Dupixent® (dupilumab)

Formulary Application Support Pack

Severe atopic dermatitis in children 6 months to 5 years of age who are candidates for systemic therapy

Prescribing Information and adverse event reporting are available in the Appendices

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Contents

General introduction: Dupilumab

Dupilumab is a biological agent that inhibits the signalling of both interleukin (IL)-4 and IL-13 to mediate the type 2 inflammatory response[1,2].

Dupilumab is indicated for the treatment of moderate-to-severe atopic dermatitis (AD) in adults and adolescents 12 years and older who are candidates for systemic therapy. Dupilumab is indicated for the treatment of severe AD in children 6 months to 11 years old who are candidates for systemic therapy[1–8].

Dupilumab is also indicated for the treatment of adults with moderate-to-severe prurigo nodularis (PN) who are candidates for systemic therapy[1,2,5-6].

In patients with moderate-to-severe AD, dupilumab improves clinical signs such as pruritis and quality of life compared with placebo in patients from 6 months of age[1–16]. In adult patients with moderate-to-severe PN, dupilumab achieved significant and clinically meaningful improvements in itch and skin lesions compared with placebo[17].

Dupilumab is indicated in adults and adolescents aged 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fractional exhaled nitric oxide (FeNO), who are inadequately controlled with high-dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment. Dupilumab is further indicated in children aged 6–11 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[1–8].

For children, adolescents, and adults with severe asthma, dupilumab, compared with placebo, has been shown in clinical trials to increase lung function, reduce severe asthma exacerbations, improve asthma control, reduce the use of oral corticosteroids, and improve asthma-related quality of life[1–8,18–20].

Additionally, dupilumab is indicated as add-on therapy with intranasal corticosteroids for the treatment of adults with severe chronic rhinosinusitis with nasal polyposis (CRSwNP) for whom therapy with systemic corticosteroids and/or surgery does not provide adequate disease control[1,2,5-6].

In adults with CRSwNP, clinical trials of dupilumab as add-on therapy in addition to standard care have shown improved clinical signs and symptoms, such as polyp size, sinus opacification, and nasal congestion, compared with placebo[1,2,5–6,21].

The most common adverse reactions observed in clinical trials and/or post-marketing settings with dupilumab are injection site reactions (includes erythema, oedema, pruritis, pain, and swelling), conjunctivitis, conjunctivitis allergic, arthralgia, oral herpes, and eosinophilia. Rare cases of serum sickness, serum sickness-like reactions, anaphylactic reactions, and ulcerative keratitis have been reported[1–8].

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
5. Dupixent 300 mg solution for injection in pre-filled pen. Summary of Product Characteristics. UK. Available at https://www.medicines.org.uk/emc/product/11321. Accessed January 2024.
6. Dupixent 300 mg solution for injection in pre-filled pen. Summary of Product Characteristics. IE. Available at https://www.medicines.ie/medicines/dupixent-300-mg-solution-for-injection-in-pre-filled-pen-34951/spc. Accessed January 2024.
7. Dupixent 200 mg solution for injection in pre-filled pen. Summary of Product Characteristics. UK. Available at https://www.medicines.org.uk/emc/product/11323. Accessed January 2024.
8. Dupixent 200 mg solution for injection in pre-filled pen. Summary of Product Characteristics. IE. Available at https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-pen-34950/spc. Accessed January 2024.
9. Simpson EL, Beiber T, Guttman-Yassky E, et al. Two Phase 3 trials of dupilumab versus placebo in atopic dermatitis. N Engl J Med. 2016;375:2335–2348.
10. Ferrandiz, C., de la Cueva Dobao, P., Simpson, E. et al. Dupilumab in Moderate-to-Severe Atopic Dermatitis: Pooled Efficacy Results from Two Identically Designed Randomized Phase 3 Trials (SOLO 1 & 2). SKIN The Journal of Cutaneous Medicine. 2017;1:s38.
11. Blauvelt A, de Bruin-Weller M, Gooderham M, et al. Long-term management of moderate-to-severe atopic dermatitis with dupilumab and concomitant topical corticosteroids (LIBERTY AD CHRONOS): A 1-year, randomised, double-blinded, placebo-controlled, phase 3 trial. Lancet. 2017;389:2287–2303.
12. Worm M, Simpson E, Thaci D, et al. Efficacy and safety of multiple dupilumab dose regimens after initial successful treatment in patients with atopic dermatitis. A randomised clinical trial. JAMA Dermatol. 2020;156:131–143.
13. de Bruin-Weller M, Thaci D, Smith CH, et al. Dupilumab with concomitant topical corticosteroid treatment in adults with atopic dermatitis with an inadequate response or intolerance to ciclosporin A or when this treatment is medically inadvisable: A placebo-controlled, randomised phase III clinical trial (LIBERTY AD CAFE). Br J Dermatol. 2018;178:1083–1101.
14. Simpson EL, Paller AS, Siegfried EC, et al. Efficacy and safety of dupilumab in adolescents with uncontrolled moderate to severe atopic dermatitis: A Phase 3 randomized clinical trial. JAMA Dermatol. 2019;156:44–56.
15. Paller AS, Siegfried EC, Thaçi D, et al. Efficacy and safety of dupilumab with concomitant topical corticosteroids in children 6 to 11 years old with severe atopic dermatitis: A randomised, double-blinded, placebo-controlled phase 3 trial. *J Am Acad Dermatol*. 2020;83:1282–1293.
16. Paller AS, Pinter A, Lee LW, et al. Efficacy and safety of dupilumab treatment with concomitant topical corticosteroids in children aged 6 months to 5 years with severe atopic dermatitis. 5th Revolutionising Atopic Dermatitis (RAD) Conference; Dec 11, 2022, Virtual.
17. Vosipovitch G, Mollanazar N, Stander S, et al. Dupilumab in patients with prurigo nodularis: Two randomized, double-blind, placebo-controlled phase 3 trials. Nat Med. 2023;29:1180–1190.
18. Castro M, Corren J, Pavord ID, et al. Dupilumab efficacy and safety in moderate-to-severe uncontrolled asthma. N Engl J Med. 2018;378:2486–2496.
19. Rabe K, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018;28;378:2475–2485.
20. Bacharier LB, Maspero JF, Katelaris CH, et al. Dupilumab in children with uncontrolled moderate-to-severe asthma. N Engl J Med. 2021;385:2230–2240.
21. Bachert C, Han J, Desrosiers M, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): Results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. Lancet. 2019;394:1638–1650.

Product characteristics

GENERIC NAME	Dupilumab[1–4]
BRAND NAME	Dupixent®[1–4]
MANUFACTURER	Sanofi
PRODUCT AVAILABILITY DATE	Indicated for use in children aged 6 months to 5 years with severe atopic dermatitis who are candidates for systemic therapy: • In England: August 2023[1,3] • In Wales: August 2023[1,3] • In Scotland: August 2023[1,3] • In Northern Ireland: June 2023[2,4]
DRUG CLASS	Recombinant human immunoglobulin G4 monoclonal antibody that inhibits interleukin (IL)-4 and IL-13 signalling[1–4]
ATC CODE	D11AH05[5]
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024. 5. WHO Collaborating Centre for Drug Statistics Methodology. Dermatologicals. Available at: https://www.whocc.no/atc_ddd_index/?code=D11AH05. Accessed January 2024.

