Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2581

deucravacitinib film-coated tablets (Sotyktu®)

Bristol Myers Squibb

10 November 2023

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

ADVICE: following a full submission

deucravacitinib (Sotyktu®) is accepted for restricted use within NHSScotland.

Indication under review: for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

SMC restriction: patients who have failed to respond to standard systemic therapies (including ciclosporin, methotrexate and phototherapy), are intolerant to, or have a contra-indication to these treatments.

In two phase III studies, deucravacitinib was superior to a phosphodiesterase type-4 inhibitor and placebo in improving the signs and symptoms of psoriasis in adults with moderate to severe plaque psoriasis, who were candidates for systemic therapy.

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

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Deucravacitinib selectively inhibits the tyrosine kinase 2 (TYK2) enzyme, which belongs to the janus kinase [JAK] family and inhibits the release of pro-inflammatory cytokines and chemokines. TYK2 mediates signalling of interleukin-23 (IL-23), interleukin-12 (IL-12), and type I interferons (IFN), which are naturally occurring cytokines involved in inflammatory and immune responses. The recommended dose of deucravacitinib is 6mg orally once daily.[1]

1.2. Disease background

Psoriasis is a chronic, immune-mediated, relapsing-remitting, inflammatory skin disease, which is characterised by red, scaly patches, plaques and pustules that usually itch. Plaque psoriasis, which typically affects the elbows, knees, scalp and back, is the most common type of psoriasis.[4]

1.3. Company proposed position

The submitting company has requested that deucravacitinib is positioned for use in patients who have failed to respond to standard systemic therapies (including ciclosporin, methotrexate and phototherapy), are intolerant to, or have a contra-indication to these treatments.

1.4. Treatment pathway and relevant comparators

Treatment options include topical therapy initially, then, in patients inadequately controlled with topical therapy, phototherapy or photochemotherapy followed, in non-responders, by conventional systemic therapy (for example, methotrexate and acitretin, with ciclosporin usually reserved for induction only in severe cases). Biologic medicines are generally used in patients who have failed to respond to conventional systemic therapies. Biologic therapies licensed for the treatment of moderate to severe plaque psoriasis in adults, that have been accepted for restricted use in NHSScotland, include tumour necrosis factor (TNF)-alpha inhibitors (infliximab, etanercept, adalimumab and certolizumab pegol), IL12/IL23 inhibitor (ustekinumab), IL23 inhibitor (guselkumab, tildrakizumab and risankizumab), IL17 inhibitors (secukinumab, ixekizumab and bimekizumab) and the IL17A receptor antagonist (brodalumab). Other potential non-biologic treatment options in this setting are dimethyl fumarate and apremilast. Deucravacitinib is unlikely to replace any one comparator in Scottish practice. It will provide an additional treatment option for patients with moderate to severe plaque psoriasis, and has the added benefit of being an oral treatment.[4, 5]

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of deucravacitinib for the treatment of moderate to severe plaque psoriasis comes from POETYK-PSO-1 and POETYK-PSO-2 (Table 2.1).

Table 2.1. Overview of relevant studies.[2, 3, 4]

