bpac^{nz} Quick Clinical Knowledge

B-QuiCK: Treatment resistant atopic dermatitis

Approach atopic dermatitis treatment in a stepwise manner; begin with **emollients** and **topical corticosteroids** (or **topical calcineurin inhibitors**, i.e. tacrolimus or pimecrolimus). Increase potency of topical corticosteroids as required.

Consider referral for **phototherapy** for patients with inadequate response to first-line treatments.

Oral systemic immunosuppressants are the usual next step. Continue emollients and topical corticosteroids alongside. Trial conventional immunosuppressants first: ciclosporin, methotrexate, mycophenolate mofetil or azathioprine.

- Consider patient-specific factors when deciding which to prescribe. In general, methotrexate may be chosen first by primary care clinicians due to familiarity (but avoid if pregnancy is possible), or ciclosporin given it is indicated for atopic dermatitis (but avoid if renal dysfunction). See Table 1 for prescribing information for all options.
- A dermatologist is usually involved (via written/verbal advice or referral) as these medicines are associated with significant adverse effects and ongoing monitoring requirements; however, dermatologist input is not a requirement for funded prescribing of most of these treatments in primary care
- Refer to NZF or check local HealthPathways for information on laboratory testing, adverse effects and monitoring requirements for each medicine, in general:
    - Perform baseline laboratory testing, e.g. FBC, LFTs, renal function and hepatitis B/C, HIV, varicella zoster, tuberculosis (Quantiferon TB-Gold) screening
    - Monitor for hepatotoxicity, neutropenia, anaemia and serious infections
- Trial for at least 12 weeks before assessing response; ongoing use depends on the medicine, e.g. ciclosporin should not be used long term

✋ **Patient still experiencing inadequate response?** If adding one of these conventional systemic immunosuppressants to the treatment regimen does not control symptoms (or is contraindicated), consider upadacitinib, **an oral JAK inhibitor**.
Take care when switching patients from a conventional systemic immunosuppressant to upadacitinib as disease flare may occur; a bridging course of oral corticosteroids may be appropriate.

Prescribing upadacitinib

- Upadacitinib is approved for the treatment of moderate to severe atopic dermatitis in people aged ≥ 12 years
- It is funded with Special Authority approval for patients (of any age) with moderate to severe atopic dermatitis (defined by an EASI score ≥ 16 or DLQI ≥ 10) who have achieved insufficient benefit from at least one month of topical treatment and three months of conventional systemic immunosuppressant treatment, where appropriate. Special Authority applications can be made by any relevant practitioner. See box for full Special Authority criteria.

Upadacitinib funded with Special Authority approval

To be eligible for funded upadacitinib the patient must meet the following Special Authority criteria:

- Currently taking upadacitinib for atopic dermatitis and met all remaining Special Authority criteria (below) prior to commencing treatment; ***OR***
- Patient has moderate to severe atopic dermatitis, i.e. EASI score ≥ 16 or DLQI score ≥ 10; ***AND***
- Patient has achieved insufficient benefit from a 28-day trial of topical treatment (including topical corticosteroids or calcineurin inhibitors) within the last six months (unless contraindicated to all); ***AND***
- Patient has trialled and achieved insufficient benefit from at least one systemic treatment (e.g. ciclosporin, azathioprine, methotrexate, mycophenolate mofetil) for at least three months (unless contraindicated to all); ***AND***
- EASI or DLQI assessment has been completed for at least the most recent prior treatment course, preferably while still on treatment, but no longer than one month following cessation of each prior treatment course; ***AND***
- The most recent EASI or DLQI assessment is no more than one month old at the time of application

N.B. Upadacitinib is approved for use in people aged ≥ 12 years, however, there is no age restriction on funding.

Initial Special Authority approval is valid for six months. Renewals require that the patient has achieved a ≥ 75% reduction in EASI score, or a DLQI improvement of ≥ 4, compared to baseline EASI/DLQI score prior to starting treatment with upadacitinib. Renewals are valid for 12 months.

Key prescribing and monitoring information for upadacitinib. N.B. Seek dermatology advice where needed.

