Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2675

danicopan film-coated tablets (Voydeya®)

Alexion Pharmaceuticals Inc

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 a full submission

danicopan (Voydeya®) is accepted for restricted use within NHSScotland.

Indication under review: as an add-on to ravulizumab or eculizumab for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia.

SMC restriction: under the advice of the national PNH service.

In a randomised phase III study, danicopan, as an add-on treatment to C5 inhibitor, was associated with a statistically significant improvement in haemoglobin concentrations at week 12 compared with placebo.

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

Danicopan is a selective, reversible inhibitor of complement factor D which blocks activation of the complement alternative pathway, which is a part of the immune system, leading to inhibition of the deposition of C3 fragments on paroxysmal nocturnal haemoglobinuria (PNH) red blood cells. The deposition of C3 fragments is a key cause of extravascular haemolysis, which is the predominant cause of residual haemolytic anaemia in patients receiving complement component (C5) inhibitors (ravulizumab or eculizumab).[1, 2] The recommended starting dose of danicopan is 150 mg three times a day administered orally, increased to 200 mg three times a day after a minimum of 4 weeks of treatment depending on clinical response. See Summary of Product Characteristics (SPC) for more details.[2]

1.2. Disease background

Paroxysmal nocturnal haemoglobinuria is a rare, life-threatening condition that can affect individuals of any age, though it is most commonly diagnosed in young adults, typically in their 30s and 40s. This condition occurs due to an acquired mutation in the phosphatidylinositol glycan A (PIG-A) gene, leading to a deficiency of crucial terminal complement inhibitor proteins on cell surfaces. The absence of these proteins in blood cells triggers uncontrolled alternative complement activation, which can lead to the premature destruction of red blood cells (haemolysis), haemolytic anaemia, thrombosis, and ultimately, death. Haemolysis in PNH occurs in two forms: within the blood vessels (intravascular haemolysis [IVH]) or outside the blood vessels (extravascular haemolysis [EVH]). Intravascular haemolysis can lead to thrombosis which, before the availability of complement inhibitors, was the leading cause of death in patients with PNH.[3, 4]

1.3. Treatment pathway and relevant comparators

There is a national PNH service based in England that has agreements in place to provide support to patients with PNH in Scotland, and there is a PNH outreach centre based in NHS Lanarkshire.[4] The current standard of care for newly diagnosed PNH is the C5 inhibitors, eculizumab or ravulizumab. Ravulizumab is given by intravenous infusion every 8 weeks and is more commonly prescribed than eculizumab which is given by intravenous infusion every 2 weeks; eculizumab is the preferred treatment during pregnancy. The inhibition of C5 helps to control IVH; EVH is believed to be mediated by C3 fragment deposition in PNH red blood cells. Approximately 20% of patients who are treated with C5 inhibitors experience clinically significant EVH.[3] The C3 inhibitor pegcetacoplan (SMC2451) was accepted for restricted use by SMC for the treatment of adult patients with PNH who are anaemic after treatment with a C5 inhibitor for at least 3 months (under the advice of the national PNH service) and is the most relevant comparator for this submission.

1.4. Category for decision-making process

Eligibility for a PACE meeting

Danicopan meets SMC orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of danicopan as an add-on therapy to ravulizumab or eculizumab in adult patients with PNH and clinically significant EVH comes from the ALPHA study (Table 2.1).

Table 2.1. Overview of relevant studies [3, 5]

