Medicines Management Programme

Managed Access Protocol for dupilumab for the treatment of severe atopic dermatitis in children 6 years to 11 years old

Medicine	Date of addition to Managed Access Protocol
Dupilumab (Dupixent®)	01/05/2022

Approved by	**Professor Michael Barry, Clinical Lead, MMP**	
Date approved	Version 1.0	10/05/2022
Date updated	Version 2.0	19/04/2023
	Version 2.1	01/08/2024

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List of abbreviations

AD	Atopic dermatitis
BSC	Best supportive care
CDLQI	Children's Dermatology Life Quality Index
EASI	Eczema Area and Severity Index
HSE	Health Service Executive
MAP	Managed Access Protocol
MMP	Medicines Management Programme
PFS	Pre-filled syringe
SmPC	Summary of product characteristics

1. Dupilumab for severe atopic dermatitis

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

From May 2022, two presentations of Dupixent® are available under the High Tech Arrangement for the treatment of severe atopic dermatitis (AD) in children aged 6 years to 11 years old:

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

1.1 Licensed indications

Dupilumab is indicated for treatment of severe AD in children 6 years to 11 years old who are candidates for systemic therapy.

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

1.2 Reimbursement

Reimbursement of dupilumab on the High Tech Arrangement for the treatment of severe AD in children 6 years to 11 years old is supported only for those who are candidates for systemic therapy , who have not adequately responded to existing systemic treatments, who cannot tolerate them, or for whom their use is not clinically advisable, 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 dupilumab for the treatment of severe AD which are relevant to this MAP. Please refer to the Summary of Product Characteristics (SmPC) for further prescribing information.

Table 1 Licensed therapeutic dosages of dupilumab in children aged 6 years to 11 years of age

Patient population	Route of administration	Dosage
Children 6 to 11 years of age, weighing 15 kg to less than 60 kg	Subcutaneous	300 mg on day 1, followed by 300 mg on day 15, followed by 300 mg every 4 weeks*, starting 4 weeks after day 15 dose
Children 6 to 11 years of age, weighing 60 kg or more	Subcutaneous	Initial dose of 600 mg followed by 300 mg every other week

kg: kilogram; mg: milligram;
*The dose may be up-titrated to 200 mg every other week in patients with body weight 15 kg to less than 60 kg based on physician's assessment (see section 1.2.1 below).

If a patient is recommended for reimbursement of dupilumab, reimbursement is supported up to the maximum licensed dosage specified in table 1. Reimbursement of dosages in excess of the licensed therapeutic dosages (as outlined in table 1) is not supported.

See Section 3.1 for further details on treatment discontinuation.

1.2.1 Children weighing 15 kg to less than 60 kg

The dose may be up-titrated to 200 mg every other week based on prescriber's assessment, on or after week 16 if the patient does not achieve a meaningful response. For the purpose of reimbursement approval, a meaningful response is defined as a 50% improvement in Eczema Area and Severity Index (EASI) score and 4-point improvement in Children's Dermatology Life Quality Index (CDLQI) score. If a patient has not achieved a meaningful response after 16 weeks and the prescriber wishes to up-titrate the dose, the prescriber must notify the MMP by emailing mmp@hse.ie, outlining the updated EASI and CDLQI scores. The MMP will support reimbursement of a dose of 200 mg every other week, only when the prescriber contacts the MMP providing details outlining that the patient did not achieve a meaningful response after at least 16 weeks of treatment at a dose of 300 mg every four weeks.

1.3 Reimbursement price

The reimbursement prices of the presentations of dupilumab available on the High Tech Arrangement are outlined in Table 2. Commercial-in-confidence arrangements are in place with the marketing authorisation holder to reduce the net acquisition cost of dupilumab to the Health Service Executive (HSE).

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

Strength (pack size)	Code	Reimbursement price*
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

mg: milligram; ml: millilitre; PFS: pre-filled syringe
*Correct as at 15/07/2024

2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for patients aged 6 years to 11 years to be recommended for reimbursement of dupilumab for severe AD under the High Tech Arrangement.

2.1 Prescribers

Applications for reimbursement approval for dupilumab for the treatment of severe AD for patients aged 6 years to 11 years 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 Dupixent® for approved patients for the treatment of AD under the High Tech Arrangement will be 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 will only be considered for individuals aged 6 years to 11 years at time of application.

Please refer to the *MAP for High Tech medicines for the treatment of moderate-to-severe atopic dermatitis* when submitting applications for the reimbursement of Dupixent® for adults and adolescents 12 years and older at the 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.

2.3.1 Eczema Area and Severity Index score

Clinicians will be required to confirm the patient's EASI score at the time of application. Reimbursement will only be supported for patients with an EASI score ≥ 21.

2.3.2 Children's Dermatology Life Quality Index score

Clinicians will be required to confirm the patient's CDLQI score at the time of application.

2.4 Patient clinical history/status

In line with SmPC for Dupixent®, applications for reimbursement approval will not be considered for individuals who meet any of the contraindications for treatment as outlined in the SmPC.

2.5 Patient's medical treatment

Reimbursement will only be supported in refractory AD, when patients:

- Have had an inadequate response (defined as failure to achieve and maintain remission or a low disease activity state) to existing systemic treatments, who could not tolerate them, or for whom their use is not clinically advisable, and
- Are using best supportive care (BSC) for AD.

Patients 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 severe AD has been trialled prior to the application. Such medicines include[i]:

- Ciclosporin
- Methotrexate
- Azathioprine
- Mycophenolate mofetil

2.5.2 Immunosuppressant medicine 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 not clinically advisable

For patients in whom treatment with an immunosuppressant medicine is not clinically advisable, details of this, including any 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.

[i] Prescribing of these medicines in children 6 years to 11 years old for the treatment of severe atopic dermatitis represents an “off-label” indication. Please refer to each individual product’s Summary of Product Characteristics (SmPC) for further details.

3.1 Treatment discontinuation

Clinical evidence indicates that the majority of patients who respond to dupilumab will show clinical benefit within 16 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 CDLQI score of ≥ 4 points.

Patients not showing these improvements after 16 weeks of treatment would be considered non-responders. As this is a condition of ongoing reimbursement:

- Non-responders who have been in receipt of 300 mg every two weeks - consider stopping treatment.
- Non-responders who have been in receipt of 300 mg every four weeks - consider up-titration (see section 1.2.1 for details) or discontinuation as deemed clinically appropriate.

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

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

[ii] 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.