

upadacitinib prolonged-release tablets (Rinvoq®)

AbbVie

10 July 2026

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 assessed under the orphan equivalent medicine process **upadacitinib (Rinvoq®)** is accepted for restricted use within NHSScotland.

Indication under review: for the treatment of giant cell arteritis in adult patients.

SMC restriction: for use in patients where tocilizumab is unsuitable, not tolerated or has failed.

Evidence from a double-blind phase III study demonstrated that upadacitinib combined with a 26-week corticosteroid taper was superior to placebo combined with a 52-week corticosteroid taper, in achieving sustained remission at 52 weeks. Indirect comparisons of upadacitinib and tocilizumab (both combined with a 26-week corticosteroid taper), were uncertain.

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.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Upadacitinib is a selective and reversible Janus kinase (JAK) inhibitor. JAK enzymes transmit cytokine and growth factor signals that are involved in a broad range of cellular processes, including inflammatory responses, haematopoiesis and immune surveillance. By blocking these enzymes, upadacitinib disrupts proinflammatory cytokine pathways that are involved in the pathogenesis of giant cell arteritis (GCA).^{1, 2}

The recommended dose of upadacitinib for GCA is 15 mg orally once daily in combination with a tapering course of corticosteroids. Upadacitinib monotherapy should not be used to treat acute relapses. Based on the chronic nature of GCA, upadacitinib can be continued as monotherapy following the discontinuation of corticosteroids. Treatment beyond 52 weeks should be guided by disease activity, physician discretion and patient choice.^{1, 2}

1.2. Disease background

Giant cell arteritis (GCA) is a systemic inflammatory vasculitis that primarily affects the large vessels, particularly the cranial branches of the aorta. GCA occurs almost exclusively in people aged 50 years and older and is three times more common in women than in men. Key symptoms include headaches, jaw pain, and scalp tenderness. There is substantial overlap between polymyalgia rheumatica (a chronic, systemic, rheumatic inflammatory disease characterised by pain and morning stiffness in the neck, shoulder, and pelvic girdle) and GCA.

Without high-dose corticosteroid treatment, GCA can lead to serious complications including blindness and stroke; therefore, it constitutes a medical emergency.²⁻⁵

1.3. Treatment pathway and relevant comparators

Corticosteroids are the main treatment used to prevent GCA-related complications. High-dose corticosteroid treatment (generally starting with a prednisolone dose of 40 to 60 mg) should be initiated immediately and continued once daily. Lower or higher doses may be appropriate depending on patient characteristics.

Once controlled (symptoms resolved, normal inflammatory markers), the corticosteroid dose should be gradually tapered. Guidelines suggest tapering over 1 to 1.5 years but recommends this should be individualised to patient. A more rapid tapering regimen may be appropriate in patients at high risk of steroid toxicity. It is reported that more than 40% of patients with GCA relapse following corticosteroid treatment, usually within 2 years of diagnosis. In patients who experience a relapse, reinstitution or dose escalation of corticosteroids is recommended.

In patients at high risk of steroid toxicity or who relapse, adjunctive therapy with the glucocorticoid-sparing agents, such as methotrexate (used off-label) or the interleukin-6 (IL-6) inhibitor, tocilizumab, may be considered with a more rapid tapering regimen.^{3, 4, 6, 7} Tocilizumab has been accepted for restricted use by SMC (with a 12-month clinical stopping rule) for this indication (SMC2014).

The submitting company considered that corticosteroid tapering and tocilizumab are the relevant comparators in this submission. Clinical experts consulted by SMC confirmed that systemic

corticosteroids are standard of care for all patients and that tocilizumab is the corticosteroid-sparing agent most commonly used in practice.

1.4. Category for decision-making process

Eligibility for a PACE meeting

Upadacitinib 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 use of upadacitinib for this indication comes from the SELECT-GCA study. Details are presented in Table 2.1.