Criteria	ALPHA study
Study design	A randomised, double-blind, placebo-controlled phase III study.
Eligible patients	• Adults with PNH • Clinically evident EVH (defined as anaemia [haemoglobin ≤ 9.5 g/dL] with absolute reticulocyte count ≥ 120 × 10^9/L) • Patients were taking C5 inhibitor for at least 6 months at the approved dose (or higher) with no change in dose for at least 24 weeks preceding day 1 of the study. • Platelet count ≥ 30,000/microlitre (30 x10^9/L) without the need for platelet transfusions • ANC ≥ 500/microlitre (0.5 x10^9/L)
Treatments	Danicopan 150 mg or placebo orally three times a day, both in combination with C5 inhibitor (ravulizumab or eculizumab) for the double-blind 12-week treatment period. At week 12, the study was unblinded and patients assigned to placebo were switched to danicopan plus C5 inhibitor and patients originally assigned to danicopan continued treatment plus C5 inhibitor for a further 12 weeks. At week 24, patients were eligible to enter an open-label long-term extension study. Dose escalation to a maximum of 200 mg three times a day was permitted at specific time points based on safety and clinical effect. Any dose escalation was done following a minimum of 4 weeks at current dose.
Randomisation	Patients were randomised to danicopan or placebo in a 2:1 ratio. Randomisation was stratified based on transfusion history (>2 versus ≤2 transfusions within 6 months of screening), haemoglobin (<8.5 g/dL versus ≥8.5 g/dL at screening) and by patients enrolled from Japan (yes versus no).
Primary outcome	Change in haemoglobin level from baseline to week 12.
Key secondary outcomes	• Proportion of patients with an increase in haemoglobin level of ≥2 g/dL at week 12 in the absence of transfusion. • Proportion of participants with transfusion avoidance (defined as patients who remain transfusion-free and do not require a transfusion as per protocol-specified guidelines) to Week 12. • Change from baseline in FACIT-Fatigue scores to Week 12. • Change from baseline in ARC to Week 12.
Statistical analysis	The primary outcome was analysed using a MMRM. A hierarchical testing procedure was applied to key secondary outcomes as ordered above with no formal testing after the first non-significant outcome in the hierarchy. Several interim analyses were planned: IA1 took place on 28 June 2022 when 75% of the target enrolled population (n=63) completed the 12-week double-blind period; IA2 took place on 20 September 2022 when 75% of the target enrolled population (n=63) completed the first 24 weeks of the study (12 week double-blind period and 12-week unblinded, cross-over period). IA3 was not pre-specified. It took place on

	31 March 2023 in the Modified Randomised Set, defined as all randomised participants excluding 3 participants who were randomised to the placebo group with their 12-week treatment period cut short due to early switching from placebo to danicopan following positive interim analysis readout and DMC recommendation.

Abbreviations: ANC = absolute neutrophil count; ARC = absolute reticulocyte count; DMC = Data Monitoring Committee; EVH = extravascular haemolysis; FACIT = Functional Assessment of Chronic Illness Therapy; IA = interim analysis; MMRM = mixed model for repeated measures; PNH = paroxysmal nocturnal haemoglobinuria.

Danicopan, as an add-on treatment to ravulizumab or eculizumab, was associated with a statistically significant improvement in haemoglobin concentrations at week 12 versus placebo. See Table 2.2 for more details.

Table 2.2 Selected key efficacy outcomes from ALPHA study.[2, 3 6, 7]

	Interim Analysis 2* (data-cut 20 September 2022)		**Interim analysis 3** (data-cut 31 March 2023)**	
	Danicopan (n= 42)	**Placebo (n= 21)**	**Danicopan (n=57)**	**Placebo (n=26)**
Primary outcome				
Change in haemoglobin from baseline to week 12, LSM, g/dL	2.94	0.50	2.81	0.41
LSM difference, g/dL (95% CI)	2.44 (1.69 to 3.20) p<0.001		2.40 (1.68 to 3.13) p<0.001	
Key secondary outcomes				
Haemoglobin increase of ≥ 2 g/dL at week 12 in the absence of transfusion	60%[a]	0%	54%[a]	0%
Transfusion avoidance through week 12	83%[a]	38%	79%[a]	31%
Change in FACIT-Fatigue score from baseline to week 12, LSM	7.97[a]	1.85	8.00[a]	2.29
Change in ARC ($\times 10^9$/L) from baseline to week 12, LSM	-83.8[a]	3.5	-93.1[a]	-3.4

* Interim Efficacy Analysis Set, defined as the first 75% (n=63) of the target enrolment of patients (n=84)

** Modified Randomised Set, defined as all randomised participants excluding 3 participants who were randomised to the placebo group with their 12-week treatment period cut short due to early switching from placebo to danicopan following positive interim analysis readout and Data Monitoring Committee (DMC) recommendation

[a] statistically significant p-value versus placebo (p<0.001)

Abbreviations: ARC = absolute reticulocyte count; CI = confidence interval; FACIT = Functional Assessment of Chronic Illness Therapy; LSM = least squares mean.