Mechanism of action

Dupilumab is a recombinant human immunoglobulin G4 monoclonal antibody that inhibits interleukin (IL)-4 andIL-13 signalling. Dupilumab inhibits IL-4 signalling via the Type I receptor (IL-4Rα/γc) and both IL-4 and IL-13 signalling through the Type II receptor (IL-4Rα/IL-13Rα)[1–4].

IL-4 and IL-13 are key drivers of human type 2 inflammatory diseases, such as atopic dermatitis and asthma. Blocking the IL-4/IL-13 pathway with dupilumab in patients decreases many of the mediators of type 2 inflammation[1–4].

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed December 2023.

Indications

MODERATE-TO-SEVERE ATOPIC DERMATITIS (AD)	**Adults and adolescents:** treatment of moderate-to-severe AD in adults and adolescents 12 years and older who are candidates for systemic therapy[1–4]. **Children 6 months to 11 years of age:** treatment of severe AD in children 6 months to 11 years old who are candidates for systemic therapy[1–4].
SEVERE ASTHMA	**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 fractional exhaled nitric oxide (FeNO), who are inadequately controlled with high-dose inhaled corticosteroids (ICS) plus another medicinal product for maintenance treatment[1–4]. **Children 6–11 years of age:** 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[1–4].
CHRONIC RHINOSINUSITIS WITH NASAL POLYPS (CRSwNP)	Add-on therapy with ICS for severe CRSwNP in adults with inadequate control with prior systemic corticosteroids and/or surgery[1,2].
PRURIGO NODULARIS (PN)	For the treatment of adults with moderate-to-severe PN who are candidates for systemic therapy[1,2].
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

Dupilumab for atopic dermatitis in children aged 6 months to 5 years

This document contains information about the use of dupilumab in children 6 months to 5 years old for the treatment of severe atopic dermatitis (AD) with inadequate response to topical corticosteroids. Efficacy is reported from the Phase 3 clinical trial, LIBERTY AD PRESCHOOL[1].

Safety is reported from experience with dupilumab in clinical trials and/or in the post-marketing setting in patients aged at least 6 years old with AD[1–5].

REFERENCES

1. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400:908–919.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
3. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
5. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

SECTION 1: INTRODUCTION – DUPILUMAB FOR SEVERE ATOPIC DERMATITIS FOR CHILDREN AGED 6 MONTHS TO 5 YEARS	
	Atopic dermatitis (AD) is a chronic, recurrently flaring, generalised skin condition that can be life-limiting, debilitating, and isolating. It has a substantial and multidimensional burden on patients from childhood through to adulthood and can affect all aspects of life (physical, psychological, social, and financial)[1]. AD incidence peaks in infancy, with an onset before the age of 6 years in an estimated 80% of patients[2]. In the UK, AD is prevalent in approximately 16–25% of children younger than 6 years[3]. AD is associated with substantially reduced quality of life in infants, young children, and their family members[4]. In addition, AD is associated with type 2 inflammation-mediated comorbidities, including asthma and food allergies, which often have an earlier age of onset in children with AD than those without AD[5–6]. Infants with AD suffer from signs and symptoms that contribute to a poor quality of life, including pruritus and sleep disturbances[7–8]. In approximately 12.5% of infants with AD, developmental delays in motor skills, communication, relationships, and play are reported[9]. In addition to the impact on quality of life for patients, paediatric patients with severe AD impose a substantial financial burden on healthcare systems, with more than half of children with severe AD experiencing at least one hospitalisation in the previous 12 months[10]. Management of AD aims to improve symptoms; however, for infants with severe AD, their disease often remains uncontrolled with conventional therapies such as topical corticosteroids. Oral corticosteroids can be prescribed for short-term management of severe flares[12]. Other currently available systemic immunosuppressants are used off-label for the management of severe AD and are associated with safety concerns, which can limit their use[13]. Dupilumab is a fully human monoclonal antibody against the interleukin (IL)-4 receptor α subunit of IL-4 and IL-4/IL-13 receptor complexes[11,13–16]. In a Phase 3, randomised trial (LIBERTY AD PRESCHOOL, post-hoc analysis), a higher proportion of children aged 6 months to 5 years with severe AD treated with dupilumab, achieved Investigator's Global Assessment scores 0-1 (clear or almost clear), and at least a 75% improvement from baseline in Eczema Area and Severity Index score, compared with those treated with placebo[13,17]. Dupilumab was generally well tolerated and showed an acceptable safety profile[13,17]. Dupilumab fulfils the current unmet need for a new treatment option with a different mode of action for children aged 6 months to 5 years with severe AD with inadequate response to current standard care[2].
REFERENCES	1. NICE. TA534. Dupilumab for treating moderate to severe atopic dermatitis. August 2018. Available at: https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485. Accessed January 2024. 2. Weidinger S, Beck, LS, Bieber T, et al. Atopic dermatitis. Nat Rev Dis Primers. 2018;4(1):1. 3. Silverberg JI, Barbarot S, Gadkari A, et al. Atopic dermatitis in the pediatric population: A cross-sectional, international epidemiologic study. Ann Allergy Asthma Immunol. 2021;126:417–428. 4. Al Shobaili HA. The impact of childhood atopic dermatitis on the patients' family. Pediatr Dermatol. 2010;27:618–623. 5. Eichenfield LF, Hanifin JM, Beck LA, et al. Atopic dermatitis and asthma: Parallels in the evolution of treatment. Pediatrics. 2003;111:608–616. 6. Martin PE, Eckert JK, Koplin JJ, et al. Which infants with eczema are at risk of food allergy? Results from a population-based cohort. Clin Exp Allergy. 2015;45:255–264. 7. Alanne S, Nermes M, Söderlund R, Laitinen K. Quality of life in infants with atopic dermatitis

and healthy infants: A follow-up from birth to 24 months. Acta Paediatr 2011;100:e65–70.
8. Ricci G, Bendandi B, Bellini F, Patrizi A, Masi M. Atopic dermatitis: Quality of life of young Italian children and their families and correlation with severity score. Pediatr Allergy Immunol. 2007;18:245–249.
9. Torun EG, Ertugrul A, Tekguc DC, Bostanci I. Sleep patterns and development of children with atopic dermatitis. Int Arch Allergy Immunol. 2020;181:871–878.
10. Weidinger S, Simpson E, Silverberg J, et al. Burden of atopic dermatitis in infants/preschoolers from EPI-CARE: An international survey. 3rd Annual RAD Virtual Conference; Dec 11–13, 2021. P025.
11. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed August 2023.
12. NICE. Eczema - atopic: NICE stepped approach to treatment. April 2023. https://cks.nice.org.uk/topics/eczema-atopic/prescribing-information/stepped-approach-to-treatment/. Accessed January 2024.
13. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400:908-919.
14. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
15. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
16. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
17. Paller AS, Pinter A, Lee LW, et al. Efficacy and safety of dupilumab treatment with concomitant topical corticosteroids in children aged 6 months to 5 years with severe atopic dermatitis. Revolutionizing Atopic Dermatitis (RAD) Virtual Conference; Dec 11, 2022. Virtual.

