimseltinib for treatment of tenosynovial giant cell tumour, localised and diffuse type (EU/3/19/2227) is not removed from the Community Register of Orphan Medicinal Products.