At week 12, patients were unblinded, and patients originally randomised to placebo were switched to danicopan. Overall, efficacy was maintained from week 12 to week 24 in patients

originally randomised to danicopan, and in patients who switched from placebo an improvement was observed in most of the efficacy outcomes (interim analysis 3).[3] Following the completion of week 24, patients were able to enrol in a long-term extension study. At interim analysis 3 (data-cut March 2023), 80 patients had entered the open-label, long-term extension study, and 32 patients had completed 1 year of treatment. Preliminary results suggest efficacy is maintained in the long-term.[3, 6]

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using; FACIT-Fatigue (key secondary outcome - see Table 2.2), European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30), EQ-5D-3L, Work Productivity and Activity Impairment Questionnaire: Anaemic Symptoms (WPAI:ANS) and Health Resource Utilization (HRU) (exploratory outcomes). No notable differences were observed between the danicopan and placebo groups for EQ-5D-3L at week 12; both groups appeared to maintain baseline quality of life. There were similar findings with EORTC QLQ-C30 scores, WPAI:ANS scores, and HRU.[6]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing danicopan with pegcetacoplan the submitting company presented an indirect treatment comparison. This analysis has not been used to inform the economic base case, but it does inform some scenario analyses. See Table 2.3 for details.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	MAIC (anchored and unanchored)
Population	Adult patients ≥18 years of age, with csEVH who were stable on eculizumab or ravulizumab
Comparators	Pegcetacoplan
Studies included	ALPHA (danicopan versus placebo [plus ravulizumab or eculizumab]) [5], PEGASUS (pegcetacoplan versus eculizumab)[8].
Outcomes	• Change in haemoglobin level from baseline • Change in LDH level from baseline • Change in FACIT-F score from baseline • Change in ARC from baseline • Proportion of patients with transfusion avoidance
Results	Results for mean difference in change in haemoglobin from baseline were inconsistent between anchored and unanchored analyses; 95% confidence intervals were wide and crossed 0, suggesting no evidence of a difference between danicopan (as an add-on to C5 inhibitor) and pegcetacoplan. Broadly similar findings were observed for the other outcomes analysed. The submitting company concluded that "results of the MAIC analyses were not considered suitable for inclusion in the economic analysis".

Abbreviations: MAIC: Matching-Adjusted Indirect Comparison; csEVH: clinically significant extravascular haemolysis; LDH: lactate dehydrogenase; FACIT-F: Functional Assessment of Chronic Illness Therapy – Fatigue; ARC: Absolute Reticulocyte Count

3. Summary of Safety Evidence

At interim analysis 3 (data-cut March 2023), the total (all treatment periods including long-term extension) median exposure to study treatment was 439 days in the danicopan group (n=57) and 381 days in the placebo group (that were switched to danicopan after the 12-week double-blind treatment period) (n=27). In the 12-week double-blind treatment period patients reporting a grade 3 or higher AE were 19% (11/57) in the danicopan group versus 14% (4/29) in the placebo group, and patients discontinuing therapy due to an AE was 5.3% versus 3.4%.[3]

In the 12-week double-blind period (data-cut 31 Mar 2023), there were 3 (5.3%) patients in the danicopan and 2 (6.9%) in the placebo group who experienced at least 1 serious AE. Serious AEs in the danicopan group included severe cholecystitis, pancreatitis, and blood bilirubin increased. During the 12-week double-blind treatment period (data-cut June 2022), two treatment-emergent AEs of haemolysis (breakthrough haemolysis [BTH]) were reported; none of these events had LDH > 1.5 times the upper limit of normal and none led to discontinuation of treatment; no new incidences of BTH were reported at data-cut March 2023.[3]

Overall, regulatory authorities concluded that the addition of danicopan to C5 inhibitor treatment results in an increase in overall incidence of AEs but does not appear to increase serious AEs or AEs of grade ≥3. Nevertheless, serious infections including meningococcal infection and malignancies/haematological abnormalities have been included as important potential risks in the SPC for danicopan. Longer-term safety data are awaited.[3]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In a randomised, double-blind, phase III study, danicopan as an add-on treatment to ravulizumab or eculizumab was associated with a statistically significant and clinically meaningful improvement in haemoglobin concentrations at week 12 versus placebo. The difference in mean change in haemoglobin from baseline to week 12 between treatment groups was 2.40 g/dL (interim analysis 3).[3]
- Danicopan also was associated with a statistically significant improvement over placebo at week 12 for all four key secondary outcomes, including the proportion of patients with an increase in haemoglobin level ≥2 g/dL in the absence of transfusion, transfusion avoidance, the patient-reported outcome FACIT-Fatigue, and absolute reticulocyte count.[3]

