Medicines Management Programme

Managed Access Protocol – Dupilumab (Dupixent®) for the treatment of severe asthma in adults and adolescents 12 years and older

Approved by:	Prof. Michael Barry, Clinical Lead, MMP.
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List of abbreviations

ACQ	Asthma Control Questionnaire
ACT	Asthma Control Test
FeNO	Fraction of exhaled nitric oxide
HSE	Health Service Executive
HTH	High Tech Hub
ICS	Inhaled corticosteroids
Ig	Immunoglobulin
IL	Interleukin
LABA	Long-acting $beta_2$-agonist
LAMA	Long-acting muscarinic antagonist
LTRA	Leukotriene receptor antagonist
MAP	Managed Access Protocol
MMP	Medicines Management Programme
OCS	Oral corticosteroids
PCRS	Primary Care Reimbursement Service
PEFR	Peak expiratory flow rate
PFP	Pre-filled pen
PFS	Pre-filled syringe
SmPC	Summary of Product Characteristics

1. Dupilumab

Dupilumab (Dupixent®) is a recombinant human immunoglobulin G4 (IgG4) monoclonal antibody that inhibits interleukin (IL)-4 and IL-13 signalling. IL-4 and IL-13 are major drivers of human type 2 inflammatory disease, including asthma.

From 1 November 2023, four presentations of Dupixent® are available on the High Tech Arrangement for the treatment of severe asthma:

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

1.1 Licensed indications

Dupixent® is indicated in adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide (FeNO), who are inadequately controlled with high-dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment.

Dupixent® is also indicated in children 6 to 11 years as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with medium- to high-dose ICS plus another medicinal product for maintenance treatment.

In addition, Dupixent® is indicated in the treatment of a number of other inflammatory diseases that are outside the scope of this managed access protocol (MAP).[i]

1.2 Reimbursement

Reimbursement of Dupixent® on the High Tech Arrangement for the treatment of severe asthma is supported only for adults and adolescents 12 years and older, who meet the criteria outlined in this MAP. All criteria must be satisfied in order for reimbursement to be supported.

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

Approved consultant respiratory physicians are required to apply for reimbursement approval on an individual patient basis through the online application system.

If a patient is recommended for reimbursement by the Health Service Executive (HSE)-Medicines Management Programme (MMP), the high tech prescription for Dupixent® should be generated on the High Tech Hub (HTH). High tech prescriptions that are not hub generated for Dupixent® will not be eligible for reimbursement by the HSE-Primary Care Reimbursement Service (PCRS).

Table 1 outlines the licensed therapeutic dosages of Dupixent® for adult and adolescents 12 years and older for the treatment of severe asthma.

Table 1: Licensed therapeutic dosages of Dupixent® for adult and adolescents 12 years and older for the treatment of severe asthma

Patient population	Route	Initial dosage	Maintenance dosage (every other week)
Patients with severe asthma and who are on oral corticosteroids, or for patients with severe asthma and co-morbid moderate-to-severe atopic dermatitis or adults with co-morbid severe chronic rhinosinusitis with nasal polyposis	Subcutaneous injection	600 mg (2 x 300 mg injections)	300 mg
All other patients	Subcutaneous injection	400 mg (2 x 200 mg injections)	200 mg

mg: milligrams

Please refer to the Summary of Product Characteristics (SmPC) for Dupixent® for further information, including the management of missed doses.

Dupixent® is available as a PFP or PFS, with one pack containing two PFP/PFS. If a patient is recommended for reimbursement of Dupixent®, reimbursement is supported in line with the licensed therapeutic dosage as outlined in the table 1, i.e. one pack of Dupixent® (containing two PFP/PFS) every four weeks for patients on the maintenance dosage, with an additional supply of one pack at time of initiation to allow for administration of the loading dosage.

Reimbursement of dosages in excess of the licensed therapeutic dosages (as outlined in table 1) is not supported.

See Section 3 for further details on Reimbursement Criteria - Continuation.

Reimbursement of Dupixent® on the High Tech Arrangement is also supported for the treatment of atopic dermatitis, in line with the relevant MAPs.

1.3 Reimbursement price

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

Table 2: Reimbursement codes and prices for the presentations of Dupixent® available on the High Tech Arrangement

Medicinal product (pack size)	Reimbursement	
	Code	Price
Dupixent® 200 mg PFP (2)	89072	€1,232.34
Dupixent® 200 mg PFS (2)	89074	€1,246.16
Dupixent® 300 mg PFP (2)	89073	€1,238.19
Dupixent® 300 mg PFS (2)	89075	€1,246.16

mg: milligrams; PFP: pre-filled pen; PFS: pre-filled syringe

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

2. Reimbursement criteria - Initiation

This section outlines the criteria that must be satisfied in order for an adult or adolescent aged 12 years and older to be recommended for reimbursement of Dupixent® under the High Tech Arrangement for the treatment of severe asthma.