SECTION 2: FORMULATION AND STRENGTH

Dupilumab 200 mg solution for injection is available in a pre-filled syringe or pen – each single-use pre-filled syringe or pen contains 200 mg of dupilumab in 1.14 mL of solution (175 mg/mL)[1–4].

Dupilumab 300 mg solution for injection is available in a pre-filled syringe or pen – each single-use pre-filled syringe or pen contains 300 mg of dupilumab in 2 mL of solution (150 mg/mL)[5–8].

The pre-filled pen is not intended for use in children younger than 12 years of age[1–8]. For children 6 months to 11 years of age with severe atopic dermatitis the dupilumab pre-filled syringe is the presentation appropriate for administration to this population[1–8].

Dupilumab is a clear, slightly opalescent, colourless to pale yellow sterile solution, which is free from visible particulates, with a pH of approximately 5.9. Dupilumab contains < 1 mmol sodium (23 mg) per 200 mg or 300 mg dose, i.e. it is essentially "sodium free"[1–8]. Excipients include arginine hydrochloride, histidine, polysorbate 80 (E433), sodium acetate trihydrate, glacial acetic acid (E260), sucrose, and water for injections[1–8].

REFERENCES

1. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
2. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled pen. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/11323. Accessed January 2024.

4. Dupixent 200 mg solution for injection in pre-filled pen. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-pen-34950/spc. Accessed January 2024.
5. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
6. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
7. Dupixent 300 mg solution for injection in pre-filled pen. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/11321. Accessed January 2024.
8. Dupixent 300 mg solution for injection in pre-filled pen. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300-mg-solution-for-injection-in-pre-filled-pen-34951/spc. Accessed January 2024.

SECTION 3: DOSAGE (ATOPIC DERMATITIS, CHILDREN 6 MONTHS TO 5 YEARS)

Recommended dose of dupilumab for subcutaneous administration in children 6 months to 5 years of age with severe atopic dermatitis[1–4]

Body weight	Initial and subsequent doses
5 kg to < 15 kg	Initial: 200 mg (one 200 mg injection) Subsequent: 200 mg Q4W
15 kg to >30 kg	Initial: 300 mg (one 300 mg injection) Subsequent: 300 mg Q4W

Q4W, every 4 weeks

Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, such as the face, neck, and intertriginous and genital areas[1–4].

Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment for atopic dermatitis. Some patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks. If dupilumab treatment interruption becomes necessary, patients can still be successfully re-treated[1–4].

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

SECTION 4: ADMINISTRATION (ATOPIC DERMATITIS, CHILDREN 6 MONTHS TO 5 YEARS)	
	Dupilumab is available as a single-use pre-filled syringe [1–4]. Dupilumab is administered by subcutaneous injection into the thigh or abdomen, except for 5 cm around the navel. The upper arm can also be used if administered by another person[1–4]. It is recommended to rotate the injection site with each injection. Dupilumab should not be injected into skin that is tender, damaged, or has bruises or scars[1–4]. The child's caregiver may administer dupilumab if their healthcare professional determines it is appropriate. Proper training should be provided to patients and/or caregivers on the preparation and administration of dupilumab before use, according to the Instructions for Use section in the package leaflet[1–4]. After removing the pre-filled syringe from the refrigerator, it should be allowed to reach room temperature (up to 25°C) by waiting 30 minutes (200 mg) or 45 minutes (300 mg) before injecting dupilumab. The pre-filled syringe should not be exposed to heat or direct sunlight and should not be shaken[1–4]. The solution should be clear to slightly opalescent, colourless to pale yellow[1–4]. If an every 4 week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, administer the dose, starting a new schedule based on this date[1–4].
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
SECTION 5: STORAGE AND DISPOSAL	
	Dupilumab should be stored in a refrigerator between 2°C and 8°C. Do not freeze[1–4]. If necessary, pre-filled syringes may be kept at room temperature up to 25°C for a maximum of 14 days. Do not store above 25°C. If the carton needs to be removed permanently from the refrigerator, the date of removal may be recorded on the outer carton. After removal from the refrigerator, dupilumab must be used within 14 days or discarded[1–4]. Any unused medicinal product or waste material should be disposed of in accordance with local requirements. After use, place the pre-filled syringe into a puncture-resistant container and discard as required by local regulations. Do not recycle the container[1–4].
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product

	Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
SECTION 6: LICENSED INDICATION (ATOPIC DERMATITIS)	
	Adults and adolescents 12 years and older: as treatment for moderate-to-severe atopic dermatitis (AD) in adults and adolescents 12 years and older who are candidates for systemic therapy[1–8]. **Children 6 months to 11 years of age:** as treatment for severe AD in children 6 months to 11 years old who are candidates for systemic therapy[1–8].
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024. 5. Dupixent 300 mg solution for injection in pre-filled pen. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/11321. Accessed January 2024. 6. Dupixent 300 mg solution for injection in pre-filled pen. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300-mg-solution-for-injection-in-pre-filled-pen-34951/spc. Accessed January 2024. 7. Dupixent 200 mg solution for injection in pre-filled pen. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/11323. Accessed January 2024. 8. Dupixent 200 mg solution for injection in pre-filled pen. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-pen-34950/spc. Accessed January 2024.
SECTION 7: DURATION OF THERAPY (ATOPIC DERMATITIS)	
	Consideration should be given when discontinuing dupilumab treatment in patients who have shown no response after 16 weeks of treatment for atopic dermatitis. Some patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks. If dupilumab treatment interruption becomes necessary, patients can still be successfully re-treated[1-4].
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

SECTION 8: PLACE IN THERAPY RELATIVE TO OTHER TREATMENTS	
	In children under the age of 12 years, NICE guidelines recommend a stepped approach to treatment to tailor the regimen according to atopic dermatitis (AD) severity. Emollients should form the basis of treatment for AD and should always be used. Management can then be stepped up or down, depending on severity, with the addition of other treatments as follows[1]: - Mild AD: Emollients; mild-potency topical corticosteroids (TCS) - Moderate AD: Emollients, moderate-potency TCS, topical calcineurin inhibitors, bandages - Severe AD: Emollients, potent TCS, topical calcineurin inhibitors, bandages, phototherapy, systemic therapy
REFERENCES	1. NICE CG57. Atopic eczema in under 12s: Diagnosis and management. December 2007. Available at: https://www.nice.org.uk/guidance/cg57/resources/atopic-eczema-in-under-12s-diagnosis-and-management-pdf-975512529349. Accessed January 2024.