Table 2.1. Overview of relevant study ^{2, 8}

Criteria	SELECT-GCA
Study design	International, randomised, double-blind, parallel group, phase III study.
Eligible patients	The key inclusion criteria were: - Adults ≥ 50 years. - Diagnosis of GCA according to the following: - History of ESR ≥ 50 mm/h or hsCRP or CRP ≥ 1.0 mg/dL. - Presence of unequivocal cranial symptoms of GCA, or unequivocal symptoms of polymyalgia rheumatica. - Presence of at least one of either temporal artery biopsy revealing features of GCA, or evidence of large vessel vasculitis by angiography or cross-sectional imaging. - Active new onset or relapsing GCA within 8 weeks of baseline: - Active disease was defined by the presence of an ESR ≥ 30 mm/hr or hsCRP/CRP ≥ 1 mg/dL and at least one of the following: unequivocal cranial symptoms of GCA, unequivocal symptoms of PMR, or other features judged by the investigator to be consistent with GCA or PMR flares. - Relapsing disease was defined as active GCA in a subject who has failed at least one attempted corticosteroid taper. - Received treatment with ≥ 40 mg prednisone (or equivalent) at any time prior to baseline and were receiving prednisone (or prednisolone) at a dose of 20 mg to 60 mg once daily at baseline. - GCA was, in the opinion of the investigator, clinically stable to allow the patient to safely initiate the protocol-defined corticosteroid taper regimen.
Treatments	During a 52-week treatment period, patients received upadacitinib at a dose of 15 mg (n=209) or 7.5 mg (n=107; dose not licensed for this indication and therefore results for this group will not be discussed further) orally once daily, plus a 26-week corticosteroid tapering regimen, or placebo orally once daily plus a 52-week corticosteroid tapering regimen (n=112). At baseline, all patients received open-label prednisone or prednisolone orally at a dose of 20 mg to 60 mg once daily per discretion of the investigator. The corticosteroid tapering regimen was open label until the dose reached 20 mg once daily, after which it was a blinded taper, tailored to each patient based on the starting dose. Patients who experienced a flare were considered non-responders and they were to stop the protocol-defined glucocorticoid taper and receive open-label corticosteroid escape therapy (starting at ≥ 20 mg/day and tapering per investigator discretion). While on open-label glucocorticoid escape therapy, the patient was to continue in the study for the full 52 weeks and receive blinded study drug (upadacitinib or placebo) or, if the

	investigator believed it necessary to permanently discontinue study drug they could switch, after 2 weeks, to a standard of care treatment (such as tocilizumab).
Randomisation	Patients were randomised in a 2:1:1 ratio to upadacitinib 15 mg, upadacitinib 7.5 mg or placebo-containing regimens and stratified according to baseline corticosteroid dose (prednisone or prednisolone >30 mg or ≤30 mg), prior use of an IL-6 inhibitor and baseline disease status (new onset or relapsing disease).
Primary outcome	Proportion achieving sustained remission at week 52, defined as the absence of signs or symptoms of GCA from week 12 through week 52 and adherence to the protocol-specified corticosteroid tapering regimen.
Hierarchically tested secondary outcomes	• Proportion of patients achieving sustained complete remission from week 12 through week 52 (defined as achieving sustained remission and normalisation of ESR to ≤30 mm/h and hsCRP to <1 mg/dL, without elevation on ≥2 consecutive visits to ≥1 mg/dL, from week 12 through week 52). • Cumulative corticosteroid exposure through week 52. • Time to first GCA flare through week 52, which was calculated from the time at which the patients had no signs and symptoms of GCA, normalisation of the ESR, and no increase in the glucocorticoid dose. Disease flare was defined as an event determined by the investigator to represent recurrence of the signs or symptoms of GCA or an ESR measurement ≥ 30 mm/hr (attributable to GCA) and requiring an increase in glucocorticoid dose. • Proportion of patients who experienced ≥1 GCA flare through week 52. • Proportion of patients achieving complete remission at week 52 (defined as achieving remission and normalisation of ESR to ≤30 mm/h and hsCRP to <1 mg/dL). • Proportion of patients achieving complete remission at week 24. • Change from baseline in the 36-item Short-Form-36 physical component summary at week 52. • A group of four outcomes: number of GCA flares per patient; change from baseline in Functional Assessment of Chronic Illness Therapy-Fatigue score at week 52; assessment of Treatment Satisfaction Questionnaire for Medication patient global satisfaction subscale at week 52; and rate of corticosteroid-related adverse events through week 52.
Statistical analysis	A hierarchical statistical testing strategy (in the order listed above) was applied in the study 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. Efficacy analyses were performed in the FAS, which included all randomised patients who received at least one dose of study medicine in Period 1 and were analysed according to randomised treatment.

