Medicines Management Programme

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

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List of abbreviations

BSC	Best supportive care
CDLQI	Children's Dermatology Life Quality Index
EASI	Eczema Area and Severity Index
HSE	Health Service Executive
HTH	High Tech Hub
IgG4	Immunoglobulin G4
IL	Interleukin
MAP	Managed Access Protocol
MMP	Medicines Management Programme
PCRS	Primary Care Reimbursement Service
PFS	Pre-filled syringe
SC	Subcutaneous
SmPC	Summary of product characteristics
TCI	Topical calcineurin inhibitors
TCS	Topical corticosteroids

1. Dupilumab (Dupixent®)

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

From 1 May 2022, two presentations of Dupixent® are available under the High Tech Arrangement for the treatment of severe atopic dermatitis in children aged 6 years to 11 years old:

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

Dupixent® pre-filled pen is not intended for use in children below 12 years of age. For children 6 years to 11 years of age with atopic dermatitis, Dupixent® PFS is the presentation appropriate for administration to this population.

1.1 Licensed indications

Dupixent® is indicated for the treatment of a number of inflammatory conditions.[i] This Managed Access Protocol (MAP) relates to its use in the treatment of severe atopic dermatitis in children 6 years to 11 years old who are candidates for systemic therapy.

1.2 Reimbursement

Conditional reimbursement of Dupixent® on the High Tech Arrangement under this MAP is confined to the treatment of severe atopic dermatitis in children 6 years to 11 years old who are candidates for systemic therapy (and who have not adequately responded to existing systemic treatments, who cannot tolerate them, or for whom their use is not clinically advisable).

Prescribers are required to apply for reimbursement approval on an individual patient basis through the online application system.

[i] Please refer to the Summary of Product Characteristics (SmPC) for full prescribing information.

If a patient is recommended for reimbursement by the MMP, the High Tech prescription for Dupixent® should be generated on the High Tech Hub (HTH). High Tech prescriptions which are not hub generated for Dupixent® will not be eligible for reimbursement by the Health Service Executive (HSE)-Primary Care and Reimbursement Service (PCRS). Treatment with Dupixent® for severe atopic dermatitis should be initiated and supervised by physicians experienced in the diagnosis and treatment of the condition.

1.2.1 Dupixent® dosing[i]

Table 1 outlines the licensed dosage regimens of dupilumab (Dupixent®) in children 6 years to 11 years of age for the treatment of severe atopic dermatitis.

Table 1: Licensed dosage regimens of Dupixent® in children 6 years to 11 years of age for severe atopic dermatitis

Body weight of patient	Route	Initial dose	Subsequent doses
≥ 15 kg to less than 60 kg	SC	300 mg (one 300 mg injection) on Day 1, followed by 300 mg on Day 15	300 mg every 4 weeks*, starting 4 weeks after Day 15 dose
60 kg or more	SC	600 mg (two 300 mg injections)	300 mg every other week

kg: kilogram; mg: milligram; SC: subcutaneous

*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 1.2.1.1 below).

Dupixent® is available as a PFS, with one pack containing two PFS. If a patient is recommended for reimbursement of Dupixent®, reimbursement will be supported as outlined in sections 1.2.1.1 and 1.2.1.2 below.

1.2.1.1 Children weighing ≥ 15 kg to less than 60 kg

If a patient is recommended for reimbursement of Dupixent®, reimbursement will be supported for one pack of Dupixent® (containing two 300 mg PFS) to cover the first four weeks of treatment (i.e. initial dose of 300 mg on day 1, followed by 300 mg on day 15). It is envisaged that the majority of children ≥ 15 kg to less than 60 kg will subsequently be treated with dupilumab 300 mg every four weeks; this equates to one 300 mg PFS of Dupixent® every four weeks.

[i] Please refer to the Summary of Product Characteristics (SmPC) for full prescribing information.

The Dupixent® 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 one pack of Dupixent® (containing two 200 mg PFS) every four weeks, i.e. 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.

1.2.1.2 Children weighing 60 kg or more

If a patient is recommended for reimbursement of Dupixent®, reimbursement will be supported for a total of two packs of Dupixent® (each containing two 300 mg PFS) to cover the first four weeks of treatment (i.e. initial dose of 600 mg then 300 mg every other week), followed by one pack of Dupixent® (containing two 300 mg PFS) every four weeks thereafter (i.e. a dose of 300 mg every other week).