SECTION 9: COMPARATIVE EFFICACY IN CHILDREN 6 MONTHS TO 5 YEARS – CLINICAL TRIAL	
	Dupilumab efficacy in children aged 6 months to < 6 years with moderate-to-severe atopic dermatitis (AD) was assessed in one Phase 3 clinical trial, LIBERTY AD PRESCHOOL[1]. A summary of the design and key results of this trial follows.
	LIBERTY AD PRESCHOOL: Dupilumab efficacy and safety in children aged 6 months to < 6 years with moderate-to-severe AD and inadequate response to topical steroids[1].
Study objectives[1]	To evaluate the efficacy and safety of dupilumab with concomitant low-potency topical steroids in patients aged 6 months to < 6 years with moderate-to-severe AD.
Eligibility criteria[1]	Children aged 6 months to < 6 years at screening, with physician-diagnosed AD according to the American Academy of Dermatology consensus criteria and: - Investigator's Global Assessment (IGA) score ≥ 3 - Eczema Area and Severity Index (EASI) ≥ 16 at screening and baseline visits - Body surface area (BSA) of AD involvement ≥ 10% at baseline visits - Baseline worst scratch/itch Numeric Rating Scale (NRS) score weekly mean score for maximum scratch/itch intensity ≥ 4 - Inadequate response to topical AD medication within last 6 months - At least 11 of 14 daily applications of medium-potency topical corticosteroids (TCS) during the 2-week TCS standardisation period (beginning on Day –14) leading up to the baseline visit (not including the day of randomisation) - At least 11 (of a total of 14) applications of a topical emollient (moisturiser) during the 7 consecutive days immediately before the baseline visit (not including the day of randomisation)
Study design[1]	A Phase 3, randomised, double-blind, placebo-controlled, parallel-group trial. A total of 162 patients were randomised 1:1 to receive dupilumab (n = 83) or placebo (n = 79) plus low-potency TCS. Patients received subcutaneous dupilumab (200 mg for baseline bodyweight ≥ 5 kg to < 15 kg or 300 mg for baseline bodyweight ≥ 15 kg to < 30 kg) or matched placebo every 4 weeks for a 16-week treatment period. From Day −14 to the end of the treatment period, patients received a standardised once-daily regimen of low-potency TCS (hydrocortisone acetate 1% cream). Once an IGA score of 2 or less was achieved, TCS use was tapered to three times per week, and at an IGA score of 0, TCS were stopped. Moisturiser use was required twice daily for at least 7 consecutive days prior to randomisation and throughout the trial. Systemic immunomodulating treatments, medium- or higher-potency TCS, crisaborole, and topical calcineurin inhibitors were prohibited, but could be used as rescue for worsening disease at the investigator's discretion after Day 14.
Primary endpoint[1]	Co-primary efficacy endpoints: - Proportion of patients with an IGA score of 0 or 1 at Week 16 - Proportion of patients with ≥ 75% improvement from baseline in EASI (EASI-75) at Week 16

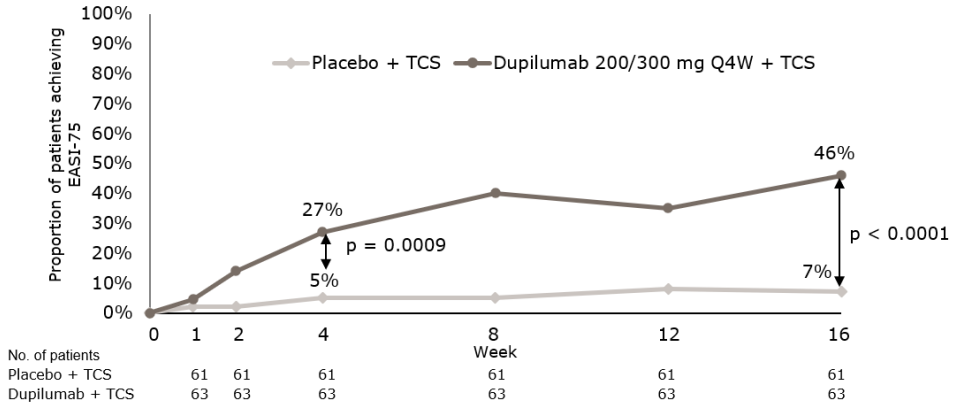
Secondary endpoints[1]	Key secondary efficacy endpoints included: - Percent change from baseline in EASI at Week 16 - Percent change from baseline in weekly mean of daily worst scratch and itch NRS score (assessed by parents or caregivers) to Week 16
Baseline characteristics[1]	Baseline demographics and disease characteristics were balanced across treatment groups. Across treatment groups, the mean age was 4.0 years, and 61% of patients were male. At baseline: - Mean duration of AD was 3.4 years - 23% of patients had an IGA score of 3 and 77% of patients had an IGA score of 4 - Mean BSA involvement was 58.4%
Key efficacy results	The co-primary efficacy endpoints, the proportion of patients with IGA score 0–1 (clear or almost clear skin) at week 16 and the proportion of patients with EASI-75 at week 16, were both met in LIBERTY AD PRESCHOOL[1]. A *post-hoc* analysis of the efficacy and safety of dupilumab compared with placebo in children aged 6 months to 5 years with severe AD from the LIBERTY AD PRESCHOOL clinical trial was completed[2]. Severe AD was defined as an IGA score of 4 at baseline[2]. This analysis reported efficacy and quality of life endpoints for children with severe AD (n = 125), including[2]: - EASI-75 - Worst scratch/itch NRS - Children's Dermatology Life Quality Index (CDLQI, for children aged ≥ 4 to < 6 years) - Infants' Dermatitis Quality of Life (IDQOL, for children < 4 years) At Week 16, significantly more patients receiving dupilumab achieved EASI-75 than those receiving placebo. Additionally, daily worst scratch itch NRS scores significantly improved with dupilumab compared with placebo after 16 weeks of treatment[2]. The table and graphs below present the key efficacy and quality of life outcomes obtained with dupilumab and placebo at Week 16, in patients with severe AD.

