Ritlecitinib for treating severe alopecia areata in people 12 years and over

PAC recommendations

1. Ritlecitinib is recommended for treating severe alopecia areata (AA) in people 12 years and over in line with NICE TA958 and its marketing authorisation.
2. Patients with severe alopecia are defined as having a Severity of Alopecia Tool (SALT) score of 50 or more and where non pharmacological treatment options (i.e. wigs, psychological support) are inadequate or unacceptable.
3. Treatment should be initiated by a consultant dermatologist experienced in the diagnosis and treatment of AA. Prior to commencing ritlecitinib a discussion should be had with the patient that treatment will need to be discontinued if limited hair regrowth is achieved or if there are significant adverse effects. It is likely that any regrown hair will be lost upon discontinuation and patients should be made aware of this prior to commencing treatment.
4. Ritlecitinib is a Janus-associated kinase (JAK) inhibitor immunosuppressant. Vaccination and immunisation status of the patient should be reviewed by the initiating clinician and any required vaccinations administered in agreement with current immunisation guidelines and locally agreed arrangements. Use of live attenuated vaccines should be avoided during or immediately prior to ritlecitinib treatment. Inactivated vaccines should ideally be administered at least two weeks before commencement of ritlecitinib.
5. Prescribing and supply should be retained in secondary care. Ritlecitinib is only recommended by NICE if the company provides it according to the commercial arrangement.
6. Patients should be reviewed by the specialist team initiating treatment and monitored for efficacy, adherence to treatment, and adverse effects, and the benefit-risk of treatment should be re-assessed.

The following review intervals are recommended in line with the NICE clinical and cost effectiveness assessment undertaken as part of TA958:

- 4 weeks after starting treatment: Blood monitoring in accordance with the Summary of Product Characteristics is required after 4 weeks treatment. See point 8 for further details.
- 24 weeks (6 months) after starting treatment: Treatment should be discontinued at this review if patients show a worsening in their condition, i.e. a higher SALT score than at initiation.
- 48 weeks (12 months) after starting treatment: Treatment should be discontinued in patients where an absolute SALT score of ≤20 is not achieved.
- Annual review: The ongoing therapeutic benefit of ritlecitinib should be reviewed at least annually thereafter and the benefits and risks of ongoing treatment discussed with the patient. Where initial therapeutic benefit has not been maintained, treatment with ritlecitinib should be discontinued.

7. The risk and benefits of treatment with ritlecitinib should be considered prior to initiating treatment, and on continuing treatment, particularly in patients with a known malignancy other than successfully treated non-melanoma skin cancer (NMSC) or cervical cancer, patients with known risk factors for thromboembolism i.e. previous VTE, patients undergoing major surgery, immobilisation, combined hormonal contraceptive or hormonal replacement therapy use or inherited coagulation disorder. Ritlecitinib treatment should be discontinued in patients with a suspected thromboembolic event.
8. Treatment with ritlecitinib should not be initiated in patients with an absolute lymphocyte count (ALC) < 0.5 × 10^3/mm^3 or a platelet count < 100 × 10^3/mm^3. Platelet count and lymphocytes should be monitored before treatment initiation, 4 weeks after initiation and at each subsequent review according to routine patient management and as set out in the Summary of Product Characteristics. Treatment with ritlecitinib may need to be interrupted or discontinued based on ALC and platelet count abnormalities. Treatment with ritlecitinib must not be initiated in patients with an active, serious infection. Treatment should be interrupted if a patient develops a serious or opportunistic infection.