Criteria	POETYK-PSO-1 and POETYK-PSO-2
Study design	International, multi-centre, randomised, double-blind, phase III studies.
Eligible patients	The key inclusion criteria were: • Age ≥ 18 years • Stable plaque psoriasis (defined as no morphology changes or significant flares of disease activity in the opinion of the investigator) for 6 months or more. • Involved BSA ≥ 10%, PASI score ≥ 12, sPGA score ≥ 3 at Screening Visit and day 1 • Patient deemed by the investigator to be a candidate for phototherapy or systemic therapy.
Treatments	Deucravacitinib 6mg orally daily, apremilast orally twice daily (titrated to 30 mg twice a day over six days), or placebo. In both studies, treatment with deucravacitinib and apremilast continued until week 24; placebo was to continue until week 16, at which point patients crossed over to deucravacitinib. From week 24 to week 52: • In POETYK-PSO-1, patients randomised to apremilast at baseline who did not achieve PASI 50 response were switched in a blinded manner to deucravacitinib through week 52, while patients achieving PASI 50 response continued apremilast through week 52. • In POETYK-PSO-2, patients randomised to deucravacitinib at baseline, who did not achieve PASI 75 response continued deucravacitinib through week 52, while patients achieving PASI 75 response, were re-randomised to either deucravacitinib or placebo (if patients relapsed on placebo they could return to deucravacitinib). Patients randomised to apremilast at baseline, who did not achieve PASI 75 response were switched to deucravacitinib, while patients achieving PASI 75 response were switched to placebo through week 52 (if patients relapsed on placebo they switched to deucravacitinib). At week 24, patients with either sPGA or ss-PGA ≥3 could receive rescue treatment with restricted topicals (such as high potency corticosteroids [WHO Classes I-V]) or shampoos at the investigator's discretion. These treatments could only be initiated at week 24 and not at subsequent time points.
Randomisation	Patients were randomised 2:1:1 to receive deucravacitinib, apremilast, or placebo. Randomisation was stratified by geographic region (U.S., Japan, China, and rest of world), previous biologic use (for psoriasis, psoriatic arthritis or other inflammatory diseases only; yes/no), and body weight (≥90 kg and <90 kg [weight strata not applied in Japan or China]).
Primary outcome	The co-primary outcomes were: • sPGA 0/1 response (score of 0 or 1): proportion of patients achieving sPGA score of 0 (clear) or 1 (almost clear), with at least a 2-point reduction from baseline at Week 16. • PASI 75 response: proportion of patients achieving at least a 75% reduction from baseline in the PASI score at Week 16.
Secondary outcomes	Key secondary outcomes include (but are not limited to) PASI 90/100 at week 16, PASI 75/90 at week 24, sPGA 0 at week 16, sPGA 0/1 at week 24, ss-PGA 0/1 at week 16, DLQI 0/1 at week 16, PSSD symptom score of 0 at week 16.
Statistical analysis	Missing data were imputed primarily using non-responder imputation. The statistical testing was split into two branches: one comparing deucravacitinib with placebo and one comparing deucravacitinib with apremilast. Each branch used a hierarchical statistical testing strategy, with no formal testing of outcomes after the first non-significant outcome in the hierarchy. Therefore, the results reported for these outcomes are descriptive only and not inferential (no p-values reported).

Abbreviations: BSA = body surface area; DLQI = Dermatology Life Quality Index; PASI = Psoriasis Area and Severity Index; PSSD = Psoriasis Symptoms and Signs Diary; sPGA = static Physician's Global Assessment (assessed on 5-point scale, where 0 = clear and 1 = almost clear); ss-PGA = scalp-specific Physician's Global Assessment; WHO = World Health Organisation.

Deucravacitinib demonstrated statistically significant benefits over apremilast and placebo for both co-primary outcomes and for almost all secondary outcomes at week 16; exceptions were nail psoriasis versus placebo, and Psoriasis Symptoms and Signs Diary (PSSD) symptom score 0 versus apremilast.[4] See Table 2.2 for details.

Table 2.2. Co-primary and key selected secondary outcomes from POETYK-PSO-1 and POETYK-PSO-2 (ITT population).[4]