Abbreviations: CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; FAS = full analysis set, GCA = giant cell arteritis; hsCRP = high sensitivity C-reactive protein; PMR = polymyalgia rheumatica.

In the SELECT-GCA study, a significantly greater proportion of patients treated with upadacitinib plus a 26-week corticosteroid taper achieved sustained remission at 52 weeks compared with those receiving placebo plus a 52-week corticosteroid taper.^{2,8} See Table 2. 2 for details.

Table 2.2. Key efficacy results of SELECT-GCA (FAS population) ^{2, 8}

	Upadacitinib 15 mg + 26- week corticosteroid taper (n=209)	Placebo + 52-week corticosteroid taper (n=112)
Primary outcome: Sustained remission at week 52		
n (%)	97 (46%)	33 (29%)
Difference versus placebo (95% CI), p-value	17% (6.3 to 28), p=0.002	
Secondary outcome: Sustained complete remission at week 52		
n (%)	78 (37%)	18 (16%)
Difference versus placebo (95% CI), p-value	21% (11 to 30), p<0.001	
Secondary outcome: Cumulative corticosteroid exposure through week 52 ^a		
Median, mg	1,615	2,882
Difference versus placebo (95% CI), p-value	-1,267 (-1,587 to -1,133), p<0.001	
Secondary outcome: Time to first GCA flare through week 52		
Median, days	>365	323
Hazard ratio (95% CI), p-value	0.57 (0.40 to 0.83), p=0.003	
Secondary outcome: Proportion of patients with ≥1 GCA flare through week 52		
%	34%	56%
Odds ratio (95% CI), p-value	0.47 (0.29 to 0.74), p=0.001	
Secondary outcome: Complete remission at week 52		
n (%)	105 (50%)	22 (20%)
Difference versus placebo (95% CI), p-value	30% (20 to 40), p<0.001	
Secondary outcome: Complete remission at week 24		
n (%)	120 (57%)	40 (36%)
Difference versus placebo (95% CI), p-value	21% (9.7 to 32), p<0.001	
Secondary outcome: Change from baseline in SF-36 PCS score at week 52		
LS mean change	2.5	-1.3
Difference versus placebo (95% CI), p-value	3.8 (1.4 to 6.1), p=0.002	
Secondary outcome: Number of GCA flares through week 52 per patient-year		
Mean	0.4	0.7
Difference versus placebo (95% CI), p-value	0.6 (0.4 to 0.8), p=0.001	
Secondary outcome: Change from baseline in FACIT-Fatigue score at week 52		
LS mean change	1.7	-2.4
Difference versus placebo (95% CI), p-value	4.0 (1.3 to 6.8), p=0.004	
Secondary outcome: TSQM score at week 52		
LS mean	72	69
Difference versus placebo (95% CI)	2.7 (-3.1 to 8.6) ^b	
Secondary outcome: Number of corticosteroid-related AEs through week 52 per patient-year		
Mean	2.0	1.7
Rate ratio (95% CI)	1.1 (0.8 to 1.6)	

^a comparison affected by the different pre-specified regimens for steroid tapering in the upadacitinib arm versus the placebo arm.

^b outcome was not statistically significant (no p-value reported).

Abbreviations: AE = adverse event; CI = confidence interval; FACIT = Functional Assessment of Chronic Illness Therapy; FAS = full analysis set; GCA = giant cell arteritis; PCS = physical component summary; SF-36 = Short-Form 36-item; TSQM = Treatment Satisfaction Questionnaire for Medication

Patients achieving remission (absence of GCA signs and symptoms and adherence to the protocol-defined corticosteroid-taper regimen or corticosteroid-free) during the initial 52-week treatment period were eligible to enter a 52-week blinded extension period. Those receiving upadacitinib who had achieved ≥ 24 weeks of remission by week 52 were re-randomised to continue upadacitinib or switch to placebo. The data suggest that patients who continued upadacitinib 15 mg were more likely to remain in remission than those switched to placebo.⁹