Key points

NICE recommendations

In March 2024, NICE published TA958, Ritlecitinib for treating severe AA in people 12 years and over.[1]

- Ritlecitinib is recommended, within its marketing authorisation, as an option for treating severe AA in people 12 years and over.
- Ritlecitinib is only recommended if the company provides it according to the commercial arrangement.[1]

AA is a chronic, inflammatory condition affecting the hair follicles which leads to sudden onset of non-scarring alopecia (hair loss where the hair follicles are generally preserved).[2]

Severity of alopecia

The main evidence for ritlecitinib considered by the NICE committee was from the ALLEGRO phase 2b/3 trial (ALLEGRO 2b/3) and the ALLEGRO long-term follow-up trial (ALLEGRO-LT). ALLEGRO 2b/3 was a multi-arm mixed methods trial including 2 phases, in people 12 years and over with severe AA (defined by a SALT score of 50 or more).[1]

The SALT score is based on percentage loss of scalp hair with severe AA defined as having at least 50% loss of scalp hair (SALT score of ≥50).[3]

In July 2024, The British Association of Dermatologists (BAD) published professional guidance supplementary to NICE TA958 which advocated adjusting the SALT-based severity rating when other additional factors are present.[3]

The guidance recommends that people with moderate-AA (absolute SALT score 21-49) may have their severity rating increased by one level to severe, if one or more of the following are present:

- Negative impact on psychological functioning resulting from AA
- Noticeable involvement of eyebrows or eyelashes
- Inadequate response after at least 6 months of treatment (treatments include topical or intralesional steroids or oral steroids, etc.)
- Diffuse (multifocal) positive hair pull test consistent with rapidly progressive AA.[3]

NICE have not assessed the clinical and cost effectiveness of ritlecitinib in patients with a SALT score <50, and use in this wider cohort of patients is not currently recommended.[1]

Review and stopping treatment

The NICE recommendations state that the committee concluded that the evidence from clinical trials shows that ritlecitinib is more effective than placebo at improving hair regrowth after 24 weeks.[1,4,5] However, the NICE committee papers indicate that the committee evaluated the clinical and cost effectiveness up to 48 weeks.[1,4,5] Absolute stopping rules were included in the clinical and cost effectiveness cases at 24 and 48 weeks, with treatment discontinued if clinical condition had worsened at 24 weeks and where an absolute SALT score of ≤20 was still not achieved at 48 weeks.[4,5] The Summary of Product Characteristics (SPC) for ritlecitinib states: Consideration should be given to discontinuing patients who show no evidence of therapeutic benefit after 36 weeks.[6]

The BAD professional guidance recommends the following:

At week 36, clinicians should consider the following, depending on treatment response:

- If no response at all, then ritlecitinib should be stopped at this point.
- If terminal regrowth has been noted on examination, but an absolute SALT score of ≤20 is not achieved, then consider extending treatment duration for a further 3 months. If at that extended point, an absolute SALT score of ≤20 is still not achieved, then treatment should be discontinued.[3]

Treatment must only be initiated and continued in accordance with the current Summary of Product Characteristics.[6] The following clinical criteria should be assessed and considered and treatment stopped if the risks outweigh the benefits of continued treatment.

Haematologic abnormalities

Treatment with ritlecitinib should not be initiated in patients with an absolute lymphocyte count (ALC) < 0.5 x 10^3/mm^3 or a platelet count < 100 x 10^3/mm^3. Platelet count and lymphocytes should be monitored before treatment initiation, 4 weeks after initiation and at each subsequent review according to routine patient management, as set out in the Summary of Product Characteristics. Treatment with ritlecitinib may need to be interrupted or discontinued based on ALC and platelet count abnormalities.[6]

Infections

Ritlecitinib is a Janus-associated kinase (JAK) inhibitor immunosuppressant. Serious infections have been reported in patients receiving ritlecitinib. The most frequent serious infections have been appendicitis, COVID-19 infection (including pneumonia), and sepsis. Treatment with ritlecitinib must not be initiated in patients with an active, serious infection.[6]

The risks and benefits of treatment should be considered in patients:

- With chronic or recurrent infection
- Who have been exposed to tuberculosis (TB)
- With a history of serious or opportunistic infection
- Who have resided or travelled in areas of endemic TB or mycoses, or
- With underlying conditions that may predispose them to infection.[6]