	POETYK-PSO-1			POETYK-PSO-2			Pooled		
	DEUC (n=332)	APREM (n=168)	PBO (n=166)	DEUC (n=511)	APREM (n=254)	PBO (n=255)	DEUC (n=843)	APREM (n=422)	PBO (n=421)
Co-primary outcomes at week 16									
sPGA 0/1	54%	32%[A]	7.2%[B]	50%	34%[A]	8.6%[B]	51%	33%	8.1%
PASI 75	58%	35%[A]	13%[B]	53%	40%[A]	9.4%[B]	55%	38%	11%
Selected secondary outcomes at week 16									
PASI 90	36%	20%[A]	4.2%[B]	27%	18%[A]	2.7%[B]	30%	19%	3.3%
PASI 100	14%	3.0%[A]	0.6%[B]	10%	4.3%[A]	1.2%[B]	12%	3.8%	1.0%
ss-PGA 0/1	70%	39%[A]	17%[B]	60%	37%[A]	17%[B]	64%	38%	17%
sPGA 0	18%	4.8%[A]	0.6%[B]	16%	6.3%[A]	1.2%[B]	16%	5.7%	1.0%
DLQI 0/1	41%	29%[A]	11%[B]	38%	23%[A]	9.8%[B]	39%	25%	10%
Selected secondary outcomes at week 24 and week 52									
PASI 75	56%	30%[A]	-	-	-	-	-	-	-
sPGA 0/1	46%	22%[A]	-	-	-	-	-	-	-

Abbreviations: APREM = apremilast; DEUC = deucravacitinib; DLQI = Dermatology Life Quality Index; ITT = intention-to-treat; PASI = psoriasis area and severity index (PASI 75/90/100 refers to an improvement of 75%, 90%, and 100%, respectively, in PASI scores); PBO = placebo; sPGA = static Physician's Global Assessment (assessed on 5-point scale, where 0 = clear and 1 = almost clear); ss-PGA = scalp-specific Physician's Global Assessment.
A = Statistically significant, multiplicity-controlled (deucravacitinib versus apremilast)
B = Statistically significant, multiplicity-controlled (deucravacitinib versus placebo)

In POETYK-PSO-2, patients who were randomised to deucravacitinib on day 1 and achieved PASI 75 response at week 24 were re-randomised to either deucravacitinib or placebo; 80% (119/148) of patients re-randomised to deucravacitinib had a PASI 75 response at week 52 compared with 31% (47/150) of patients who were re-randomised to placebo. Among patients re-randomised from deucravacitinib to placebo at week 24, the loss of sPGA 0/1 response and PASI 75 response occurred as early as the first assessment, approximately 4 weeks after withdrawal of therapy;

median time to loss of sPGA 0/1 response or PASI 75 response was approximately 8 weeks and 12 weeks respectively.[4]

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using PSSD scores and Dermatology Life Quality Index (DLQI). The results of DLQI have been reported in Table 2.2. Overall, quality of life outcomes were generally statistically significant (some HRQoL outcomes were not hierarchically tested and therefore descriptive only) in favour of deucravacitinib over apremilast and placebo, and were considered clinically relevant by regulatory authorities for the overall population.[4]

2.3. Supportive studies

POETYK-PSO-LTE is a multi-centre, open-label, phase IIIb study to evaluate the long-term safety, tolerability, and efficacy of deucravacitinib in the treatment of psoriasis of patients who were previously enrolled in the parent studies, including POETYK-PSO-1 and 2. At data-cut 15 June 2021, the mean duration of exposure to deucravacitinib was 358 days. At week 0, PASI 75 response rate was 65%, which improved through week 48 (76%) and maintained through week 60 (75%); sPGA 0/1 response rates were 51% at week 0 and improved through week 48 (56%) and week 60 (57%).[4]

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

In the absence of direct evidence comparing deucravacitinib with relevant comparators, the submitting company presented a series of indirect treatment comparisons. One of the sensitivity analyses has been used to inform the economic base case.

