Medicines Management Programme

Managed Access Protocol for high tech medicines for the treatment of moderate-to-severe atopic dermatitis

Medicine	Date of addition to Managed Access Protocol
Dupilumab (Dupixent®)	01/04/2021
Upadacitinib (RINVOQ®)	01/02/2022
Tralokinumab (Adtralza®)	01/03/2022
Abrocitinib (Cibinqo®)	01/07/2022

Approved by	**Professor Michael Barry, Clinical Lead, MMP**	
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	Version 5.0	19/04/2023
	Version 6.0	25/07/2024
	Version 6.1	02/01/2025

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AD	Atopic dermatitis
BSC	Best supportive care
CDLQI	Children's dermatology life quality index
DLQI	Dermatology life quality index
EASI	Eczema area and severity index
HSE	Health Service Executive
IgG4	Immunoglobulin G4
IL	Interleukin
JAK	Janus kinase inhibitor
MACE	Major adverse cardiovascular events
MAP	Managed access protocol
MMP	Medicines Management Programme
PFP	Pre-filled pen
PFS	Pre-filled syringe
SmPC	Summary of medicinal product characteristics
TYK	Tyrosine kinase
VTE	Venous thromboembolism

1. High tech medicines for the treatment of atopic dermatitis

There are currently four medicines referenced in this Managed Access Protocol (MAP) that are available under the High Tech Arrangement for the treatment of moderate-to-severe atopic dermatitis (AD); abrocitinib (Cibinqo®), dupilumab (Dupixent®), tralokinumab (Adtralza®) and upadacitinib (RINVOQ®).

Cibinqo® contains abrocitinib. Abrocitinib is a janus kinase (JAK) 1 inhibitor. In biochemical assays, abrocitinib has selectivity for JAK1 over the other three JAK isoforms; JAK2, JAK3 and tyrosine kinase 2 (TYK2). In cellular settings, it preferentially inhibits cytokine-induced signal transducers and activators of transcription phosphorylation by signalling pairs involving JAK1, and spares signalling by JAK2/JAK2, or JAK2/TYK2 pairs. AD is driven by pro-inflammatory cytokines, including interleukin (IL)-4, IL-13, IL-22, thymic stromal lymphopoietin, IL-31 and interferon gamma, that transduce signals via the JAK1 pathway.

From July 2022, three presentations of abrocitinib (Cibinqo®) are available on the High Tech Arrangement for the treatment of moderate-to-severe AD:

- Cibinqo® 50 mg film-coated tablets
- Cibinqo® 100 mg film-coated tablets
- Cibinqo® 200 mg film-coated tablets.

Dupixent® contains dupilumab. Dupilumab is a recombinant human immunoglobulin G4 (IgG4) monoclonal antibody that inhibits IL-4 and IL-13 signalling. It is produced in Chinese hamster ovary cells by recombinant DNA technology.

From April 2021, two presentations of dupilumab (Dupixent®) are available on the High Tech Arrangement for the treatment of moderate-to-severe AD:

- Dupixent® 200 mg solution for injection pre-filled pen (PFP)
- Dupixent® 300 mg solution for injection PFP.

From May 2021, a further two presentations of dupilumab (Dupixent®) are available on the High Tech Arrangement for the treatment of moderate-to-severe AD:

- Dupixent® 200 mg solution for injection pre-filled syringe (PFS)
- Dupixent® 300 mg solution for injection PFS.

Adtralza® contains tralokinumab. Tralokinumab is fully human IgG4 monoclonal antibody that specifically binds to the type 2 cytokine IL-13 and inhibits its interaction with the IL-13 receptors. It is produced in mouse myeloma cells by recombinant DNA technology.

From March 2022, one presentation of tralokinumab (Adtralza®) is available on the High Tech Arrangement for the treatment of moderate-to-severe AD:

- Adtralza® 150 mg solution for injection in PFS.

From August 2024, a further presentation of tralokinumab (Adtralza®) is available on the High Tech Arrangement for the treatment of moderate-to-severe AD:

- Adtralza® 300mg solution for injection PFP.

RINVOQ® contains upadacitinib. Upadacitinib is a selective and reversible JAK inhibitor. In human cellular assays, upadacitinib preferentially inhibits signalling by JAK1 or JAK1/3 with functional selectivity over cytokine receptors that signal via pairs of JAK2.