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with ritlecitinib. Treatment should be interrupted if a patient develops a serious or opportunistic infection. A patient who develops a new infection during treatment with ritlecitinib should undergo prompt and complete diagnostic testing appropriate for an immunocompromised patient, appropriate antimicrobial therapy should be initiated, and the patient should be closely monitored. If interrupted, ritlecitinib may be resumed once the infection is controlled.[6]

Prior to initiating ritlecitinib, it is recommended that patients are brought up to date with all immunisations, including prophylactic herpes zoster vaccinations. The initiating healthcare professional

should review vaccination status and arrange for any needed vaccinations to be administered in agreement with current immunisation guidelines and locally agreed arrangements. Use of live attenuated vaccines should be avoided during or immediately prior to ritlecitinib treatment.[6] For individuals due to commence immunosuppressive treatments, inactivated vaccines should ideally be administered at least two weeks before commencement.[7]

Patients should be screened for TB before starting therapy with ritlecitinib. Ritlecitinib must not be given to patients with active TB. Anti-TB therapy should be started prior to initiating therapy with ritlecitinib in patients with a new diagnosis of latent TB or previously untreated latent TB. In patients with a negative latent TB test, anti-TB therapy should still be considered before initiating treatment with ritlecitinib in those at high risk and screening for patients at high risk for TB during treatment with ritlecitinib should be considered.[6]

Viral reactivations, including cases of herpes virus reactivation (e.g. herpes zoster), have been reported. If a patient develops herpes zoster, temporary interruption of treatment may be considered until the episode resolves.[6]

Screening for viral hepatitis should be performed in accordance with clinical guidelines before starting therapy with ritlecitinib. Patients with evidence of hepatitis B or C infection were excluded from studies with ritlecitinib. Monitoring for reactivation of viral hepatitis according to clinical guidelines is recommended during ritlecitinib treatment. If there is evidence of reactivation, a liver specialist should be consulted.[6]

Malignancy

Malignancies, including non-melanoma skin cancer (NMSC) have been reported in patients receiving ritlecitinib. Limited clinical data are available to assess the potential relationship of exposure to ritlecitinib and the development of malignancies. The risks and benefits of ritlecitinib treatment should be considered prior to initiating or continuing therapy in patients with a known malignancy other than a successfully treated NMSC or cervical cancer.

Periodic skin examination is recommended for patients who are at increased risk of skin cancer.[6]

Suspected Thromboembolic Events

Ritlecitinib treatment should be discontinued and treatment re-evaluated promptly in patients with a suspected thromboembolic event. Ritlecitinib should be used with caution in patients with known risk factors for thromboembolism (i.e. previous VTE, patients undergoing major surgery, immobilisation, combined hormonal contraceptive or hormonal replacement therapy use or inherited coagulation disorder).[6]

Neurological events

Treatment with ritlecitinib should be discontinued in cases of unexplained neurological symptoms occur.[6]

Interactions

Ritlecitinib is a moderate inhibitor of CYP3A; caution should be exercised with concomitant use of ritlecitinib with CYP3A substrates (e.g. quinidine, ciclosporin, dihydroergotamine, ergotamine, pimozide) where moderate concentration changes may lead to serious adverse reactions. Dose adjustment recommendations for the CYP3A substrate (e.g. colchicine, everolimus, tacrolimus, sirolimus) should be considered. Caution should be exercised with concomitant use of ritlecitinib with OCT1 substrates (e.g. sumatriptan) where small concentration changes may lead to serious adverse reactions. Ritlecitinib is a moderate inhibitor of CYP1A2; caution should be exercised with concomitant use of ritlecitinib with other CYP1A2 substrates (e.g. tizanidine) where moderate concentration changes may lead to serious adverse reactions. Dose adjustment recommendations for the CYP1A2 substrate (e.g. theophylline, pirfenidone) should be considered.[6]

Women of child bearing potential

Ritlecitinib is contraindicated during pregnancy. Ritlecitinib is not recommended in women of childbearing potential not using contraception. Women of childbearing potential have to use effective contraception during treatment and for 1 month following the final dose of ritlecitinib.[6]

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Document history

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