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

2.2. Health-related quality of life outcomes

Health-related quality of life (HRQoL) was assessed using: Short-Form (SF)-36 item (a generic HRQoL measure assessing eight domains; it can provide two summary scores [a physical component [PCS] and mental component score], all ranging from 0 to 100, with higher scores indicating better HRQoL), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue (a 13-item measure assessing fatigue and its impact on daily functioning, particularly in chronic disease; scores range from 0 to 52, with higher values indicating less fatigue and better HRQoL) and Treatment Satisfaction Questionnaire for Medication (TSQM; a 14-item measure of treatment satisfaction, with domain scores ranging from 0 to 100; higher scores indicate greater satisfaction and better perceived HRQoL). These questionnaires were used at baseline (except for TSQM) and at weeks 8, 12, 24 and 52.⁸

As shown in Table 2.2, statistically significant improvements from baseline at week 52 in SF-36 PCS and FACIT-Fatigue score were observed with upadacitinib compared with placebo. Regulators considered these improvements clinically relevant but close to the lower threshold for clinical meaningfulness. No statistically significant difference in TSQM scores was observed between treatment groups.^{2, 8}

The EuroQol Five Dimensions Five Levels Questionnaire (EQ-5D-5L) was also used, and the results generally suggested a trend in favour of upadacitinib, however these were not formally tested.^{8, 10}

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

In the absence of direct evidence comparing upadacitinib with tocilizumab, the submitting company presented an indirect treatment comparison (ITC) in the form of matching-adjusted indirect comparisons (MAICs). An unanchored MAIC was used to inform the comparison with tocilizumab in the economic base case and scenario analyses. An anchored MAIC was also included in a scenario analysis. See Table 2.3 for further details.

Table 2.3. Summary of indirect treatment comparison

Criteria	Overview
Design	Unanchored and anchored MAIC. The submitting company preferred the unanchored MAIC due to differences in cumulative corticosteroid dose between the placebo arms. The anchored MAIC was also included in a scenario analysis.
Population	Adults with active GCA and receiving corticosteroids.
Comparators	Upadacitinib (15 mg orally once daily) compared with tocilizumab (162 mg SC every week), both in combination with a 26-week corticosteroid taper.
Studies included	SELECT-GCA ⁸ (for upadacitinib) and GiACTA ¹¹ (for tocilizumab).
Outcomes	Sustained remission, the proportion of patients experiencing flares, cumulative corticosteroid dose and time-to-first flare (all assessed at week 52).

Results	In both MAICs, the point estimates of the results (which the submitting company consider confidential), generally favoured tocilizumab however the 95% confidence intervals for the ORs or HRs crossed 1, suggesting there was no evidence of a difference between treatments.
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Abbreviations: CI = confidence interval; GCA = giant cell arteritis; HR = hazard ratio; MAIC = matching adjusted indirect comparison; NR = not reported; OR = odds ratio; SC = subcutaneous

[*Other data were also assessed but remain confidential.**](#)

3. Summary of Safety Evidence

The SELECT-GCA study provides evidence on the relative safety of upadacitinib plus a 26-week corticosteroid tapering regimen versus placebo plus a 52-week corticosteroid tapering regimen, which is considered one of the relevant comparators for this submission.

The safety analysis included all patients in SELECT-GCA (data cut-off: 06 February 2024) who received at least one dose of study treatment in Period 1 (up to week 52).

In the 52-week Period 1 of SELECT-GCA, any treatment-emergent adverse event (AE) was reported by 97% (202/209) of patients in the upadacitinib 15 mg group and 95% (106/112) of patients in the placebo group. These were considered potentially related to study treatment in 53% versus 44% and potentially related to corticosteroids in 66% versus 58%. In the upadacitinib 15 mg and placebo group respectively, patients reporting serious AEs were 23% versus 21% and the proportion of AEs that led to withdrawal of upadacitinib 15 mg or matching placebo was 17% versus 26%. One unexplained death in the upadacitinib 15 mg group was evaluated by the investigator as having reasonable possibility of being related to both study drugs (upadacitinib/placebo and prednisone/prednisolone/placebo).