Table 2.3: Summary of indirect treatment comparisons

Criteria	Overview
Design	Network meta-analyses (NMAs).
Population	Adult patients with moderate to severe plaque psoriasis who are candidates for systemic therapies.
Comparators	Apremilast, etanercept (50mg weekly and twice weekly), dimethyl fumarate, certolizumab pegol (200mg and 400mg), tildrakizumab (100mg and 200mg), ixekizumab, ustekinumab (45/90 mg and 90mg), bimekizumab, adalimumab, guselkumab, secukinumab (150mg and 300mg), infliximab, brodalumab, risankizumab.
Studies included	The full network included 84 studies.
Outcomes	PASI 50/75/90/100 at three different time points: 10-16 weeks, 24-28 weeks, and 44-60 weeks.
Results	In the short-term analysis (10-16 weeks, PASI 75 response), deucravacitinib was significantly more efficacious than placebo, apremilast, dimethyl fumarate, and etanercept 25mg twice weekly or 50mg weekly. There was no evidence of a difference between deucravacitinib and etanercept 50mg twice weekly or tildrakizumab 100mg. Deucravacitinib was significantly less efficacious than certolizumab pegol 200mg or 400mg, tildrakizumab 200mg, ixekizumab, ustekinumab 45mg or 90 mg, bimekizumab, adalimumab, guselkumab, secukinumab 150mg or 300mg, infliximab, brodalumab, and risankizumab. Similar results were observed for the mid-term (24-28 weeks) and long-term (44-60 weeks) results; notably, there was no evidence of a difference between deucravacitinib and adalimumab, ustekinumab 45mg or 90mg or secukinumab 150mg in the long-term analysis.

3. Summary of Safety Evidence

Safety data were pooled for the POETYK-PSO-1 and POETYK-PSO-2 studies; out of the 1,364 patients who had received at least one dose of deucravacitinib, 77% had at least 26 weeks of continuous exposure and 37% had at least 52 weeks of continuous exposure. Between week 0 to 16, adverse events (AEs) were reported by 56%, 58%, and 50% in the deucravacitinib, apremilast, and placebo groups respectively. Between week 0 to week 52, these were 73%, 71%, and 52% respectively; serious AEs were observed in 4.0%, 2.1%, and 2.1% of the deucravacitinib, apremilast, and placebo groups respectively; patients discontinuing therapy due to treatment emergent AE was 3.2% versus 6.2% and 3.5%.[4]

The most common treatment-related AEs occurring in ≥ 1% of patients between week 0 and week 52 (deucravacitinib, apremilast, placebo) were nasopharyngitis (2.4% versus 1.2% and 0.9%); upper respiratory tract infection (2.2% versus 2.8% and 1.4%); diarrhoea (2.1% versus 7.3% and 2.4%); headache (1.7% versus 4.7% and 1.2%); blood creatine phosphokinase increased (1.0% versus 0.2% and 0.6%); nausea (1.0% versus 8.5% and 0.6%).[4]

Overall, the safety profile was considered acceptable by regulatory bodies and consistent with its mechanism of action. The most notable AEs are related to increased risk of infections, such as upper respiratory tract infections and skin disorders. These AEs were largely mild to moderate in severity. At present it is unknown if deucravacitinib may be associated with adverse reactions of JAK inhibition, which has led regulatory bodies to place warnings in the SPC for malignancies, major adverse cardiovascular event (MACE), and venous thromboembolism (VTE) until further post-authorisation data are available.[4]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- As a TYK2 inhibitor, deucravacitinib offers a novel mechanism of action compared with other medicines used in moderate to severe plaque psoriasis. It can be administered orally, which is convenient for both patients and the service.
- Two phase III studies that randomised 1,686 patients demonstrated that deucravacitinib is associated with substantial skin clearance and clinical improvement in the extent and severity of plaque psoriasis compared with apremilast and placebo.
- The efficacy of deucravacitinib has also been shown to be maintained over time; to date there are data to support maintenance of treatment effect up to and beyond two years.

4.2. Key uncertainties

- Direct evidence for deucravacitinib versus active comparators is limited to apremilast, a non-biologic oral treatment.
- In the absence of direct evidence comparing deucravacitinib with various relevant comparators, the submitting company presented an indirect treatment comparison, which had the following limitations:

- The population in the NMA is broader than the company's proposed positioning.
- There was heterogeneity in the PASI levels reported and the timing of assessment in the studies included in the networks.
- There was heterogeneity in baseline patient characteristics including age, weight, duration of disease, and comorbid psoriatic arthritis. The studies included in the NMA also included both treatment naïve and experienced patients.
- Several of the studies included in the network did not use the licensed dose regimen for comparators.
- No safety or health-related quality of life outcomes were included in the NMA.