From February 2022, two presentations of RINVOQ® are available on the High Tech Arrangement for the treatment of moderate-to-severe AD:

- RINVOQ® 15 mg prolonged-release tablets
- RINVOQ® 30 mg prolonged-release tablets.

1.1 Licensed indications

Abrocitinib, dupilumab, tralokinumab and upadacitinib are indicated for the treatment of moderate-to-severe AD in adults and adolescents 12 years and older who are candidates for systemic therapy. Additionally, dupilumab is indicated or the treatment of severe atopic dermatitis in children 6 months to 11 years old who are candidates for systemic therapy.

In addition, dupilumab and upadacitinib are indicated in a number of other disease areas that are outside the scope of this managed access protocol (MAP).

1.2 Reimbursement

Reimbursement of the high tech medicines for the treatment of moderate-to-severe AD under this MAP is supported only for adult patients (abrocitinib, dupilumab, tralokinumab and upadacitinib) and adolescent patients aged 12 years and older (dupilumab and upadacitinib) for whom immunosuppressant treatment has failed, or is not tolerated or is contraindicated, and who meet

the criteria outlined in this MAP. All criteria must be satisfied in order for reimbursement to be supported.

An application for reimbursement approval is required to be submitted on an individual patient basis through the online application system.

Table 1 outlines the licensed therapeutic dosages of the high tech medicines for the treatment of moderate-to-severe AD for adults (abrocitinib, dupilumab, tralokinumab and upadacitinib) and adolescents aged 12 years and older (dupilumab and upadacitinib), which are relevant to this MAP. Please refer to the relevant Summary of Product Characteristics (SmPC) for further prescribing information.

Table 1 Licensed therapeutic dosages of the high tech medicines for the treatment of atopic dermatitis

Medicine	Route of administration	Dosage
Abrocitinib in adults	Oral	100 mg or 200 mg once daily, based on individual patient characteristics[i]
Dupilumab in adolescents aged 12 to 17 years, weighing < 60 kg	Subcutaneous	Initial dose of 400 mg followed by 200 mg every other week
Dupilumab in adolescents aged 12 to 17 years, weighing ≥ 60 kg	Subcutaneous	Initial dose of 600 mg followed by 300 mg every other week
Dupilumab in adults	Subcutaneous	Initial dose of 600 mg followed by 300 mg every other week
Tralokinumab in adults	Subcutaneous	Initial dose of 600 mg followed by 300 mg every other week[ii]
Upadacitinib in adolescents aged 12 to 17 years weighing at least 30 kg	Oral	15 mg once daily. If the patient does not respond adequately to 15 mg once daily, the dose can be increased to 30 mg once daily.
Upadacitinib in adults	Oral	15 mg or 30 mg once daily, based on individual patient presentation[iii]

kg: kilogrammes; mg: milligram; SC: subcutaneous

[i] A starting dose of 100 mg once daily is recommended for patients at higher risk of venous thromboembolism (VTE), major adverse cardiovascular event (MACE) and malignancy. A dose of 200 mg once daily may be appropriate for patients who are not at higher risk of VTE, MACE and malignancy with high disease burden. During treatment, the dose of abrocitinib may be decreased or increased based on tolerability and efficacy. The lowest effective dose for maintenance should be considered. The maximum daily dose of abrocitinib is 200 mg.

[ii] At the prescriber's discretion, every fourth week dosing may be considered for patients who achieve clear or almost clear skin after 16 weeks of treatment. The probability of maintaining clear or almost clear skin may be lower with every fourth week dosing.

[iii] A dose of 15 mg is recommended for patients at higher risk of VTE, MACE and malignancy. A dose of 30 mg once daily may be appropriate for patients with high disease burden who are not at higher risk of VTE, MACE and malignancy or patients with an inadequate response to 15 mg once daily. The lowest effective dose to maintain response should be used. For patients ≥ 65 years of age, the recommended dose is 15 mg once daily.

If a patient is recommended for reimbursement of abrocitinib, dupilumab, tralokinumab or upadacitinib, reimbursement is supported up to the relevant maximum licensed dosage specified in Table 1. Reimbursement of dosages in excess of the licensed therapeutic dosages (as outlined in this MAP) is not supported. Reimbursement is not supported for concomitant use of high tech medicines for the treatment of moderate-to-severe AD.

See Section 3.1 for further details on treatment discontinuation.