The most commonly reported treatment-emergent AEs were worsening GCA (23% versus 31%), headache (16% versus 12%), arthralgia (14% versus 13%), COVID-19 (13% versus 11%) and hypertension (13% versus 12%).^{1, 2, 8, 10}

Some long-term safety data were also presented for patients who continued treatment in Period 2 (up to week 104); the safety profile appeared consistent with that seen in Period 1.²

Overall, the safety profile of upadacitinib in patients with GCA was generally consistent with the known safety profile (peripheral oedema observed in SELECT-GCA was added as a new common adverse reaction to the summary of product characteristics [SmPC]) and no new safety concerns were identified.²

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In SELECT-GCA, upadacitinib with a 26-week corticosteroid taper achieved higher sustained remission at 1 year than placebo with a 52-week taper, with a statistically significant 17% adjusted difference between groups.⁸ Regulators considered the effect size to be clinically relevant in relation to both remission and probable potential to be steroid-sparing.²

- Results for several secondary outcomes, including complete remission and time to first flare, were consistent and favoured upadacitinib over placebo.⁸

4.2. Key uncertainties

- There is no direct evidence versus tocilizumab, a relevant comparator, therefore, an ITC was presented. The submitting company preferred an unanchored MAIC as there were substantial differences in cumulative corticosteroid dose between the placebo arms, with an anchored MAIC included as a scenario analysis. The submitting company noted that the reason for this difference is unclear but is likely due to differences in the use of escape therapy. The key uncertainty is the company's choice of ITC method in the base case; an anchored MAIC was considered more appropriate. Unanchored MAICs have stronger assumptions than anchored MAICs and it is uncertain whether these were met, considering that some prognostic variables and treatment effect modifiers could not be matched. Of note, large vessel vasculitis could not be matched as this was not reported in the GiACTA study. While the results were generally consistent, the point estimates of the results were generally less favourable in the anchored MAIC. In addition, the effective sample size was reduced considerably after matching, wide confidence intervals suggest uncertainty in the point estimates, outcomes were assessed at week 52 (meaning long-term relative efficacy is uncertain) and safety and health-related quality of life were not assessed. Due to these limitations, the results are uncertain.
- In SELECT-GCA, different corticosteroid taper durations were used (26 weeks with upadacitinib versus 52 weeks with placebo), making corticosteroid-related outcomes difficult to interpret and potentially biased in favour of upadacitinib.^{2, 8} Although guidelines suggest tapering over 12 to 18 months, with faster tapering possible in patients on glucocorticoid-sparing therapy or at high risk of toxicity, tapering is individualised in practice.^{3, 4} Clinical experts consulted by SMC had mixed views on whether the study tapering schedules reflect Scottish clinical practice, with some noting that tapering may be longer in routine care.
- Supportive evidence from a real-world evidence study^{12, 13} was presented by the submitting company to address concerns that corticosteroid-related AEs observed in the SELECT-GCA trial were unrealistically low and not reflective of clinical practice, and to provide longer term safety data. Compared with matched control groups, patients with GCA experienced substantially higher rates of corticosteroid-related AEs. Some of the results were used to inform corticosteroid-related AEs in the economic case; however, the study had important limitations. This was not a study of patients receiving upadacitinib and neither control cohort was diagnosed with GCA, making it difficult to interpret the results and to distinguish the impact of corticosteroid exposure from underlying disease-related inflammation.

4.3. Clinical expert input

Clinical experts consulted by SMC generally agreed that upadacitinib addresses an unmet need in this therapeutic area, particularly for patients with GCA who would benefit from more rapid glucocorticoid tapering and for whom tocilizumab, the only currently licensed glucocorticoid-sparing option, is unsuitable. Experts also considered upadacitinib to represent a therapeutic advancement, as it would provide an additional licensed treatment option with an alternative

mechanism of action and an oral route of administration, with the potential to reduce long-term reliance on systemic corticosteroids and the associated morbidity.

4.4. Service implications

Clinical experts consulted by the SMC considered that the introduction of this medicine is not expected to have a substantial impact on patients or on service delivery.

