NCPE Assessment

Technical Summary

Ritlecitinib (Litfulo®)

23071

02 December 2025

Applicant: Pfizer

Ritlecitinib for the treatment of severe alopecia areata in adults and adolescents 12 years of age and older.

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of ritlecitinib (Litfulo®) for the treatment of severe alopecia areata (AA) in adults and adolescents 12 years of age and older.

Following assessment of the Applicant's submission, the NCPE recommends that ritlecitinib not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Pfizer) Health Technology Assessment of ritlecitinib (Litfulo®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In February 2025, Pfizer submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of ritlecitinib (Litfulo®) for the treatment of severe alopecia areata (AA) in adults and adolescents 12 years of age and older. Pfizer is seeking reimbursement of ritlecitinib on the High-Tech Drug Arrangement.

The severity of AA is commonly assessed by the Severity of Alopecia Tool (SALT) which reflects the area of scalp hair loss. SALT scores are graded as mild (SALT ≤20; 1-20% scalp hair loss), moderate (SALT 21-49; 21–49% scalp hair loss) or severe (SALT ≥50; ≥50% scalp hair loss). The Alopecia Areata Scale (AAS) considers the SALT score and additional criteria (e.g. associated psychosocial functioning) capturing the wider impact of AA on an individual.

Ritlecitinib, a Janus Kinase (JAK) inhibitor, is administered at a dose of 50mg once daily (o.d.) orally. The Summary of Product Characteristics (SmPC) outlines that consideration should be given to discontinuing patients who show no evidence of therapeutic benefit after 36 weeks. JAK inhibitors are positioned as a first-line treatment for severe AA by the British Association of Dermatologists, the European Academy of Dermatology and Venereology and in the updated Australian Expert Consensus Statement. Standard of care in Ireland, for severe AA, varies with some patients opting for no pharmacological treatment whilst others may attend a dermatologist with a special interest in AA. Treatment options, available in Ireland, consist of topical corticosteroids, oral corticosteroids and immunosuppressants. These are unlicensed for this indication. Clinical opinion to the Review Group indicated that a small number of patients with severe AA have received treatment with a JAK inhibitor such as baricitinib and tofacitinib. These are not reimbursed, in Ireland, for this indication. Best supportive care (BSC) consisting of non-pharmacological management, such as wigs, is the most relevant comparator in this appraisal.

1. Comparative effectiveness of ritlecitinib

The efficacy and safety data for ritlecitinib are from the ALLEGRO-2b/3 and ALLEGRO-LT clinical trials. ALLEGRO-2b/3 was a phase 2b/3 randomised, double-blind, placebo-controlled, 48-week dose ranging trial, completed in 2021. A total of 718 participants aged

12 years and older with at least 50% scalp hair loss were enrolled. The study consisted of a 4-week loading phase, followed by a 20-week maintenance phase, followed by a 24-week extension phase. Ritlecitinib at a dose of 200/50mg o.d., 200/30mg o.d., 50/50mg o.d. and 30/30mg o.d. were tested for superiority versus placebo. The primary endpoint for the EMA was a SALT ≤10 score at Week 24. SALT ≤20 at Week 24 was the primary endpoint for the FDA and a secondary outcome for the EMA. Patient's Global Impression of Change (PGI-C) response rate of 'moderately improved' or 'greatly improved' at Week 24 was a key secondary endpoint. Ritlecitinib showed a statistically significant and clinically relevant benefit compared with placebo in SALT ≤10 score at Week 24 for all ritlecitinib doses. Regimens with and without loading doses showed similar efficacy at Week 48. Only results from the ritlecitinib 50mg o.d. group, the licensed dose, are discussed below. For the primary endpoint, SALT ≤10 at Week 24, the absolute difference in response rate versus placebo was 11.88% (95% Confidence Interval (CI); 5.42 to 18.33). Treatment effects were more pronounced with the less stringent secondary outcome, SALT ≤20 at Week 24; the difference versus placebo was 21.43% (95% CI; 13.37 to 29.48). PGI-C response at Week 24 was also met with a difference in response rate of 39.96% (95% CI; 28.85 to 51.06) versus placebo. Participants treated with ritlecitinib reported an improvement in AA patient priority outcomes (AAPPO) emotional symptom scores; other Health Related Quality of Life (HRQoL) outcomes (including the EQ-5D), reported small increases or no change with ritlecitinib treatment.