Sub-population of children aged 6 months to 5 years with severe AD (n = 125): Endpoints at Week 16[2]

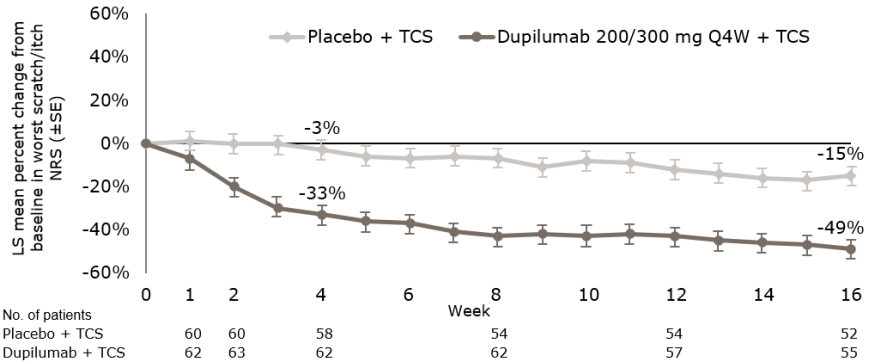
	Dupilumab plus TCS (n = 63)	Placebo plus TCS (n = 62)	Difference vs placebo (95% CI)	P value
EASI percent change from baseline (LS mean [SE]; 0–72)	–55.4 (5.0)	–10.3 (5.2)	–45.1 (–59.2 to –31.0)	<0.0001
Proportion of patients with IGA ≤ 2 (%)	42.9%	8.1%	34.8%	<0.0001
CDLQI change from baseline (LS mean [SE]; 0–30)	–9.1 (1.1)	–2.6 (1.2)	–6.6 (–9.7 to –3.4)	<0.0001
IDQOL change from baseline (LS mean [SE]; 0–30)	–9.1 (1.3)	–0.6 (1.1)	–8.5 (–11.9 to –5.1)	<0.0001

AD, atopic dermatitis; **CDLQI,** Children's Dermatology Life Quality Index; **CI,** confidence interval; **EASI,** Eczema Area and Severity Index; **IDQOL,** Infants' Dermatitis Quality of Life index; **IGA,** Investigator's Global Assessment; **LS,** least squares; **SE,** standard error; **TCS,** topical corticosteroids.

Proportion of patients achieving EASI-75[2]



Change from baseline in weekly average of daily worst scratch/itch NRS score[2]



Conclusions	Dupilumab significantly improved AD signs and symptoms and quality of life in children aged 6 months to 5 years with severe AD compared with placebo[2].
REFERENCES	1. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400:908–919. 2. Paller AS, Pinter A, Lee LW, et al. Efficacy and safety of dupilumab treatment with

	concomitant topical corticosteroids in children aged 6 months to 5 years with severe atopic dermatitis. Revolutionizing Atopic Dermatitis (RAD) Virtual Conference; Dec 11, 2022. Virtual.

SECTION 10: COMPARATIVE SAFETY – CLINICAL TRIALS

SAFETY OVERVIEW

The most common adverse reactions observed in clinical trials and/or post-marketing settings with dupilumab in asthma, atopic dermatitis (AD), and chronic rhinosinusitis with nasal polyposis (CRSwNP) are injection site reactions (includes erythema, oedema, pruritis, pain, bruising and swelling), conjunctivitis, conjunctivitis allergic, arthralgia, oral herpes, and eosinophilia. Rare cases of serum sickness, serum sickness-like reaction, anaphylactic reaction, and ulcerative keratitis have been reported[1–4].

Dupilumab was studied in 12 randomised, placebo-controlled trials including AD, asthma, and CRSwNP patients. The pivotal controlled studies involved 4,206 patients receiving dupilumab and 2,326 patients receiving placebo during the controlled period[1–4].

The safety of dupilumab with concomitant topical corticosteroids (TCS) was assessed in a study of 161 patients aged 6 months to 5 years with moderate-to-severe AD, which included a subgroup of 124 patients with severe AD (AD-1539). The safety profile of dupilumab with concomitant TCS in these patients through Week 16 was similar to the safety profile from studies in adults and paediatric patients aged 6–17 years with AD[1–4].

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

ADVERSE REACTIONS

Great Britain: Adverse reactions from 12 randomised, placebo-controlled trials, including AD, asthma, and CRSwNP patients, and from post-marketing surveillance[1,3]

MedDRA System Organ Class	Frequency	Adverse reaction
Infections and infestations	Common (≥ 1/100 to < 1/10)	Conjunctivitis[a] Oral herpes[a]
Blood and lymphatic system disorders	Common (≥ 1/100 to < 1/10)	Eosinophilia
Immune system disorders	Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000)	Angioedema[b] Anaphylactic reaction Serum sickness reaction Serum sickness-like reaction
Skin and subcutaneous tissue disorders	Uncommon (≥ 1/1,000 to < 1/100)	Facial rash[b]
Eye disorders	Common (≥ 1/100 to < 1/10) Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000)	Conjunctivitis allergic[a] Keratitis[a,b] Blepharitis[a,c] Eye pruritus[a,c] Dry eye[a,c] Ulcerative keratitis[a,b,c]
Musculoskeletal and connective tissue disorders	Common (≥ 1/100 to < 1/10)	Arthralgia[b]
General disorders and administration site concerns	Common (≥ 1/100 to < 1/10)	Injection site reactions (includes erythema, oedema, pruritis, pain, swelling and bruising)

[a]Eye disorders and oral herpes occurred predominately in AD studies.
[b]From post-marketing reporting.
[c]The frequencies for eye pruritus, blepharitis, and dry eye were common and ulcerative keratitis was uncommon in AD studies.
AD, atopic dermatitis; **CRSwNP,** chronic rhinosinusitis with nasal polyposis

Northern Ireland/Republic of Ireland: Adverse reactions from 12 randomised, placebo-controlled trials, including AD, asthma, and CRSwNP patients, and from post-marketing surveillance[2,4]

MedDRA System Organ Class	Frequency	Adverse reaction
Infections and infestations	Common (≥ 1/100 to < 1/10)	Conjunctivitis[a] Oral herpes[a]
Blood and lymphatic system disorders	Common (≥ 1/100 to < 1/10)	Eosinophilia
Immune system disorders	Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000)	Angioedema[b] Anaphylactic reaction Serum sickness reaction Serum sickness-like reaction
Skin and subcutaneous tissue disorders	Uncommon (≥ 1/1,000 to < 1/100)	Facial rash[b]
Eye disorders	Common (≥ 1/100 to < 1/10) Uncommon (≥ 1/1,000 to < 1/100) Rare (≥ 1/10,000 to < 1/1,000)	Conjunctivitis allergic[a] Keratitis[a,b] Blepharitis[a,c] Eye pruritus[a,c] Dry eye[a,c] Ulcerative keratitis[a,b,c]
Musculoskeletal and connective tissue disorders	Common (≥ 1/100 to < 1/10)	Arthralgia[b]
General disorders and administration site concerns	Common (≥ 1/100 to < 1/10)	Injection site reactions (includes erythema, oedema, pruritis, pain, swelling, and bruising)

[a]Eye disorders and oral herpes occurred predominately in AD studies.
[b]From post-marketing reporting.
[c]The frequencies for eye pruritus, blepharitis and dry eye were common and ulcerative keratitis was uncommon in AD studies.

AD, atopic dermatitis; **CRSwNP,** chronic rhinosinusitis with nasal polyposis

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

CLINICAL TRIALS

Safety data from one atopic dermatitis (AD) clinical trial, LIBERTY AD PRESCHOOL, are detailed below[1].

LIBERTY AD PRESCHOOL: Children aged 6 months to < 6 years with moderate-to-severe AD and an inadequate response to low-potency topical corticosteroids (TCS)[1].