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of **upadacitinib**, as an **orphan-equivalent** medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- GCA is a serious, chronic and potentially life-threatening condition associated with severe and often incapacitating physical symptoms (including persistent headache, pain, fatigue and functional limitation) and a risk of irreversible complications such as permanent sight loss and stroke; this is accompanied by a substantial psychological burden, including stress, anxiety, and cognitive difficulties, with the relapsing and unpredictable course further impacting overall quality of life.
- The impact extends to family and carers, including through increased support needs and disruption to usual roles. Although many affected individuals are older, they may still be working or have caregiving responsibilities (including childcare), at the time of diagnosis. The condition may lead to shifts in responsibilities, reduced involvement in family life, and broader social or financial strain.
- Management requires high-dose corticosteroid use with the aim of tapering over time. This approach carries a substantial treatment burden, including challenging tapering schedules, which may last for years, and a risk of serious adverse effects (such as infections, metabolic, musculoskeletal, and psychological complications). Corticosteroids are often combined with the IL-6 inhibitor tocilizumab to facilitate dose reduction. Alternative treatment options are limited.
- Upadacitinib provides an additional treatment option with a different mechanism of action and the potential to reduce reliance on corticosteroids, which may lessen treatment burden and reduce the risk of long-term steroid-related adverse effects, and is expected to be associated with improvements in symptoms.
- Improved disease control and reduced treatment burden may increase patient quality of life and independence, reduce reliance on family/carers, and lessen the emotional and practical impact on all, while potentially supporting continued caring roles, family functioning, and, for some patients, employment.
- It may offer practical and clinical advantages over tocilizumab, including oral administration and greater flexibility in treatment interruption (with a shorter duration of action).

- Its use may be limited in practice due to safety considerations in older patients and those with cardiovascular risk factors, with a likely role mainly in patients unsuitable to receive, or who have not responded to other treatments, such as IL-6 inhibitors.

Additional Patient and Carer Involvement

We received patient group submissions from Vasculitis UK and PMR-GCA Scotland. Vasculitis UK is a charitable incorporated organisation. PMR-GCA Scotland is a Scottish charitable incorporated organisation. Vasculitis UK has received 1% pharmaceutical company funding in the past two years, with none from the submitting company. PMR-GCA Scotland has not received any pharmaceutical company funding in the past two years. Representatives from both organisations participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An economic case was provided by the submitting company and is summarised in Table 6.1.

Table 6.1. Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	A lifetime time horizon of 28.9 years was used
Population	Adult patients with a diagnosis of active GCA
Comparators	The intervention was upadacitinib + 26 weeks corticosteroid taper (CS-T). There were two comparators for the economic analysis: • Placebo + 52 weeks CS-T • Tocilizumab (1 year) + 26 weeks CS-T
Model description	A semi-Markov model comprising of four health states was developed: • Pre-flare remission • Flare • Post-flare remission • Death Patients enter the model in the 'pre-flare remission' state and remain until their first flare. In the 'flare' state which lasts 4 weeks, it is assumed that patients do not experience another flare within that time. Patients then proceed to the 'post-flare remission' state, which includes tunnel states to track corticosteroid dose, ensuring this does not exceed the CS-T schedule duration. Once patients have experienced their first flare, their probability of subsequent flares is increased. Patients transition between the 'flare' and 'post-flare remission' states until death.
Clinical data	Treatment efficacy data was sourced from SELECT-GCA for the upadacitinib and placebo arms, and the GiACTA study for the tocilizumab arm. ^{8,11} The Kaplan-Meier curves from these studies were adjusted using unanchored MAIC methods. These curves were then used to fit parametric models for each of the treatment arms, which informed the transition probabilities for the 'pre-flare remission to flare' health state. The SELECT-GCA and GiACTA studies also informed the transition probability for 'post-flare remission to flare (subsequent flare)' states, with constant rates applied.
Extrapolation	As clinical data from the SELECT-GCA and GiACTA studies were not available beyond 52 weeks, extrapolation methods were used.

	Time to first flare (TTFF) were extrapolated from SELECT-GCA, using log-normal for upadacitinib and log-normal for placebo. The gamma curve was extrapolated from the GiACTA study and used for tocilizumab TTFF. The probability of subsequent flares was calculated using regression methods from SELECT-GCA for the upadacitinib and placebo arms, and NICE TA518 for the tocilizumab arm.^{8, 14} Transition probabilities to the death state were derived from Scottish life tables in the first instance and adjusted for GCA-specific excess mortality.¹⁵ These adjustments included short-term mortality during flare and long-term mortality in the remission state, with these rates sourced from the literature. A mortality risk ratio was also applied to account for long-term mortality risk due to AEs.
Quality of life	Utility values were derived from SELECT-GCA and were based on flare status:⁸ • Flare = 0.7098 • No flare (remission) = 0.7685 Disutilities were also included to account for long-term complications of GCA, and AEs associated with patients taking Janus kinase (JAK) inhibitor treatment and corticosteroids. These were sourced from the literature and NICE technology appraisals.
Costs and resource use	Costs included medicine acquisition for upadacitinib, tocilizumab and prednisolone (the choice of corticosteroid), as well as treatment for AEs. Health state-specific disease management costs were also included, as well as monitoring services.
PAS/contract price	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. A PAS discount and a national framework contract price is in place for tocilizumab. The national framework contract price was included in the results used for decision-making by using estimates of the comparator price.