ALLEGRO-LT is an ongoing phase 3, open-label, long-term trial which enrolled 1,052 participants. The ALLEGRO-LT study included de-novo participants with SALT ≥25 and roll over participants with severe AA (SALT ≥50). Only the roll over participant population can be considered when assessing the long-term effects of ritlecitinib in patients with severe AA (SALT ≥50). Rollover participants received ritlecitinib 50mg o.d. Efficacy analyses were descriptive in nature. The ALLEGRO-LT results provide some evidence of the durability of effectiveness of ritlecitinib but are subject to uncertainty.

The Review Group noted a number of limitations of the clinical trial evidence including the open-label nature of studies (ALLEGRO-LT and after Week 24 in ALLEGRO-2b/3), uncertainty over the optimal duration of treatment for ritlecitinib, lack of data on a continued treatment

effect after discontinuation and the lack of direct comparative evidence versus other JAK inhibitors.

2. Safety of ritlecitinib

Safety data for ritlecitinib were obtained from five studies (including ALLEGRO-2b/3 and ALLEGRO-LT). Overall, 1,011 participants (including 133 adolescents) were exposed to ritlecitinib at a dose of 50mg o.d. or higher for ≥12 months. In the one-year exposure pool (OYEP), the proportion of participants with at least one treatment related treatment emergent adverse event (TEAE) was 44%, the proportion of participants with at least one serious adverse event (SAE) was 2.3% and the proportion of participants who permanently discontinued ritlecitinib due to adverse events (AEs) was 3%. The most common TEAEs in participants receiving ritlecitinib 50mg o.d. were nasopharyngitis (14.2%), headache (12.6%), upper respiratory tract infection (11.1%), diarrhoea (8.0%), folliculitis (7.3%), acne (6.9%), urticaria (6.1%), nausea (5.4%), dizziness (5.0%), fatigue (3.8%) and myalgia (3.4%). Infections, malignancies (including non-melanoma skin cancer), major adverse cardiovascular events and thromboembolic events, neurological, and audiological events were identified as AEs of special interest. The safety data set is considered too limited for detection of infrequent serious AEs considered class effects of JAK inhibitors (major adverse cardiovascular events, venous thromboembolism, malignancies, serious infections).

3. Cost effectiveness of ritlecitinib

Methods

A semi-Markov model included eight health states based on different ranges of SALT scores (SALT ≥50, SALT 21-49, SALT 11-20 and SALT ≤10) and treatment (ritlecitinib or BSC) and an additional health state for death. The model population consisted of patients with severe AA and thus all patients enter the model with SALT ≥50 and may transition between SALT-score states during each model cycle, with transition probabilities depending on treatment. In the model, response to treatment was defined as achieving SALT ≤20, with non-responders at Week 48 and patients who lose response at any time assumed to discontinue ritlecitinib. The Review Group presented a scenario using the more stringent response criterion of SALT ≤10 as the basis for ritlecitinib discontinuation. Transition probabilities between SALT score

states and ritlecitinib discontinuation rates were estimated using data from ALLEGRO 2b/3 and ALLEGRO-LT and extrapolated over a lifetime horizon.

The Applicant claimed that the EQ-5D and SF-36 data from the trial did not adequately capture changes in Health-Related Quality of Life (HRQoL) with AA due to a perceived insensitivity towards hair loss. The Applicant chose AA health state vignette study data to model utilities in the cost-effectiveness analysis rather than those collected in the clinical trial. Insufficient information on the vignette study was provided by the Applicant, and the Review Group considered the resulting utility values to lack face-validity. Furthermore, the use of generic preference-based methods such as EQ-5D are recommended in Irish HTA guidelines. To address this, utility weights from Hanson et al (2025), which were derived from EQ-5D, were used in the NCPE adjusted base case.