	Placebo plus TCS (n = 78)[a]	Dupilumab plus TCS (n = 83)
Any TEAE, n (%)	58 (74%)	53 (64%)
Any serious TEAE, n (%)	4 (5%)	0
Any severe TEAE, n (%)	10 (13%)	2 (2%)
Treatment discontinuation owing to TEAE, n (%)	1 (1%)[b]	1 (1%)[c]
Any TEAE leading to death, n (%)	0	0
TEAE related to study drug, n (%)	5 (6%)	9 (11%)
TEAEs in ≥ 3% of patients		
Infections and infestations	40 (51%)	35 (42%)
Nasopharyngitis	7 (9%)	7 (8%)
Upper respiratory tract infection	6 (8%)	5 (6%)
Molloscum contagiosum	2 (3%)	4 (5%)
Conjunctivitis	0	3 (4%)
Viral gastroenteritis	0	3 (4%)
Impetigo	6 (8%)	3 (4%)
Viral respiratory tract infection	3 (4%)	0
Staphylococcal skin infection	3 (4%)	0
Skin and subcutaneous tissue disorders	28 (36%)	17 (20%)
AD[d]	25 (32%)	11 (13%)
Urticaria	4 (5%)	1 (1%)
Respiratory, thoracic, and mediastinal disorders	15 (19%)	9 (11%)
Rhinorrhoea	1 (1%)	4 (5%)
Asthma	5 (6%)	3 (4%)
Cough	5 (6%)	0
Gastrointestinal disorders	6 (8%)	8 (10%)
Dental caries	0	4 (5%)
Blood and lymphatic system disorders	7 (9%)	6 (7%)
Lymphadenopathy	6 (8%)	3 (4%)
General disorders and administration site conditions	9 (12%)	5 (6%)
Pyrexia	7 (9%)	1 (1%)

[a]One patient in the placebo plus TCS group was excluded from the safety analysis set because they were randomly assigned in error and did not receive study treatment. [b]Patient discontinued owing to TEAE of AD flare. [c]Patient discontinued owing to TEAE of nightmares due to blood draws. [d]Exacerbation of AD.

AD, atopic dermatitis; **TCS,** topical corticosteroids; **TEAE,** treatment-emergent adverse events

REFERENCES

1. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400:908–919.

MANAGEMENT OF ADVERSE REACTIONS	
Special warnings and precautions for use	
Traceability	In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded[1–4].
Acute asthma exacerbations	Dupilumab should not be used to treat acute asthma symptoms or acute exacerbations. Dupilumab should not be used to treat acute bronchospasm or status asthmaticus[1–4].
Corticosteroids	Systemic, topical, or inhaled corticosteroids should not be discontinued abruptly upon initiation of therapy with dupilumab. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy. Biomarkers of type 2 inflammation may be suppressed by systemic corticosteroid use. This should be taken into consideration to determine type 2 status in patients taking oral corticosteroids[1–4].
Conjunctivitis, dry eye, and keratitis-related events	Conjunctivitis, dry eye, and keratitis-related events have been reported with dupilumab, predominantly in atopic dermatitis (AD) patients. Some patients reported visual disturbances (e.g. blurred vision) associated with conjunctivitis or keratitis. Patients should be advised to promptly report new-onset or worsening eye symptoms to their healthcare provider. Sudden changes in vision or significant eye pain that does not settle warrant urgent review. Patients treated with dupilumab who develop conjunctivitis or dry eye that does not resolve following standard treatment or signs and symptoms suggestive of keratitis should undergo ophthalmological examination, as appropriate[1–4].
Hypersensitivity	If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of dupilumab should be discontinued immediately and appropriate therapy initiated. Cases of anaphylactic reaction, angioedema, and serum sickness/serum sickness-like reaction have been reported. Anaphylactic reactions and angioedema have occurred from minutes to up to 7 days after the dupilumab injection[1–4].
Eosinophilic conditions	Cases of eosinophilic pneumonia and cases of vasculitis consistent with eosinophilic granulomatosis with polyangiitis (EGPA) have been reported with dupilumab in adult patients who participated in the asthma development program. Cases of vasculitis consistent with EGPA have been reported with dupilumab and placebo in adult patients with co-morbid asthma in the CRSwNP development program. Physicians should be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in their patients with eosinophilia. Patients being treated for asthma may present with serious systemic eosinophilia sometimes presenting with clinical features of eosinophilic pneumonia or vasculitis consistent with eosinophilic granulomatosis with polyangiitis, conditions which are often treated with systemic corticosteroid therapy. These events usually, but not always, may be associated with the reduction of oral corticosteroid therapy[1–4].
Helminth infections	Patients with known helminth infections were excluded from participation in clinical studies. Dupilumab may influence the immune response against helminth infections by inhibiting interleukin (IL)-4/IL-13 signalling. Patients with pre-existing helminth infections should be treated before initiating dupilumab. If patients become infected while receiving treatment with dupilumab and do not respond to anti-helminth treatment, treatment with dupilumab should be discontinued until infection resolves. Cases of enterobiasis were reported in children 6–11 years old who participated in the dupilumab arm of the paediatric asthma development programme[1–4].

Patients with comorbid asthma	Patients on dupilumab who also have co-morbid asthma should not adjust or stop their asthma treatments without consultation with their physicians. Patients with comorbid asthma should be monitored carefully following discontinuation of dupilumab[1–4].
Vaccinations	Concurrent use of live and live attenuated vaccines with dupilumab should be avoided as clinical safety and efficacy have not been established. It is recommended that patients should be brought up to date with live and live attenuated immunisations in agreement with current immunisation guidelines prior to treatment with dupilumab. Clinical data are not available to support more specific guidance for live or live attenuated vaccines administration in patients treated with dupilumab. Immune responses to TdaP vaccine and meningococcal polysaccharide vaccine were assessed[1–4].
Sodium content	This medicinal product contains less than 1 mmol sodium (23 mg) per 300 mg dose, that is to say essentially 'sodium-free'[1–4].
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.

SECTION 11: REPLACEMENT OF EXISTING ATOPIC DERMATITIS TREATMENTS

In the UK, dupilumab was the first licensed biologic treatment for severe atopic dermatitis (AD) in children aged 6 months to 5 years[1–4]. While NICE guidelines recommend a stepwise approach to treatment with systemic immunosuppressants[5,6], these therapies are used off-license. In addition, systemic immunosuppressants are associated with safety concerns and have a significant negative impact on patient and caregiver burden owing to routine laboratory monitoring associated with blood draws, risk of infection, and renal and hepatic toxicity[7–10].

In children aged < 12 years, NICE recommends using a stepped approach to tailor the treatment regimen according to AD severity. Emollients should form the basis of treatment for AD and should always be used. Management can then be stepped up or down, depending on severity, with the addition of other treatments as follows[6]:

- Mild AD: Emollients; mild potency topical corticosteroids
- Moderate AD: Emollients, moderate potency topical corticosteroids, topical calcineurin inhibitors, bandages
- Severe AD: Emollients, potent topical corticosteroids, topical calcineurin inhibitors, bandages, phototherapy, systemic therapy

For children aged 6 months to 5 years with severe AD managed within NHS England specialist dermatology centres, Dupixent is reimbursed through the 'Commissioning Medicines for Children in Specialised Services' policy[11] in line with the recommendations set out in the NICE Technology Appraisal TA534 for Dupixent in adults with moderate-to-severe AD[5,a]. Eligible patients should be discussed at a multidisciplinary team meeting that includes at least two consultants (one being a consultant paediatrician) and a paediatric pharmacist[11].