2.1 Prescribers

Applications for reimbursement approval for Dupixent® for the treatment of severe asthma under the High Tech Arrangement will only be considered from consultant respiratory physicians registered with the Irish Medical Council, who specialise in severe asthma and are practicing within a severe asthma centre, and who have agreed to the terms of this MAP and been approved by the HSE ('approved consultants').

The prescribing of Dupixent® for approved patients for the treatment of severe asthma 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.

The Severe Asthma Advisory Sub-Group of the National Clinical Programme for Respiratory will assist the MMP in identifying consultant respiratory physicians who specialise in severe asthma and are practicing within a severe asthma centre.

2.2 Patient age

Applications for reimbursement approval of Dupixent® for the treatment of severe asthma will only be considered for adults and adolescents 12 years and older at time of application.

2.3 Patient diagnosis: Severe Refractory Eosinophilic Asthma

Approved consultants are required to confirm a diagnosis of severe refractory eosinophilic phenotype asthma at time of application. This diagnosis should be made in line with the criteria outlined in the National Severe Asthma Network Briefing Paper published by the Severe Asthma Advisory Sub-Group of the National Clinical Programme for Respiratory.

For reimbursement to be supported, patients are required to have a history of raised blood eosinophils. For the purposes of this MAP, this is defined as:

- a blood eosinophil count ≥ 300 cells/microlitre (0.3×10^9 cells/litre) in the previous 12 months, or
- in patients on long-term maintenance oral corticosteroids (OCS) with a blood eosinophil count < 300 cells/microlitre (0.3×10^9 cells/litre), a blood eosinophil level taken prior to commencement of long-term maintenance OCS should be provided to confirm the eosinophilic phenotype of asthma.

Approved consultants are required to provide the blood eosinophil count and date of corresponding blood test at time of application.

2.4 Patient clinical history/status

In line with the exclusion criteria from the Liberty Asthma Quest and the Liberty Asthma Venture trials, and the SmPC of Dupixent®, applications for reimbursement approval of Dupixent® will not be considered in individuals who:

- have a blood eosinophil count ≥ 1,500 cells/microlitre (1.5 x 10^9 cells/litre), either historically or at time of application
- are a current smoker.

A baseline assessment of asthma symptom control using a validated asthma control questionnaire, e.g. Asthma Control Questionnaire (ACQ)/Asthma Control Test (ACT), must be included as part of application for reimbursement approval. This baseline assessment should have been undertaken in the 30-day period preceding the date of application.

2.5 Adherence to maintenance treatment

In line with the licensed indication of Dupixent®, patients are required to be in receipt of and fully adherent to a high-dose ICS plus another medicinal product for maintenance treatment of their severe asthma, unless evidence is provided to demonstrate the patient has previously been intolerant to such treatment or has a contraindication to treatment.

Table 3 outlines suggested total daily doses that are indicative of treatment with high-dose ICS for those corticosteroids that are available in inhaler presentation on the Community Drug Schemes.

Table 3: Total daily dose of inhaled corticosteroid indicative of treatment with high-dose inhaled corticosteroids

Inhaled Corticosteroid	Total daily dose for high-dose ICS (mcg)
Beclomethasone dipropionate (pMDI, standard particle, HFA)	> 1,000
Beclomethasone dipropionate (pMDI, extrafine particle, HFA)	> 400
Budesonide (DPI)	> 800
Ciclesonide (pMDI, extrafine particle, HFA)	> 320
Fluticasone furoate (DPI)	200
Fluticasone propionate (DPI)	> 500
Fluticasone propionate (pMDI, standard particle, HFA)	> 500
Mometasone furoate (DPI)	See note below*

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant; ICS: inhaled corticosteroids; mcg: micrograms; pMDI: pressurised metered dose inhaler

** The classification of high-dose for mometasone furoate (DPI) is dependent on the individual medicinal product. The licensed daily dosage of Atectura® Breezhaler 125 mcg/260 mcg inhalation powder and Enerzair® Breezhaler 114 mcg/46 mcg/136 mcg inhalation powder delivers a quantity of mometasone furoate that would be classified as a high-dose inhaled corticosteroid.*

Medicines that are used in combination with high-dose ICS as the other element of maintenance treatment include:

- long-acting beta$_2$-agonists (LABA)
- long-acting muscarinic antagonists (LAMA)
- leukotriene receptor antagonists (LTRA)
- oral corticosteroids.