The Review Group made a number of other adjustments, to the model, relating to spontaneous remission, the interim stopping rule (at Week 24), choice of time to treatment discontinuation (TTD) curve, calculation of transition probabilities, extrapolation of long-term transitions, general population mortality and carer disutility.

Results

The results of the Applicant and NCPE-adjusted base case incremental cost-effectiveness analysis are presented in Tables 1 and 2, respectively. The most influential change in incremental cost effectiveness results in the NCPE adjusted base case was the alternative source of utility values used.

Table 1: Applicant base case incremental cost-effectiveness results[a]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
BSC	29,188	11.0	-	-	-
Ritlecitinib	68,455	12.4	39,267	1.37	28,612

BSC: best supportive care; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality-adjusted life years
a Corresponding probabilistic ICER using 10,000 iterations =€29,136/QALY.
Figures in the table are rounded, and so calculations may not be directly replicable. Costs and outcomes are discounted at 4%.

Table 2: NCPE adjusted base case incremental cost-effectiveness results[a]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
BSC	28,783	16.26	-	-	-

Ritlecitinib	54,014	16.44	25,230	0.18	140,324

BSC: best supportive care; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality-adjusted life years
a Corresponding probabilistic ICER using 1,000 iterations = €160,936/QALY
Figures in the table are rounded, and so calculations may not be directly replicable. Costs and outcomes are discounted at 4%.

Sensitivity analysis

The probability of cost-effectiveness for ritlecitinib versus BSC in the Applicant and NCPE-adjusted base cases are shown in Table 3.

Table 3: Probability of cost effectiveness for ritlecitinib versus BSC[a]

Threshold (€/QALY)	Applicant base case (%)	NCPE adjusted base case (%)
20,000	0.1	0
45,000	99.8	0

BSC: best supportive care; **NCPE:** National Centre for Pharmacoeconomics; **QALY:** quality-adjusted life years
a Results based on probabilistic analyses using 10,000 iterations (Applicant base case) and 1,000 iterations (NCPE adjusted base case).

Results of a price-ICER analysis for ritlecitinib versus BSC, conducted using the NCPE-adjusted base case are shown in Table 4.

Table 4: Results of Price-ICER analysis

Threshold (€/QALY)	Reduction in ritlecitinib PtW[a]
20,000	94%
45,000	77%

ICER: incremental cost-effectiveness ratio; **PtW:** price-to-wholesaler; **QALY:** quality-adjusted life years
a Expressed as a total rebate, inclusive of the Framework Agreement Rebate (9.0%)

4. Budget impact of ritlecitinib

The price-to-wholesaler (PtW) of one pack of ritlecitinib 50mg (30-capsule pack) is €774.18. The total cost per patient per year of ritlecitinib is estimated at €10,076 (VAT not applicable to oral medicines).

Certain data sources, informing the Applicant's estimated patient population, are not validated. The Review Group considered that the Applicant's estimated eligible population may potentially be underestimated; the Applicant considered prevalent, but not incident, patients. The Applicant estimated that 54 patients will be treated with ritlecitinib in Year 1, increasing to 127 patients in Year 5. The Review Group considered the Applicant's anticipated market share for ritlecitinib to be underestimated given a lack of available treatment options in Ireland.

The Applicant estimated the five-year cumulative gross and net drug budget impact to be €4.73 million. The Review Group did not apply the NCPE-base case assumptions in relation to the interim stopping rule, the discontinuation rule and general population mortality to the Applicant's budget estimates as these were deemed to have minimal impact on the overall budget estimates. Budget impact estimates are highly uncertain and likely underestimated.

5. Patient Organisation Submission

A patient organisation submission was received from Alopecia Ireland.

6. Conclusion

The NCPE recommends that ritlecitinib not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments*.

* This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.