4.2. Key uncertainties

- There is no direct evidence comparing danicopan with the most relevant comparator in Scottish clinical practice, pegcetacoplan. The indirect comparison conducted by the submitting company had the limitations relating to substantial heterogeneity between the danicopan and pegcetacoplan studies and effective sample size following adjustment, suggesting poor overlap between study populations and generating further uncertainty. Also, results of the indirect comparisons were inconsistent, and 95% confidence intervals were wide suggesting uncertainty. Overall, the submitting company's conclusion that it is

not possible to draw reliable conclusions about the relative efficacy of danicopan (in combination with C5 inhibitor) versus pegcetacoplan based on the indirect comparison seems reasonable.

- There are limited long-term efficacy and safety data for danicopan. Evidence beyond 12 weeks is limited by the lack of a control group, and only 32 patients to date have completed one year of treatment. This is particularly relevant in a chronic condition such as PNH. Further data are awaited.[3]
- ALPHA had a limited sample size (n=82 entered treatment period 2 at interim analysis 3), however this may be expected given the rare nature of PNH and the subset of patients that danicopan aims to treat. The data on the use of danicopan in patients aged ≥75 years are also limited.[3]
- Patients in ALPHA could be considered to have severe clinically significant extravascular haemolysis, based on the relatively strict inclusion criteria (haemoglobin ≤ 9.5 g/dL with absolute reticulocyte count ≥ 120 × 10^9/L) and that all patients had received transfusions in the last 6 months before screening.[5] It is uncertain whether the treatment effect observed in ALPHA is generalisable to patients with less severe but still clinically significant extravascular haemolysis. Clinically significant extravascular haemolysis in practice is assessed on an individual basis, using a range of clinical parameters and patient-reported symptoms.[1]

4.3. Service implications

Danicopan is an oral treatment, which is a convenient route of administration. However, as an add-on treatment, patients will still require intravenous administration of C5 inhibitor. Given that PNH is a rare condition, there are no major service implications anticipated with the introduction of danicopan.

5. Summary of Patient and Carer Involvement

The following information reflects the views of the specified Patient Group.

- We received a patient group submission from PNH Scotland, which is a registered charity.
- PNH Scotland has not received any pharmaceutical company funding in the past two years.
- PNH is a debilitating, incurable condition that leaves patients exhausted, in pain and at risk of death due to thrombosis. Patients experience debilitating symptoms of fatigue, difficulty swallowing, erectile dysfunction, muscle weakness and abdominal pain, all of which can limit their daily functioning, with impacts on relationships, families and employment.
- Currently patients may receive the monoclonal antibody medicines eculizumab or ravulizumab. Both treatments are C5 complement inhibitors administered as an intravenous infusion with eculizumab given every 2 weeks and ravulizumab every 8 weeks.

Patients who have persistent anaemia while on a C5 complement inhibitor require a C3 complement inhibitor, pegcetacoplan which is administered as a sub-cutaneous infusion twice weekly.

- Danicopan is a self-administered medication that is taken in conjunction with a C5 complement inhibitor. It is taken three times a day in tablet form. An oral treatment is generally more convenient for patients although it would be alongside a C5 inhibitor.