1.3 Reimbursement price

The reimbursement price of the presentations of abrocitinib, dupilumab, tralokinumab and upadacitinib available on the High Tech Arrangement are outlined in table 2. Commercial-in-confidence arrangements are in place with the marketing authorisation holders to reduce the net acquisition cost of these medicines to the Health Service Executive (HSE).

Table 2 Reimbursement codes and prices for the presentations of abrocitinib, dupilumab, tralokinumab and upadacitinib available on the High Tech Arrangement

Strength (pack size)	Code	Reimbursement price*
Cibinqo® 50 mg film-coated tablets (28 pack)	89195	€1,085.40
Cibinqo® 100 mg film-coated tablets (28 pack)	89196	€1,085.40
Cibinqo® 200 mg film-coated tablets (28 pack)	89198	€1,085.40
Dupixent® 200 mg PFP (2 x 1.14 ml)	89072	€1,232.34
Dupixent® 300 mg PFP (2 x 2 ml)	89073	€1,228.07
Dupixent® 200 mg PFS (2 x 1.14 ml)	89074	€1,222.64
Dupixent® 300 mg PFS (2 x 2 ml)	89075	€1,227.32
Adtralza® 150 mg PFS (2 packs of 2 x 1 ml)	89167	€1,103.80
Adtralza® 300 mg PFP (2 x 2ml)	89051	€1,103.80
RINVOQ® 15 mg prolonged-release tablets (28 pack)	89057	€846.16
RINVOQ® 30 mg prolonged-release tablets (28 pack)	89155	€1,246.16

mg: milligram; ml: millilitre; PFP: pre-filled pen; PFS: pre-filled syringe
*Correct as at 02/01/2025

2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for a patient to be recommended for reimbursement of high tech medicines for the treatment of moderate-to-severe AD under the High Tech Arrangement.

2.1 Prescribers

Applications for reimbursement approval for abrocitinib, dupilumab, tralokinumab or upadacitinib for the treatment of moderate-to-severe AD under the High Tech Arrangement will only be considered from consultant dermatologists registered with the Irish Medical Council, practising in the healthcare system in the Republic of Ireland, and who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants').

Approved consultants are responsible for ensuring that the patient or their representative/guardian is aware that the application for reimbursement approval is being made on their behalf.

The prescribing of Cibinqo®, Dupixent®, Adtralza® and RINVOQ® for approved patients for the treatment of AD under the High Tech Arrangement is confined to the approved consultants and their teams. The governance of the team on the High Tech Hub, including access, rests with the approved consultant.

2.2 Patient age

Applications for reimbursement approval of Dupixent® and RINVOQ® will only be considered for individuals aged 12 years or older at time of application.

Applications for reimbursement approval of Cibinqo® and Adtralza® will only be considered for individuals aged 18 years or older at time of application.

2.3 Patient diagnosis

Clinicians will be required to confirm a diagnosis of AD at the time of application. This diagnosis should be made in line with the American Academy of Dermatology criteria, as outlined in Appendix 1.

Reimbursement under the High Tech Arrangement will only be supported for patients who are classified as having chronic AD for:

- At least one year prior to the application date in adolescent patients aged 12 to 17 years, or
- At least three years prior to the application date in patients aged 18 years and older.

2.3.1 Eczema Area and Severity Index score

Clinicians will be required to confirm the patient's eczema area and severity index (EASI) score at the time of application. Reimbursement will only be supported for patients with an EASI score ≥ 16.

2.3.2 Children's Dermatology Life Quality Index/Dermatology Life Quality Index score

Clinicians will be required to confirm either the children's dermatology life quality index (CDLQI) score or the dermatology life quality index (DLQI) score for the patient at the time of application.

2.4 Patient clinical history/status

In line with SmPCs for Cibinqo®, Dupixent®, Adtralza® and RINVOQ®, applications for reimbursement approval will not be considered for individuals who meet any of the contraindications for treatment as outlined in the relevant SmPCs.

2.5 Patient's medical treatment

Reimbursement will only be supported in refractory AD, when:

- The patient has had an inadequate response (defined as failure to achieve and maintain remission or a low disease activity state) to an immunosuppressant medicine, or where such treatment is not tolerated or is contraindicated, and
- The patient is using best supportive care (BSC) for AD.

The patient may or may not have trialled other treatments (such as phototherapy).

2.5.1 Immunosuppressant medicine response inadequate

Reimbursement will be supported for patients who have had an inadequate response to a trial of at least one immunosuppressant medicine. For the purpose of reimbursement approval, an adequate trial of a medicine is defined as a period of at least three consecutive months. The trial of an immunosuppressant medicine must have taken place within three years prior to the application date.