Approved consultants are required to provide details of the current maintenance treatment for the patient as part of the application for reimbursement approval. Patients must be adherent to maintenance treatment (i.e. high-dose ICS plus another medicinal product) for a period of at least 12 months at the time of application.

In addition, approved consultants are required to confirm that the patient is fully adherent to maintenance treatment at the time of application:

- confirmation that inhaler technique assessed and patient educated on inhaler use
- confirmation that compliance assessed by three consecutive monthly visits to a clinical nurse specialist, with provision of adherence advice, review of peak expiratory flow rate (PEFR) diary and reported asthma outcomes.

When reviewing applications, the MMP may request evidence to validate that the patient has been in receipt of a high-dose ICS plus another medicinal product as maintenance treatment for a period of at least 12 months at the time of application, e.g. printout of dispensed medicinal products.

2.5.1 Intolerance to maintenance treatment

In cases where a patient did not tolerate a maintenance treatment and experienced a clinically significant adverse reaction which necessitated discontinuation of treatment, information in relation to the medicine, the duration of treatment and the adverse reaction experienced should be provided as part of the application for reimbursement approval. The MMP may request evidence to validate the information provided, e.g. printout of dispensed medicinal products.

2.5.2 Contraindication to maintenance treatment

For patients in whom maintenance treatment is contraindicated, details of the contraindication, including supporting evidence, should be provided as part of the application for reimbursement approval.

2.6 Inadequate control

Approved consultants are required to provide information to demonstrate that the patient's asthma remains inadequately controlled despite being fully adherent to a high-dose ICS plus another medicinal product for a period of at least 12 months at the time of application.

In order for reimbursement to be supported, patients must either:

- have experienced two or more exacerbations requiring systemic corticosteroids in the 12-month period preceding the date of application, or
- have been taking continuous OCS at a dose ≥ 5 mg of prednisolone daily or equivalent for the six-month period preceding the date of application.

When reviewing applications, the MMP may request evidence to validate that the patient has been in receipt of systemic or continuous oral corticosteroids.

2.7 Treatment with other biological medicines for severe asthma

There is currently no robust evidence available supporting the use of more than one biological medicine at the same time to improve outcomes in patients with severe asthma. Reimbursement of Dupixent®, therefore, will not be supported if used in combination with other biological medicines that are licensed for the treatment of severe asthma.

Approved consultants are required to confirm if the patient is currently, or has previously been, in receipt of another biological medicine for the treatment of severe asthma, e.g. benralizumab, mepolizumab, omalizumab, reslizumab. The approved consultant should provide details of the current/previous treatment with another biological medicine, and outline the reasons for switching treatment. Where the patient is currently in receipt of another biological medicine for the treatment of severe asthma, the approved consultant will be required to confirm that treatment with the biological medicine will be ceased if reimbursement of Dupixent® is supported.

3. Reimbursement criteria - Continuation

Response to treatment with Dupixent® should be reviewed by the consultant respiratory physician at three-monthly intervals. The need for continued therapy should be considered at least on an annual basis as determined by physician assessment of the patient's level of asthma control.

A definite decision to continue treatment with Dupixent® should be made after 12 months of treatment, considering factors such as disease severity and level of exacerbation control. Treatment with Dupixent® should be stopped if the patient's asthma has not responded adequately to treatment.

An adequate response is defined as:

- a clinically meaningful reduction in the number of asthma exacerbations that required systemic corticosteroids or hospitalisation, or
- a clinically significant reduction in continuous oral corticosteroid use while maintaining improved asthma control.

Therefore, following approval of a patient for reimbursement of Dupixent® under the High Tech Arrangement, the approved consultant will be required to submit follow-up data by secure email to the MMP (mmp@hse.ie). This can include details of response to treatment with Dupixent®, e.g. details of adherence, asthma symptom control, exacerbations, General Practitioner visits and continuous OCS dose. The approved consultant should also indicate if they intend to continue or discontinue treatment with Dupixent®.

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

4. Prescribing of Dupilumab (Dupixent® 200 mg PFP/PFS, Dupixent® 300 mg PFP/PFS)

Please refer to the SmPC for Dupixent® for full prescribing information including monitoring and patient counselling requirements. Prescriptions must be generated through the HTH (details outlined separately) and only approved consultants and their teams will have access to prescribe dupilumab (Dupixent®).

The following confirmations are required when prescribing dupilumab (Dupixent®) on the HTH:

- confirmation that dupilumab (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 the approved consultant 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.