Moderate to severe atopic dermatitis	15 mg, once daily, increased to 30 mg, once daily, for patients aged under 65 years if there is inadequate response. N.B. Doses > 15 mg are not recommended for patients aged ≥ 65 years, or patients with severe renal impairment.
Before starting	• **Assess** for cardiovascular risk factors, including risk/history of thromboembolism, history of malignancy, pregnancy and breast-feeding status (consider a pregnancy test if relevant) and the presence of an active infection • **Check immunisation status**. Ensure patients are up to date with National Immunisation Schedule vaccinations, as well as influenza and COVID-19. Offer catch-up vaccinations prior to starting treatment, including varicella zoster (Shingrix; recommended but not funded for patients before, during or after immunosuppressant treatment, unless they meet other criteria for funding). Immunisation with live vaccines is not recommended during treatment. • **Request baseline laboratory testing,** including FBC, LFTs, renal function and lipids. Screen for tuberculosis (Quantiferon TB-Gold), HIV, varicella zoster serology and hepatitis B and C. Include "pre-immunosuppression screen" on these requests. N.B. These screening tests may have previously been requested if the patient was recently started on a conventional systemic immunosuppressant, but consider repeating relevant tests if subsequent disease exposure is possible. See Table 2 for contraindications and cautions
Ongoing monitoring	• Initially, monitoring should occur more often, e.g. after one month, and reduce in frequency over time, e.g. every three months or as clinically indicated • **Monitor for adverse effects**, in particular infection and venous thromboembolism or MACE. Temporarily stop treatment if an infection or signs of venous thromboembolism occur; evaluate/manage as indicated. • **Perform skin examinations** periodically, especially for patients at increased risk of skin cancer • **Monitor laboratory parameters** (e.g. FBC, LFTs, lipids) throughout treatment as clinically indicated. Usually, re-check levels one month after treatment initiation, and then every three months or as clinically indicated. • Temporarily stop treatment if laboratory parameters become abnormal (Table 2) or if

	medicine-induced liver injury is suspected. Initiate or optimise lipid-lowering treatment as needed. • **Monitor response to treatment.** Repeat EASI and DLQI to assess severity and quality of life compared to baseline. Special Authority renewals every six months need a ≥ 75% reduction in EASI score, or a DLQI improvement of ≥ 4, compared to baseline.
Notes	• Females of child-bearing potential should use effective contraception during, and for four weeks after, treatment. Upadacitinib should be stopped if patients become pregnant during treatment.

✋ **Refer following inadequate response**

Seek dermatology advice (verbal or written) or refer the patient for dermatology assessment if intolerable adverse effects are experienced or response to upadacitinib is insufficient following six months of treatment.

✍ **Best Practice Tip.** Ensure dermatology referral requests contain as much information as possible, including photographs showing the size and extent of the affected areas(s), information about treatments trialled and their duration and the impact on the patient's quality of life (e.g. DLQI score).

B-QuiCK provides short clinical summaries from some of the full articles available on our website. Relevant sections from these resources have been condensed into "notepad pages" or algorithms designed to offer rapid access to practical clinical advice and knowledge. It is strongly recommended to review the original resource at your convenience for full details of recommendations and evidence. See full article here: **https://bpac.org.nz/2025/atopic-dermatitis.aspx**

www.bpac.org.nz/b-quick

Tables

Table 1. Conventional immunosuppressants used for patients with treatment resistant atopic dermatitis. N.B. There is an extensive list of contraindications and cautions for these medicines which should be assessed for each patient prior to prescribing. See individual medicines monographs in the NZF for specific contraindications and cautions.