6.2. Results

The base case results for the cost utility analysis are shown in Table 6.2. In addition to the base case results, cost-minimisation results were requested from the company for upadacitinib versus tocilizumab. Despite some limitations, a cost-minimisation analysis was felt to be informative for decision-making.

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

Table 6.2. Base case results (inclusive of all relevant discounts)

	Total costs (£)	Total QALYs	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
<i>Versus PBO</i>					
UPA + 26-WK CS-T	CIC	CIC	CIC	CIC	Dominant
PBO + 52-WK CS-T	CIC	CIC	-	-	-
<i>Versus TOCI</i>					
UPA + 26-WK CS-T	CIC	CIC	CIC	CIC	CIC
TOCI + 26-WK CS-T	CIC	CIC	-	-	-

Abbreviations: CIC, commercial in confidence; CS-T, corticosteroid taper; ICER, incremental cost-effectiveness ratio; Inc, incremental; PBO, placebo; QALYs, quality-adjusted life years; TOCI, tocilizumab; UPA, upadacitinib; WK, week

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in Tables 6.3 and 6.4. SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present results comparing upadacitinib against tocilizumab due to competition law issues.

Table 6.3. Scenario analyses versus corticosteroids (inclusive of PAS discount on upadacitinib)

	Parameter	Base case	Scenario	ICER (£/QALY)
	Base case			Dominant
1	Probability of severe flare	20%	0%	1,040
2a	Annual decline in subsequent flare rate (both arms)	0%	5%	67
2b			10%	2,593
3a	Upadacitinib treatment duration	2 years	1 year	Dominant
3b			3 years	1,316
3c			5 years	3,153
4a	Treatment-waning to placebo	Immediate	None	Dominant
4b			1-year period	Dominant
5	Placebo arm CS taper	1 year	2 years	Dominant
6	Utility value source	SELECT-GCA	GiACTA	Dominant
7a	Time horizon	Lifetime (28.9 years)	10 years	1,827
7b			15 years	Dominant
8a	Patients enter model age	71.1 years	60 years	Dominant
8b			65 years	Dominant
9	Upadacitinib TTFF extrapolation	Log-normal	Generalised gamma (best statistical fit)	Dominant
10	Previous CS use	None	Yes	Dominant
11	Treatment duration	Annual discontinuation included	Fixed	4,186
12a	Retreatment	No retreatment	Maximum total treatment duration 209 weeks (4 years)	Dominant
12b			Maximum total treatment duration 261 weeks (5 years)	Dominant

Abbreviations: CS: corticosteroid; Inc: incremental; LY: life year; ICER: incremental cost-effectiveness ratio; mg: milligram; QALY: quality-adjusted life year; TTFF: time to first flare

Table 6.4. Scenario analyses versus tocilizumab (inclusive of all relevant discounts)

	Parameter	Base case	Scenario
	Base case		
1	Probability of severe flare	20%	0%
2a	Annual decline in subsequent flare rate (both arms)	0%	5%
2b			10%
3a	Upadacitinib treatment duration	2 years	1 year

	Parameter	Base case	Scenario
3b			3 years
3c			5 years
4a	Treatment-waning to placebo	Immediate	None
4b			1 year
5	Utility value source	SELECT-GCA	GiACTA
6a	Time horizon	Lifetime (28.9 years)	10 years
6b			15 years
7a	Patients enter model age	71.1 years	60 years
7b			65 years
8a	Modelling upadacitinib TTFF	Independent parametric methods	Relative to tocilizumab (unanchored MAIC HR)
8b			Relative to tocilizumab (anchored MAIC HR)
8c			Relative to tocilizumab (anchored MAIC HR upper confidence interval (conservative))
9	Upadacitinib TTFF extrapolation	Log-normal	Generalised gamma
10	Tocilizumab TTFF extrapolation	Gamma	Weibull
11	Previous CS use	None	Yes
12	Treatment duration	Annual discontinuation included	Fixed
13a	Retreatment	No retreatment	Maximum total treatment duration 209 weeks (4 years)
13b			Maximum total treatment duration 261 weeks (5 years)
C1	Upadacitinib and tocilizumab treatment durations	UPA: 2 years TCZ: 1 year	2 years both arms
C2			5 years both arms
C3	TTFF extrapolations (all arms)	UPA: log-normal TCZ: gamma PBO: log-normal	UPA: generalised gamma TCZ: gamma PBO: exponential (Best statistical fit)

