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Advice document
SMC2728

crovalimab solution for injection/infusion (Piasky®)

Roche Products Limited

06 December 2024

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

crovalimab (Piasky®) is accepted for restricted use within NHSScotland.

Indication under review: as monotherapy for the treatment of adult and paediatric patients 12 years of age or older with a weight of 40 kg and above with paroxysmal nocturnal haemoglobinuria (PNH):

- In patients with haemolysis with clinical symptom(s) indicative of high disease activity.
- In patients who are clinically stable after having been treated with a complement component 5 (C5) inhibitor for at least the past 6 months.

SMC restriction: under the advice of the national PNH service

Crovalimab offers an additional treatment choice in the therapeutic class of complement C5 inhibitors.

Another complement C5 inhibitor was accepted for restricted use under the orphan equivalent process.

This advice applies only in the context of approved NHSScotland Patient Access Scheme (PAS) arrangements delivering the cost-effectiveness results upon which the decision was based, or PAS/ list prices that are equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Crovalimab (Piasky®)[1] is a recombinant humanised immunoglobulin G1 (IgG1)-based monoclonal antibody that specifically binds with high affinity to component 5 (C5) of the complement system, causing terminal complement activity inhibition. In patients with PNH, crovalimab inhibits terminal complement-mediated intravascular haemolysis. Crovalimab is administered by subcutaneous injection after an initial intravenous infusion, according to two weight-based dosing bands (≥ 40 kg to < 100 kg and ≥ 100kg). Patients receive loading doses on days 1, 2, 8, 15 and 22 followed by maintenance dosing every four weeks. Please refer to the Summary of Product Characteristics for full dosing information.[1]

1.2. Relevant comparator(s)

Ravulizumab (Ultomiris®)[2, 3] and eculizumab are recombinant monoclonal antibodies that inhibit terminal complement activation at the C5 protein, thereby reducing haemolysis and thrombotic microangiopathy. Following initial loading dosing, ravulizumab is administered every eight weeks by intravenous administration. Eculizumab is given every two weeks by intravenous administration (following initial loading dosing). Ravulizumab was accepted for restricted use by SMC (SMC2305).[3] Eculizumab (Soliris®)[4, 5] was not recommended by SMC (SMC1130/16).

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

The COMMODORE II study[6] is a phase III, multicentre, randomised study comparing crovalimab with eculizumab. Adult complement inhibitor-naïve patients (n=204) with PNH and weighing ≥ 40 kg were randomised in a 2:1 ratio to receive crovalimab (n=135) or eculizumab (n=69). The study demonstrated non-inferiority of crovalimab to eculizumab for the co-primary outcomes of proportion of patients with haemolysis control from week five to week 25 (79.3% versus 79.0%; odds ratio, 1.0 [95% confidence interval [CI]: 0.6 to 1.8]) and the proportion of patients achieving transfusion avoidance from baseline to week 25 (65.7% versus 68.1%; difference - 2.8 [95% CI:-15.7, 11.1]). Additionally, crovalimab was non-inferior to eculizumab for secondary outcomes of breakthrough haemolysis and haemoglobin stabilisation.

The COMMODORE I study[7] is an ongoing, multicentre, randomised study of crovalimab versus eculizumab in adult patients with PNH weighing ≥ 40 kg who had received eculizumab for at least a 24-weeks prior. Patients were randomised to crovalimab (n=45) or to continue eculizumab (n=44). The primary outcome was to evaluate the safety and tolerability of crovalimab with efficacy as an exploratory outcome. The safety profile of crovalimab was consistent with other complement C5 inhibitors with the exception of the formation of immune complexes which vary in their formation due to C5 inhibitors binding to different C5 epitopes. Exploratory efficacy outcomes comparing crovalimab and eculizumab included haemolysis control, transfusion avoidance, breakthrough haemolysis and haemoglobin

stabilisation and these were similar in both crovalimab and eculizumab group during 24-week primary treatment period. Patients who switched from eculizumab to crovalimab following the 24-week randomised period maintained disease control in the extension phase.

An indirect treatment comparison was conducted to compare crovalimab with eculizumab and ravulizumab, which the submitting company considered was the most relevant comparator used in NHSScotland. The indirect comparison indicated that there was a high likelihood that crovalimab was non-inferior to eculizumab and ravulizumab across efficacy outcomes assessed, including transfusion avoidance, breakthrough haemolysis and haemoglobin stabilisation.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

The company estimated that there would be 41 patients eligible for treatment with crovalimab in years one to five. The company estimated that there would be one patient treated with crovalimab in year one rising to 10 patients in year five.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

References

1. Electronic Medicines Compendium. Summary of product characteristics. crovalimab (Piasky) 340 mg solution for injection/infusion. Available at: https://www.medicines.org.uk/emc/product/15875/smpc#about-medicine (Accessed 11.11.2024).
2. European Medicines Agency (EMA). Summary of product characteristics. ravulizumab (Ultomiris). 19 April 2024 (last updated) www.ema.europa.eu.
3. Scottish Medicines Consortium, SMC2305: Ravulizumab. 2021. Available at: https://scottishmedicines.org.uk/medicines-advice/ravulizumab-ultomiris-full-smc2305/ (Accessed 18/10/2024).
4. European Medicines Agency (EMA). Summary of product characteristics. eculizumab (Soliris). 18 August 2023 (last updated) www.ema.europa.eu.
5. Scottish Medicines Consortium, eculizumab (Soliris) 1130/16. 2016. Available at: https://scottishmedicines.org.uk/medicines-advice/eculizumab-soliris-for-pnh-fullsubmission-113016/ (Accessed 18/10/2024).
6. Röth A, He G, Tong H, Lin Z, Wang X, Chai-Adisaksopha C*, et al.* Phase 3 randomized COMMODORE 2 trial: Crovalimab versus eculizumab in patients with paroxysmal nocturnal hemoglobinuria naive to complement inhibition. American journal of hematology. 2024;99(9):1768-77. Epub 2024/06/17. 10.1002/ajh.27412
7. Scheinberg P, Clé DV, Kim JS, Nur E, Yenerel MN, Barcellini W*, et al.* Phase 3 randomized COMMODORE 1 trial: Crovalimab versus eculizumab in complement inhibitor-experienced patients with paroxysmal nocturnal hemoglobinuria. American journal of hematology. 2024;99(9):1757-67. Epub 2024/06/26. 10.1002/ajh.27413

This assessment is based on data submitted by the applicant company up to and including 25 November 2024.

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.