Systemic immunosuppressant	Dose	Notes
Ciclosporin	2.5 mg/kg/day in two divided doses, increased to 5 mg/kg/day if insufficient response N.B. 5 mg/kg/day can be prescribed initially if atopic dermatitis is very severe.	• Can cause nephrotoxicity so regular renal function and blood pressure monitoring is required, usually monthly. Stop treatment if patients are not adhering to regular monitoring. • Not suitable for long-term use (generally six months to two years) • Preferred option for females of child-bearing potential, however, use with care in younger patients with co-morbidities such as hypertension or high BMI • In practice it is not generally prescribed to patients aged over 40 – 45 years due to increased risk of age-related renal decline • Hirsutism may limit use • More rapid onset of action compared to methotrexate, azathioprine and mycophenolate mofetil
Methotrexate (unapproved indication)	Oral 5 – 25 mg, once per week.* In practice, a dose of 10 – 20 mg, once per week is often prescribed.	• Some formulations and strengths of methotrexate have a funding restriction, including the available oral tablets (2.5 mg and 10 mg): *Retail pharmacy-specialist*. See NZF for affected formulations and strengths. This means that the medicine will only be funded in the community on prescription by a specialist or with recommendation by a specialist. For further details, see the Pharmaceutical Schedule rules. The definition of a specialist is not specified in the restriction for methotrexate; many primary care prescribers will initiate this medicine in consultation with a dermatologist, however, vocationally

		registered general practitioners who feel comfortable initiating methotrexate may do so (as the specialist) without seeking input from a dermatologist. The medicine datasheet notes that methotrexate should only be prescribed by physicians with expertise in its use and a full understanding of the risks. The prescriber should also feel confident that the patient will adhere to the once-weekly regimen. • Highlight differences in the appearance of 2.5 mg and 10 mg tablets, especially when a patient is transferred from one tablet strength to another; prescribe only one strength of tablet at once to avoid accidental ingestion of 10 mg tablets in place of 2.5 mg tablets • Folic acid (5 mg per week, on an alternate day to methotrexate, e.g. methotrexate Mondays, folic acid Fridays; unapproved indication) should also be prescribed • Nausea may limit use (subcutaneous administration may overcome this adverse effect) • Teratogen and possible mutagen – not first choice for females of child-bearing potential or males planning parenthood • Some severe medicine interactions, e.g. with trimethoprim + sulfamethoxazole, which is often used for infected atopic dermatitis
Mycophenolate mofetil (unapproved indication)	1 – 3 g/day*	• There is inconsistency between international guidelines as to whether mycophenolate mofetil is recommended for patients with atopic dermatitis. In New Zealand, it is included in local HealthPathways as a medicine that could be trialled, and is listed as an option for one of the pre-requisites in the Special Authority criteria for upadacitinib. • Teratogen – not first choice for females of child-bearing potential
Azathioprine	Normal or high thiopurine	• Requires TPMT to be measured prior to starting treatment. TPMT is an enzyme

(unapproved indication)	methyltransferase (TPMT) activity: 1 – 3 mg/kg/day Intermediate TPMT activity: 0.5 – 1.5 mg/kg/day	that metabolises azathioprine (and other thiopurine medicines). The activity of the enzyme can help to predict those at risk of myelosuppression; low activity is associated with higher risk, and therefore a dose reduction is necessary. High activity may require dose up-titration. Azathioprine is usually avoided in patients with low TPMT activity. • Lower risk in pregnancy than other options • Increased risk of UV-induced skin cancers with long-term use • Many medicine interactions, e.g. allopurinol, ACE inhibitors
Dupilumab (IV; Section 29, not funded) is a biologic often used in preference to other conventional systemic immunosuppressants; however, it is neither approved nor readily available in New Zealand.		

* Dosing recommended in international guidelines; dosing not provided by NZF

Table 2. Contraindications and cautions for upadacitinib.

Contraindications	Cautions
• Active serious infection, e.g. active tuberculosis* • Absolute lymphocyte count < 0.5 × 10^9/L* • Absolute neutrophil count < 1 × 10^9/L* • Haemoglobin < 80 g/L* • Severe hepatic impairment • Pregnancy • Breast-feeding	• Age ≥ 65 years • Diverticular disease • Risk factors for cardiovascular disease or thrombosis • Diabetes • Current or past malignancy (except successfully treated non-melanoma skin cancer) • Concomitant use of potent CYP3A4 inhibitors or inducers, e.g. grapefruit juice, rifampicin • Chronic or recurrent infection, history of serious or opportunistic infection or predisposition to infection • Hepatitis B or herpes zoster reactivation • End-stage renal impairment (no dose adjustment is required for patients with mild to moderate renal impairment; a maximum dose of 15 mg, daily, should be given in severe impairment)

* Treatment can begin once the active infection is controlled, or parameters return above these values