1.3 Reimbursement price

A commercial-in-confidence arrangement is in place with the marketing authorisation holder to reduce the net acquisition cost of Dupixent® to the HSE.

1.3.1 Dupixent® reimbursement price

The reimbursement price of the PFS presentations of Dupixent® available on the High Tech Arrangement as of 1 April 2023 are outlined in table 2.

Table 2: Reimbursement price of PFS presentations of Dupixent® available on the High Tech Arrangement as of 1 April 2023

Strength (pack size)	Reimbursement	
	Code	Price
Dupixent® 200 mg PFS (2 x 1.14 ml)	89074	€ 1,246.16
Dupixent® 300 mg PFS (2 x 2 ml)	89075	€ 1,246.16

mg: milligram; ml: millilitre; PFS: Pre-filled syringe

2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for a child aged 6 years to 11 years old to be recommended for reimbursement of Dupixent® for the treatment of severe atopic dermatitis under the High Tech Arrangement.

2.1 Prescribers

The prescribing of Dupixent® for the treatment of severe atopic dermatitis in children 6 years to 11 years old under the High Tech Arrangement is confined to consultant dermatologists who have agreed to the terms of this MAP and have been approved by the HSE. Applications for reimbursement approval will only be considered from these prescribers.

2.2 Patient age

Applications for the reimbursement of Dupixent® submitted under this MAP will only be considered for children 6 years to 11 years old at the 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 Diagnosis

Clinicians will be required to confirm a diagnosis of atopic dermatitis 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 atopic dermatitis for at least one year prior to the application date.

2.3.1 Eczema Area and Severity Index (EASI) 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 (CDLQI) score

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

2.4 Patient's medical treatment for atopic dermatitis

Reimbursement will only be supported in refractory atopic dermatitis, when patients:

- Have had an inadequate response[ii] 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 atopic dermatitis.

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

2.4.1 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 atopic dermatitis has been trialled prior to the application. Such medicines include[iii]:

- Ciclosporin
- Methotrexate
- Azathioprine
- Mycophenolate mofetil

When reviewing applications, the MMP may request evidence to demonstrate that the patient has been adherent to the specified medicine for a period of at least three months.

2.4.2 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.

[ii] Inadequate response is defined as failure to achieve and maintain remission or a low disease activity state.
[iii] 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.

2.4.3 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.

2.4.4 Best supportive care for atopic dermatitis

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

3. Reimbursement criteria – Continuation

Clinical evidence indicates that the majority of patients who respond to dupilumab will show clinical benefit within 16 weeks.

In patients with atopic dermatitis, 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 1.2.1.1 for details) or discontinuation as deemed clinically appropriate.

Therefore, following approval of a patient for reimbursement of Dupixent® for the treatment of severe atopic dermatitis under the High Tech Arrangement, the prescribing clinician may be required to submit follow-up information to the MMP as requested. Follow-up data may be requested by the HSE/MMP for audit purposes and provision of same is a condition of ongoing reimbursement.

4. Prescribing of Dupixent® for the treatment of severe atopic dermatitis in children aged 6 years to 11 years old

Please refer to the Dupixent® Summary of Product Characteristics (SmPC) for full prescribing information including monitoring and patient counselling requirements.

Prescriptions must be generated through the HTH (details outlined separately) and only approved prescribers will have access to prescribe Dupixent® for the treatment of severe atopic dermatitis in children aged 6 years to 11 years old.

The following confirmations are required when prescribing High Tech medicines for the treatment of severe atopic dermatitis on the HTH:

- Confirmation that Dupixent® is being prescribed for a MMP approved patient in accordance with the MAP established in line with the terms of reimbursement approval given by the HSE
- Confirmation that prescriber will assist the HSE/MMP in their conduct of audits* through provision of information as requested, to provide assurance that the product is being prescribed in line with HSE reimbursement approval and the MAP
- Confirmation that the patient is aware that the application for reimbursement approval is being made on their behalf and that audits may occur during which their personal data will be reviewed

** Follow-up data may be requested by the HSE/MMP for audit purposes and provision of same is a condition of ongoing reimbursement.*

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

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

[1]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.