Clinicians will be required to demonstrate that at least one of the medicines from the current standard of care for moderate-to-severe AD has been trialled prior to the application. Such medicines include[iv]:

- Ciclosporin

[iv] Not all medicines are licensed for the treatment of moderate-to-severe atopic dermatitis. Please refer to each individual product's Summary of Product Characteristics (SmPC) for further details.

- Methotrexate
- Azathioprine
- Mycophenolate mofetil.

When reviewing applications, the HSE-Medicines Management Programme (MMP) may request evidence to demonstrate that the patient has been adherent to the specified medicine for a period of at least three months.

2.5.2 Immunosuppressant medicine is not tolerated

In cases where a patient did not tolerate a medicine and experienced a clinically significant adverse reaction which led to discontinuation of treatment prior to completion of an adequate trial, information in relation to the duration of treatment and the adverse reaction experienced should be provided.

2.5.3 Immunosuppressant medicine is contraindicated

For patients in whom treatment with an immunosuppressant medicine is contraindicated, details of the contraindication, including supporting evidence, must be provided at time of application for reimbursement approval.

2.5.4 Best supportive care for atopic dermatitis

Reimbursement will only be supported for patients who are in receipt of BSC for AD. For the purpose of reimbursement approval, BSC consists of emollients, low-to-medium potency topical corticosteroids, topical calcineurin inhibitors and as-needed short-term use of rescue treatments to manage disease exacerbations (including high-potency topical corticosteroids, topical calcineurin inhibitors or systemic corticosteroids). Evidence to demonstrate the utilisation of BSC must be provided at the time of application for reimbursement approval.

3. Reimbursement criteria – Requirement for outcome data

Follow-up data may be requested by the MMP for audit purposes and provision of same is a condition of ongoing reimbursement. It is the responsibility of the approved consultant to ensure that the patient or their representative/guardian is aware that the provision of follow-up data is a condition of reimbursement, and that audits may occur during which their personal data will be reviewed.

3.1 Treatment discontinuation

Clinical evidence indicates that:

- The majority of patients who respond to abrocitinib show clinical benefit within 24 weeks
- The majority of patients who respond to dupilumab or tralokinumab show clinical benefit within 16 weeks
- The majority of patients who respond to upadacitinib show clinical benefit within 12 weeks.

In patients with AD, the following is considered a clinically meaningful response to treatment:

- an improvement in EASI score of ≥ 50%, and
- an improvement in DLQI score of ≥ 4 points.

As this is a condition of reimbursement, patients not showing these improvements in the appropriate timeframe would be considered non-responders and consideration should be given to discontinuing treatment in such patients.

Appendix 1: American Academy of Dermatology criteria for the diagnosis of atopic dermatitis[i]:

ESSENTIAL FEATURES - Must be present:

- Pruritus
- Eczema (acute, subacute, chronic)
    - Typical morphology and age-specific patterns*
    - Chronic or relapsing history

*Patterns include:

1. Facial, neck, and extensor involvement in infants and children
2. Current or previous flexural lesions in any age group
3. Sparing of the groin and axillary regions

IMPORTANT FEATURES - Seen in most cases, adding support to the diagnosis:

- Early age of onset
- Atopy
    - Personal and/or family history
    - Immunoglobulin E reactivity
- Xerosis

ASSOCIATED FEATURES - These clinical associations help to suggest the diagnosis of atopic dermatitis but are too nonspecific to be used for defining or detecting atopic dermatitis for research and epidemiologic studies:

- Atypical vascular responses (e.g. facial pallor, white dermographism, delayed blanch response)
- Keratosis pilaris/pityriasis alba/hyperlinear palms/ichthyosis
- Ocular/periorbital changes
- Other regional findings (e.g. perioral changes/periauricular lesions)
- Perifollicular accentuation/lichenification/prurigo lesions

EXCLUSIONARY CONDITIONS - It should be noted that a diagnosis of atopic dermatitis depends on excluding conditions, such as:

- Scabies
- Seborrheic dermatitis
- Contact dermatitis (irritant or allergic)
- Ichthyoses
- Cutaneous T-cell lymphoma
- Psoriasis
- Photosensitivity dermatoses
- Immune deficiency diseases
- Erythroderma of other causes

[i] Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. J Am Acad Dermatol 2014; 71: 116-32.