Abbreviations: CIC: commercial in confidence; CS: corticosteroids; HR: hazard ratio; Inc: incremental; LY: life year; ICER: incremental cost-effectiveness ratio; MAIC: matching-adjusted indirect comparison; PBO: placebo; QALY: quality-adjusted life year; TCZ: tocilizumab; TTFF: time to first flare; UPA: upadacitinib

6.4. Key strengths

- The chosen comparators for the economic analysis appear appropriate and align with clinical guidelines and practice.
- The patient population in the SELECT-GCA and GiACTA studies reflected the patient population in the economic analysis.
- Utility values were sourced from SELECT-GCA, relevant to the patient population of the economic analysis. Flare and remission activity were recorded during SELECT-GCA, ensuring

that utility values reflected disease activity.

6.5. Key uncertainties

- Scenarios 3a-c in Tables 6.3 and 6.4 suggest that a longer treatment duration for upadacitinib has upwards impact on results versus corticosteroids, whereas a 1-year treatment duration for upadacitinib (as conducted in SELECT-GCA) has upwards impact on results versus tocilizumab. Although a conservative scenario exploring longer corticosteroid taper duration in the upadacitinib arm was requested from the company, this was not conducted as they viewed it as clinically implausible.
- The ITC is subject to several uncertainties, and the choice of unanchored MAIC methods in the base case relies upon many assumptions. Scenarios 8a-c in Table 6.4 applied both anchored and unanchored MAIC methods; the anchored MAICs had upwards impact on results. Given the limitations with the ITC, the Committee considered the case against corticosteroids to be more robust.
- Some clinical experts consulted by SMC suggested that upadacitinib may be used as second-line treatment after tocilizumab. There is uncertainty in the economic case surrounding results for patients with previous tocilizumab use, likely due to paucity of data in this area.
- The company used real-world data from a US study rather than SELECT-GCA to estimate the incidence of CS-related AEs. Although a scenario was requested which applies SELECT-GCA data, the company viewed this to be methodologically infeasible, and did not provide this.
- The proportion of patients receiving procedures and services and the frequency of disease management resource use in the remission state was sourced from a UK market research study rather than SELECT-GCA. A scenario was requested that explored the use of SELECT-GCA data, but the company did not conduct this as they viewed it as clinically implausibility.
- Some clinical experts consulted by SMC suggested that upadacitinib may be used in younger patients, noting that JAK inhibitors are not advised in those aged over 65 unless no suitable alternative is available. Patients entering the model at 71.1 years of age may be considered later than suggested. However, patients entering the model at ages 60 and 65 was explored in Scenarios 8 in Table 6.3 and Scenarios 7 in Table 6.4, and found to have downwards impact on results.

7. Conclusion

The Committee considered the benefits of upadacitinib in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as upadacitinib is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted upadacitinib for restricted use in NHSScotland.

8. Guidelines and Protocols

The British Society for Rheumatology (BSR) and British Health Professionals in Rheumatology (BHPR) published guidelines on the management of giant cell arteritis in 2010. The BSR published updated guidelines in 2020.^{3, 16}

The European League Against Rheumatism (EULAR) published guidelines on the management of large vessel vasculitis in 2009, which were updated in 2018.^{4, 17}

9. Additional Information

9.1. Product availability date

24 June 2025

Table 9.1. List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
upadacitinib	15 mg orally once daily in combination with a tapering course of corticosteroids. Treatment beyond 52 weeks should be guided by disease activity, physician discretion, and patient choice.	£10,472

Costs from BNF online on 31 March 2026. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

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 **15 June 2026**.

*[*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/](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 includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS 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. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees 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.