- Patients on danicopan report they experienced greater energy levels and a better quality of life enabling them to return to work and live a more normal family life.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	Lifetime time horizon assuming a maximum age of 100 years (45.7 years)
Population	Adult patients with PNH who have residual haemolytic anaemia as an add-on to C5 inhibitors (eculizumab or ravulizumab)
Comparators	Pegcetacoplan
Model description	Markov cohort model with mutually exclusive and mutually exhaustive health states: • Low Hb: Haemoglobin level <9.5 g/dL and not currently receiving a transfusion • Moderate Hb: Haemoglobin level ≥9.5 g/dL and not currently receiving a transfusion • Transfusion: Currently receiving a transfusion • Death Subsequent treatment, with C5 inhibitor monotherapy, was also modelled for patients who discontinued initial treatment.
Clinical data	Transition probabilities for patients receiving danicopan as an add-on to eculizumab or ravulizumab were derived from individual patient data (IPD) from all treatment periods (TP1 [Baseline–Week 12], TP2 [Week 13–24], and LTE [Week 25–52]) of the ALPHA study (IA2; data cut-off of 20 Sep 2022).[5] The adopted approach to the transition probabilities framework assumes that current haemoglobin levels have a log-linear relationship with baseline haemoglobin levels. Transition probabilities for patients receiving pegcetacoplan were sourced directly from Hakimi et al. (2022)[9], which were derived from IPD from the PEGASUS study.[8]
Extrapolation	Efficacy of the treatments was based on data up to 52 weeks (ALPHA) and 48 weeks (PEGASUS) with the treatment effect assumed to be maintained beyond this time point for the duration of the model. Discontinuation was included for danicopan and pegcetacoplan in the base case informed by treatment specific non-BTH discontinuation rates from the relevant studies. BTH events were managed with dose escalation in pegcetacoplan arm. For C5 inhibitor with or without danicopan, BTH events were managed with increased dosing frequency of C5 inhibitor. Upon discontinuation, patients in both arms were assumed to switch to C5 inhibitor monotherapy . No discontinuations were assumed beyond year 1.

Quality of life	Health state-specific utilities were derived from the ALPHA study through the commonly used and validated EQ-5D-3L instrument; a mixed model repeated measures model was then used to generate UK-specific health state index scores across timepoints in TP1, TP2 and the LTE. Utility decrements were included for increased ALT, eculizumab and pegcetacoplan administration, BTH and iron overload.
Costs and resource use	The model included acquisition, subcutaneous injection self-administration training, monitoring (blood test, GP and haematologist visit), blood transfusion, antibiotic prophylaxis, BTH management, iron overload management, AE management costs
PAS	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland Under the PAS, a discount was offered on the list price of danicopan. A PAS discount is in place for pegcetacoplan and this was included in the results used for decision-making by using estimates of the comparator PAS price.

Abbreviations: ALT= alanine aminotransferase; BTH= breakthrough haemolysis; C5i= complement component 5 inhibitor; ESS= effective sample size; Hb= haemoglobin; HSUV= health state utility value; IA= Interim Analysis; ICER= incremental cost-effectiveness ratio; ITC= indirect treatment comparison; LTE= long term extension; MAIC= matching-adjusted indirect comparison; PAS= Patient Access Scheme; PASAG= Patient Access Scheme Assessment Group; QALY= quality-adjusted life year; TA= technology appraisal; TP= Treatment period.

6.2. Results

SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

The quality-adjusted life year (QALY) gain for danicopan versus pegcetacoplan estimated from the cost-effectiveness model was 0.43.

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in table 6.2 below.

Table 6.2 Sensitivity and Scenario Analysis

No.	Parameter	Base case	Scenario
	Base case	-	-
1	Time horizon	Lifetime	10 Years
2			20 Years
3	Patients on danicopan with dose escalation to 200 mg for Week 53+	0%	100%
4	Discontinuation Year 1+	No discontinuation	Sustained discontinuation
5	Management of BTH event	0% patients on any dose discontinuing to C5i and 100% dose escalation	Pegcetacoplan discontinuation/escalation from PEGASUS study
6	C5 inhibitor distribution	Distribution of each dose from ALPHA study	Overall distribution based on ALPHA study (41.3% eculizumab and 58.7% ravulizumab)
7			Distribution of eculizumab dosing based on licensed dose (900mg)

8	Model structure	Health states based on 9.5 Hb cut-off	Health states based on 10.5 Hb cut-off (Transitions informed by MAIC)
9			Health states based on 10.5 Hb cut-off (Transitions informed by MAIC, Max ESS weights)
10			Health states based on 10.5 Hb cut-off (Transitions informed by MAIC, Utilities from Hakimi 2022)
11	Utilities	HSUV from ALPHA study	HSUV derived from arithmetic means
12			Eculizumab and pegcetacoplan utility decrement aligned with NICE TA698

Abbreviations: BTH= breakthrough haemolysis; C5i= complement component 5 inhibitor; ESS= effective sample size; Hb= haemoglobin; HSUV= health state utility value; ICER= incremental cost-effectiveness ratio; ITC= indirect treatment comparison; MAIC= matching-adjusted indirect comparison; QALY= quality-adjusted life year; TA= technology appraisal.