[a]NICE recommends dupilumab as an option for treating moderate-to-severe AD in adult patients whose disease has not responded to at least one other systemic therapy, such as ciclosporin, methotrexate, azathioprine, and mycophenolate mofetil, or when systemic therapies are contraindicated or not tolerated[5].

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024.
3. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024.
4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
5. NICE. TA534. Dupilumab for treating moderate-to-severe atopic dermatitis. August 2018. Available at: https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485. Accessed January 2024.
6. NICE CG57. Atopic eczema in under 12s: Diagnosis and management. December 2007. Available at: https://www.nice.org.uk/guidance/cg57/resources/atopic-eczema-in-under-12s-diagnosis-and-management-pdf-975512529349. Accessed January 2024.
7. Sandimmun Neoral (cyclosporine A). Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/referral/sandimmun-neoral-article-30-referral-annex-iii_en.pdf. Accessed January 2024.
8. Nordimet (methotrexate). Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/nordimet-epar-product-information_en.pdf. Accessed January 2024.
9. Proudfoot LE, Powell AM, Ayis S, et al. The European treatment of severe atopic eczema in children taskforce (TREAT) survey. Br J Dermatol. 2013;169:901–909.

10. Siegfried EC, Jaworski JC, Kaiser JD, Hebert AA. Systematic review of published trials: Long-term safety of topical corticosteroids and topical calcineurin inhibitors in pediatric patients with atopic dermatitis. BMC Pediatr. 2016;16:75.
11. NHS England. Commissioning Medicines for Children in Specialised Services. 2017. Available at: https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/?UNLID=511760278202282219511 4. Accessed January 2024.

SECTION 12: BURDEN OF DISEASE (ATOPIC DERMATITIS)

Atopic dermatitis (AD) is a chronic, recurrently flaring, generalised skin condition that can be life-limiting, debilitating, and isolating. It has a substantial and multidimensional burden on patients from childhood through to adulthood, and can affect all aspects of life (physical, psychological, social, and financial). Severe disease is associated with pruritus and viral or bacterial skin infections that disrupt sleep, and there is a higher risk of depression and suicide[1,2].

AD incidence peaks in infancy, with an onset before the age of 6 years in an estimated 80% of patients[3]. In the UK, AD is prevalent in approximately 16–25% of children younger than 6 years[4]. AD is associated with substantially reduced quality of life in infants, young children, and their family members[5]. In addition, AD is associated with type 2 inflammation-mediated comorbidities, including asthma and food allergies, which often occur at an earlier age in children with AD than in those without AD[6,7].

Severe AD greatly impacts quality of life and daily functioning, with children reporting an average of 7.3 days of school missed in a 4-week period and up to 83% of adolescents reporting that they avoid everyday activities owing to their AD and regularly feel unhappy or depressed[8,9].

Patients with severe AD have limited access to effective treatments, resulting in a significant impact on clinical symptoms and infants' and caregivers' quality of life, while imposing an economic burden on caregivers and healthcare systems[2,10]. A short course of oral corticosteroids may be prescribed off-licence for children to control severe flares of AD[11,12]. However, oral corticosteroids and other immunosuppressants such as ciclosporin, azathioprine, mycophenolate mofetil, and methotrexate have safety concerns and therefore are not recommended for chronic use[2,13].

REFERENCES

1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024.
2. NICE. TA534. Dupilumab for treating moderate to severe atopic dermatitis. August 2018. Available at: https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485. Accessed January 2024.
3. Weidinger S, Beck, LS, Bieber T, et al. Atopic dermatitis. Nat Rev Dis Primers. 2018;4(1):1.
4. Silverberg JI, Barbarot S, Gadkari A, et al. Atopic dermatitis in the pediatric population: A cross-sectional, international epidemiologic study. Ann Allergy Asthma Immunol. 2021;126:417–428.
5. Al Shobaili HA. The impact of childhood atopic dermatitis on the patients' family. Pediatr Dermatol. 2010;27:618–623.
6. Eichenfield LF, Hanifin JM, Beck LA, et al. Atopic dermatitis and asthma: Parallels in the evolution of treatment. Pediatrics. 2003;111:608–616.
7. Martin PE, Eckert JK, Koplin JJ, et al. Which infants with eczema are at risk of food allergy? Results from a population-based cohort. Clin Exp Allergy. 2015;45:255–264.
8. Weidinger S, Simpson EL, Eckert L, et al. The patient-reported disease burden in pediatric patients with atopic dermatitis: A cross-sectional study in the United States, Canada, Europe, and Japan. J Am Acad Dermatol. 2020;83(suppl):AB1–302. Poster 15115.
9. Zuberbier T, Orlow SJ, Paller A, et al. Patients perspectives on the management of atopic dermatitis. J Allergy Clin Immunol. 2006;118:226–232.
10. Ariens LFM, van Nimwegen KJM, Shams M, et al. Economic burden of adult patients with moderate to severe atopic dermatitis indicated for systemic treatment. Acta Derm Venereol. 2019;99:762–768.
11. National Eczema Society. Oral steroids (Prednisolone). Available at: https://eczema.org/information-and-advice/treatments-for-eczema/oral-steroids/. Accessed

January 2024.
12. NICE CKS. Eczema - atopic: Oral corticosteroids. Available at: https://cks.nice.org.uk/topics/eczema-atopic/prescribing-information/oral-corticosteroids/. Accessed January 2024.
13. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400:908–919.

SECTION 13: UNMET CLINICAL NEED (ATOPIC DERMATITIS, CHILDREN 6 MONTHS TO 5 YEARS)

Although clinicians individualise therapy for patients, a typical treatment pathway involves emollients and topical corticosteroids (first line); topical calcineurin inhibitors (second line); phototherapy (third line); and systemic immunosuppressant therapies (fourth line), including ciclosporin, methotrexate, azathioprine, and mycophenolate mofetil. These systemic therapies can have serious adverse effects, and if a drug is no longer effective, it will be stopped and another drug will be offered. For people whose disease does not respond to multiple systemic therapies, the only remaining treatment option is best supportive care, which may include education, psychological support, emollients, topical corticosteroids, bandages, and hospitalisation. Managing exacerbations in atopic dermatitis (AD) includes using short-term potent topical corticosteroids, oral corticosteroids, and systemic therapy[1].

For infants with severe AD, their disease often remains uncontrolled with conventional therapies such as topical corticosteroids. As a result, physicians may resort to the use of off-label systemic immunosuppressants, which require additional monitoring and are associated with safety concerns[2,3].