Despite these limitations, the results and conclusions drawn from the NMA seem reasonable.

- The study populations of POETYK-PSO-1 and POETYK-PSO-2 are broader than the company's proposed positioning (for use in patients who have failed to respond to standard systemic therapies (including ciclosporin, methotrexate and phototherapy), are intolerant to, or have a contra-indication to these treatments). Although it is not clear exactly how many patients in the key studies would meet these criteria, the study populations could be less heavily pre-treated than the proposed population in Scotland. Across the two phase III studies, 42% of patients were naïve to any systemic psoriasis treatments; 58% had received some type of systemic psoriasis treatment; 35% of patients had previously received a biologic systemic treatment. Subgroup analyses on the number of prior systemic therapies were consistent with the overall study population results; highest response rates were observed in patients naïve to biologics. It is important however, to interpret subgroup analyses with caution.[4]
- Dose adjustments have not been studied; it is not known if some patients would benefit from dose adjustments, either to prevent unnecessarily high exposure or under dosing. The recommended dose for all patients is 6mg orally once daily.[1, 4]
- Data for use of deucravacitinib in patients aged 75 years or older are limited, and it should therefore be used with caution in this group.[1, 4]

4.3. Clinical expert input

Clinical experts consulted by SMC considered that deucravacitinib meets an unmet need. They considered that deucravacitinib is a therapeutic advancement due to its novel mechanism of action and that it is a useful treatment option for patients who do not wish to have injection therapy or who have exhausted all other treatment options.

4.4. Service implications

Deucravacitinib is not anticipated to have any major service implications.

5. Summary of Patient and Carer Involvement

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

- We received patient group submissions from the Psoriasis Association and the Psoriasis and Psoriatic Arthritis Alliance (PAPAA). The Psoriasis Association is a charitable incorporated organisation and PAPAA is a registered charity.
- The Psoriasis Association has received 11.85% pharmaceutical company funding in the past two years, including from the submitting company. PAPAA has not received any pharmaceutical company funding in the past two years.
- Psoriasis is a life-long condition with varying degrees of severity. Those with moderate to severe disease, will have a degree of psoriasis that will not only be visible to others, but will also be itchy, painful and produce excess scales. Relationships, education and work are all impacted.
- For those who have moderate to severe psoriasis, the currently available medicines provide a wide choice of therapies. The convenience of oral therapies or regular injections has made psoriasis care easier, but often people become 'used-to' or intolerant of treatments, therefore a wide choice is needed to offer ongoing relief for this life-long condition.
- If deucravacitinib provides clearance it will improve a patient's quality of life. It is an oral medication, which is an advantage for many patients over injections. By being able to take a tablet once a day, people are gaining back control of treating the disease.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The submitting company provided an economic case as described in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	Lifetime (defined as 53 years, based on a mean-average starting age of 46 years) with a 2-week cycle length.
Population	The population used in the economic evaluation was a sub-population of the licensed indication for deucravacitinib and was consistent with the company's proposed positioning: adult patients with moderate to severe plaque psoriasis who have failed to respond to standard systemic therapies (including ciclosporin, methotrexate and phototherapy) are intolerant to, or have a contra-indication to these treatments.
Comparators	Deucravacitinib and comparators were each modelled as part of treatment sequences consisting of three lines of active therapy followed by best supportive care (BSC). Details of the comparator treatment sequences are presented in Table 6.2.
Model description	A Markov cohort model was used to characterise the clinical pathway for patients. Patients entered the model on active treatment in the induction phase. At the end of each treatment's induction phase, patients were distributed according to their PASI response. Patients were