6.4. Key strengths

- The health-related quality of life data was directly captured from patients using the three-level EuroQoL 5 dimensions (EQ-5D-3L) during the ALPHA study.
- The submitting company reports having validated the modelling approach and outcomes with clinical experts.

6.5. Key uncertainties

- In the absence of direct evidence for comparisons of danicopan plus C5 inhibitors with pegcetacoplan, the submitting company attempted anchored and unanchored MAICs to compare two studies (ALPHA and PEGASUS). The sample size limitations meant that few factors were adjusted, and baseline characteristics still differed considerably between the studies. This heterogeneity was reflected in the results where the mean difference in treatment effect had wide confidence intervals. Therefore, the submitting company's conclusion of not using MAIC results seems reasonable. However, the same concerns associated with heterogeneity introduces biases associated with the alternative approach of using naïve (unadjusted) estimates, adding to the uncertainty. The Scenarios 8 – 10 explored health states based on MAIC and did not change the cost-effectiveness conclusion.
- The model assumption that ravulizumab and eculizumab have comparable efficacy is a source of uncertainty in the analysis. This approach was accepted in previous submissions in this area and the company has provided evidence to support this. In addition, patients receiving C5 inhibitor monotherapy and danicopan as an add-on to C5 inhibitor were assumed to have the same probability of BTH events and iron overload. This is an area of uncertainty. However, alternate values for BTH rates explored in one-way sensitivity analysis did not change the overall cost-effectiveness conclusion.
- There is a lack of long-term data to support lifetime benefit of danicopan plus C5 inhibitors over pegcetacoplan. The assumption of BTH events, non-BTH events and corresponding discontinuation or dose escalation assumptions after year 1 in both treatment arms are

uncertain. Longer-term assumptions were explored in Scenarios 3 - 5 and did not alter the cost-effectiveness conclusion. Treatment waning was not explored through sensitivity analysis and remains a source of uncertainty. This aligns with approach applied in previous submissions in this area.

- The company's assumption that all patients switch to C5 inhibitor monotherapy after discontinuation is uncertain.

- Health-state-specific utility values were used, meaning that patients in the danicopan plus C5 inhibitor and pegcetacoplan arms of the model experienced same quality of life in all four health states. However, utility decrements associated with administration of pegcetacoplan and eculizumab, elevated alanine aminotransferase (ALT), BTH and iron overload were applied based on corresponding proportions. This resulted in an overall quality-adjusted life year (QALY) gain in danicopan plus C5 inhibitor arm compared to pegcetacoplan arm. The company provided evidence to justify this approach and explored other health-state-specific utility values in sensitivity analysis which did not alter the cost-effectiveness conclusion. Treatment specific utilities were not explored.

*Other data were also assessed but remain confidential.**

7. Conclusion

After considering all the available evidence, the Committee accepted danicopan (Voydeya®) for restricted use within NHSScotland.

8. Guidelines and Protocols

The National PNH Service was established in April 2009 to care for and support patients with PNH from throughout England. There are agreements in place with the Healthcare Commissioners in Scotland, Wales and Northern Ireland for the National PNH Service to provide support to patients with PNH from the rest of the UK. The PNH Service is now funded by NHS England as a Highly Specialised Service. The management of PNH in Scotland is largely guided by the National PNH Service in England and shared care agreements with local haematology units.[4]

9. Additional Information

9.1. Product availability date

06 November 2024

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
danicopan	**The recommended starting dose of danicopan is 150 mg three times a day administered orally, increased to 200 mg three times a day after a minimum of 4 weeks of treatment depending on clinical response.**	**150 mg three times a day:** £49,861 **200 mg three times a day:** £66,481

Costs from company submission on 27 September 2024. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 12 patients in year 1 rising to 16 patients in year 5 eligible for treatment with danicopan, to which confidential estimates of treatment uptake were applied.

SMC is unable to publish the with PAS budget impact due to commercial-in-confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS discounts associated with comparator medicines.

*Other data were also assessed but remain confidential.**

References

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This assessment is based on data submitted by the applicant company up to and including 15 November 2024.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal*:https://www.scottishmedicines.org.uk/about-us/policies-publications/

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 represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. 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.