	considered treatment responders if they achieved a ≥ PASI 75 response and continued into the maintenance phase; conversely, patients with a < PASI 75 response were assumed to discontinue treatment and move on to the next treatment within the sequence. An implicit stopping rule at the end of each treatment's induction phase was therefore applied. After discontinuation of the third-line of treatment, patients transition to BSC. It was assumed that patients could die (and transition to the death state) at any time point.
Clinical data	The source of clinical data used in the economic evaluation differed depending on the clinical outcome considered. Treatment effectiveness was informed by a NMA conducted by the company and treatment discontinuation was estimated using results from a real world evidence (RWE)[6]. Serious adverse events (SAE) requiring hospitalisation were based on a variety of published literature sources including treatment-specific clinical studies and SPCs. Life expectancy was informed by age- and gender-dependent all-cause mortality rates using National Life Tables for Scotland (2018-2020).
Extrapolation	Long-term differences in the effectiveness of deucravacitinib versus comparators were linked to differences in the proportion of patients estimated to achieve a ≥ PASI 75 response at the end of the induction phase for each treatment. Beyond this time point, the proportion of patients that discontinue treatment was assumed to be equal for all treatments (annual all-cause probability of discontinuation of 14.3%) based on the study by Yiu et al (2020).[6]
Quality of life	Health benefits were measured using pooled EuroQol-5-Dimension-3-Level (EQ-5D-3L) data collected during the POETYK-PSO-1 and POETYK-PSO-2 trials[2, 3], valued using a UK tariff, combined with health state utility values used in prior National Institute for Health and Care Excellence (NICE) Technology Appraisals (TAs). Health state utility values from these two sources were harmonised by weighting the estimates by the sample size of the datasets used to derive them. The health state utility values were combined with data on life expectancy to estimate quality-adjusted life-years (QALYs) associated with each treatment sequence. An AE disutility was included but covered severe infections only.
Costs and resource use	Medicine costs included treatment acquisition costs, administration costs and SAE costs. Other NHS costs estimated included healthcare resource use associated with BSC, non-responder costs, and monitoring for all treatment options in each treatment sequence.
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 simple discount was offered on the list price. PAS discounts are in place for apremilast, dimethyl fumarate, certolizumab pegol, secukinumab, ixekizumab, brodalumab, tildrakizumab, risankizumab or bimekizumab. These were included in the results used for decision-making by using estimates of the comparator PAS price. SMC would wish to present the with-PAS cost-effectiveness estimates that informed the SMC decision. However, owing to the commercial in confidence concerns regarding the PAS, SMC is unable to publish these results. As such, only the list price results can be presented.

6.2. Results

Base case results, using list prices for all treatments, are shown in Table 6.2. The comparison between the deucravacitinib sequence and the apremilast sequence, the dimethyl fumarate sequence and the etanercept sequence (Rows 1, 2 and 7 in Table 6.2) indicated that the deucravacitinib sequence was more costly but led to greater health outcomes than the comparator.

The deucravacitinib sequence was dominant compared to the adalimumab sequence (Row 3) meaning it was estimated as resulting in lower costs and better health outcomes for patients.

The comparison between the deucravacitinib sequence and the remaining comparator sequences results in a cost-outcome pairing sitting in the South-West quadrant of the cost-effectiveness

plane. This means that the deucravacitinib sequence was estimated as resulting in lower total costs and worse health outcomes than the comparator sequences. When this is the case, a larger incremental cost-effectiveness ratio (ICER) indicates higher savings relative to the projected health loss.

Table 6.2: Base case results [list price for all treatments]

	Sequence	ICER (£ per QALY gained)
-	Deucravacitinib → Secukinumab → Risankizumab	-
1	Apremilast → Secukinumab → Risankizumab	20,946
2	Dimethyl fumarate → Secukinumab → Risankizumab	54,937
3	Adalimumab → Secukinumab → Risankizumab	Dominated
4	Bimekizumab → Secukinumab → Risankizumab	SW quadrant: 146,205
5	Brodalumab → Secukinumab → Risankizumab	SW quadrant: 159,676
6	Certolizumab pegol → Secukinumab → Risankizumab	SW quadrant: 41,104
7	Etanercept → Secukinumab → Risankizumab	11,641
8	Guselkumab → Secukinumab → Risankizumab	SW quadrant: 135,722
9	Ixekizumab → Secukinumab → Risankizumab	SW quadrant: 132,455
10	Risankizumab → Secukinumab → Ustekinumab	SW quadrant: 130,931
11	Secukinumab → Ustekinumab → Risankizumab	SW quadrant: 116,380
12	Tildrakizumab → Secukinumab → Risankizumab	SW quadrant: 98,625
13	Ustekinumab → Secukinumab → Risankizumab	SW quadrant: 62,205

Abbreviations: QALY = quality-adjusted life-years; ICER = incremental cost-effectiveness ratio; SW = Southwest

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

6.3. Sensitivity analyses

A number of sensitivity analyses were provided by the company. Key scenarios considered during decision making were:

- alternate NMA results where the time point for assessing treatment response was varied
- incorporation of a higher probability of discontinuation during the maintenance phase for each treatment
- inclusion of a treatment waning effect for second and third-line treatments.

Overall, the results of these scenario analyses did not alter conclusions based on the base case economic results.

6.4. Key strengths

- The model type and structure used to characterise the clinical pathway was consistent with prior submissions to SMC for this indication.
- Two completed Phase III, randomised studies were available to provide direct evidence for the efficacy and safety of deucravacitinib versus apremilast and placebo within the licensed indication. The pooled data from these studies provided a large sample of patients from which to draw clinical conclusions relevant to the economic evaluation.
- Various types of sensitivity analysis were reported by the submitting company, facilitating insight into the relative contributions to uncertainty of specific model parameters, the

combined effect of multiple parameters, and key structural assumptions used in the analysis on economic results.

6.5. Key uncertainties

- The large number of comparators, and the potential for patients to receive those in a different sequence to that specified by the company in their analysis, created uncertainty regarding economic results. While it was considered necessary to assume specific sequences of treatments to create a manageable number of results for interpretation by SMC, it is possible that more cost-effective sequences were available.
- An absence of direct evidence, comparing deucravacitinib with potentially relevant comparators, reduced the robustness of the economic evaluation.
- The 'treat-through' design of the direct evidence for deucravacitinib, where patients continued to received treatment regardless of response, meant that discontinuation rates in these studies were unlikely to be reflective of clinical practice. It was therefore necessary for the company to utilise data from the RWE study by Yiu et al (2020) to inform discontinuation rates in the economic evaluation. This study did not include data on deucravacitinib, thus its appropriateness relied on the validity of assuming that discontinuation rates associated with deucravacitinib are comparable to the treatments included in this study (i.e. adalimumab, ustekinumab, and secukinumab).
- The NMA results for the relative effectiveness of deucravacitinib versus comparators that were used to inform the economic evaluation were subject to a number of limitations as noted in Section 4.2. These limitations reduced the robustness of the conclusions that could be drawn from the NMA, increasing the uncertainty associated with the economic results.

7. Conclusion

After considering all the available evidence, the Committee accepted deucravacitinib for use in NHSScotland.

8. Guidelines and Protocols

British Association of Dermatologists guidelines for biologic therapy for psoriasis 2020: a rapid update.[5]

9. Additional Information

9.1. Product availability date

16 August 2023

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year

deucravacitinib	**6mg orally once a day**	£8,970

Costs from MIMS online on 31 October 2023. 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 2,217 patients eligible for treatment with deucravacitinib in year 1 and 2,280 in year 5.

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 or PAS associated with medicines used in a combination regimen.

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

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This assessment is based on data submitted by the applicant company up to and including 13 October 2023.

**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.