There is a significant unmet need for a more precise treatment option that effectively controls severe AD in young children, while exhibiting a low rate of side effects and an acceptable safety profile, and is acceptable for long-term, chronic use[1].

REFERENCES

1. NICE. TA534. Dupilumab for treating moderate-to-severe atopic dermatitis. August 2018. Available at: https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485. Accessed January 2024.
2. Wu J, Guttman-Yasky E. Efficacy of biologics in atopic dermatitis. Expert Opin Biol Ther. 2020;20:525–538.
3. Paller AS, Simpson EL, Siegfried EC, et al. Dupilumab in children aged 6 months to younger than 6 years with uncontrolled atopic dermatitis: A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet. 2022;400:908–919.

SECTION 14: RELEVANT GUIDELINES/APPRAISALS

ENGLAND[1,2]

For children aged 6 months to 5 years with severe AD, dupilumab is reimbursed within NHS England specialist dermatology centres, through the 'Commissioning Medicines for Children in Specialised Services' policy[1] in line with the recommendations set out in the NICE Technology Appraisal TA534 for Dupixent in adults with moderate-to-severe AD[2]. Eligible patients should be discussed at a multidisciplinary team meeting that includes at least two consultants (one being a consultant paediatrician) and a paediatric pharmacist)[1]. Provider organisations must seek prior approval for all patients[1].

WALES

Appraisal by the All Wales Therapeutics and Toxicology Centre (AWMSG) is no longer required for medicines with a minor paediatric licence extension where the medicine is already recommended for use by NICE or AWMSG in the adult population[3].

SCOTLAND

Abbreviated submissions for paediatric licence extensions are no longer requested by the Scottish Medicines Consortium (SMC). Area Drugs and Therapeutics Committees (ADTCs) will be updated when paediatric licence extensions are granted and highlight advice for the corresponding indication in adults, however no SMC advice statement will be issued. ADTCs may make formulary decisions on paediatric licence extensions for medicines that are accepted for use (or restricted use) in adults. The Patient Access

	Scheme Assessment Group (PASAG) will liaise with companies to extend any existing Patient Access Scheme (PAS) to include the younger age group and will confirm arrangements with Boards[4].
NORTHERN IRELAND[1,2]	As per England (see above).
REFERENCES	1. NHS England. Commissioning Medicines for Children in Specialised Services. 2017. Available at: https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/?UNLID=511760278202282219511 4. Accessed January 2024. 2. NICE. TA534. Dupilumab for treating moderate-to-severe atopic dermatitis. August 2018. Available at: https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485. Accessed January 2024 3. AWMSG. Form A: Initial Submission. June 2023. Available at: https://awttc.nhs.wales/accessing-medicines/make-a-submission/pharmaceutical-industry-submissions/submit-for-awmsg-appraisal/invisible/initial-information-form-a1/. Accessed January 2024. 4. SMC. Minor process changes introduced. Available at: https://www.scottishmedicines.org.uk/about-us/latest-update/minor-process-changes-introduced/. Accessed January 2024.
SECTION 15: COST	
	The list price for dupilumab is £1,264.89 per pack containing 2 × pre-filled syringes of any dose[1]. For children 6 months to 5 years of age with severe atopic dermatitis, dupilumab dosing is weight based: 5 kg to <15 kg, 200 mg every 4 weeks (Q4W); 15 kg to <30 kg, 300 mg Q4W[2–5]. A pack of 2 syringes will provide 8 weeks of treatment (Q4W), for children aged 6 months to 5 years, equating to six and a half packs per patient per year. Therefore, the cost of treatment with dupilumab is £8,221.79 per patient per year of treatment.
REFERENCES	1. NICE. Dupilumab. Medicinal forms. Available at: https://bnf.nice.org.uk/drugs/dupilumab/medicinal-forms/. Accessed January 2024. 2. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 3. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc. Accessed January 2024. 4. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/10619/smpc#gref. Accessed January 2024. 5. Dupixent 200 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. IE. Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc#tabs. Accessed January 2024.
SECTION 16: IMPACT OF PRESCRIBING ON SERVICE PROVISION	
	Dupilumab is expected to be prescribed in tertiary centres by dermatology specialists. In many of these tertiary centres, this service is likely to be already established. Ongoing therapy may be administered by patients at home, and dupilumab will be offered with a homecare delivery service and a patient support programme. As with other biologics delivered in this way, there may be beneficial service implications in administering the drug through this type of scheme.
MONITORING	
	Monitoring for organ toxicities is not a requirement for the introduction and ongoing management of patients treated with dupilumab[1]. Immunosuppressant therapies including ciclosporin and methotrexate may be used off-label for the treatment of children aged 6 months to 5 years with severe atopic dermatitis (AD) and are associated with safety concerns; therefore, these therapies require additional monitoring[2–4].

	Reducing the side effects associated with treatment and the need for monitoring could reduce the number of outpatient appointments required. This could potentially help the NHS reduce healthcare costs and resource use associated with managing patients with severe AD.
REFERENCES	1. Dupixent 300 mg solution for injection in pre-filled syringe. Summary of Product Characteristics. UK. Available at: https://www.medicines.org.uk/emc/product/8553/smpc#gref. Accessed January 2024. 2. Sandimmun Neoral (cyclosporine A). Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/referral/sandimmun-neoral-article-30-referral-annex-iii_en.pdf. Accessed January 2024. 3. Nordimet (methotrexate). Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/nordimet-epar-product-information_en.pdf. Accessed January 2024. 4. Proudfoot LE, Powell AM, Ayis S, et al. The European treatment of severe atopic eczema in children taskforce (TREAT) survey. Br J Dermatol. 2013;169:901–909.

SECTION 17: OTHER RESOURCES

SUPPORT FOR PATIENTS

Dupixent MyWay® is a patient support programme providing patients with educational resources and support services throughout their treatment, which aims to empower patients who have been prescribed dupilumab (https://www.dupixentmyway.co.uk/).

The range of services provided is entirely optional and aims to provide assistance to healthcare teams managing the treatment of patients through:

- Homecare: Easy registration to home delivery
- Nurse training visits: Up to three home visits from their homecare nurse to teach patients how to administer dupilumab
- Text messaging reminder: Quick and simple reminders regarding the injections, deliveries, and nurse visits
- Ongoing support: With regular support calls and quarterly review

ORDERING INFORMATION[1,2]

GMID		PIP	
Code	**Description**	**Code**	**Description**
681314	Dupixent 300MG/2ML INJ PS2 G1	**4064721**	Dupixent pre-filled **syringe** with safety shield 300mg. Strength = 300mg; Quantity = 2
		4094926	Dupixent pre-filled **syringes** 300mg 2ml 6. Strength = 300mg; Quantity = 6; Pack size = 2ml
749333	Dupixent 200MG/+ INJ PS2 SAFE M18 GB	**4122891**	Dupixent solution for injection in pre-filled **syringe** 200 mg 2. Strength = 200mg; Quantity = 2

GTIN CODE/EAN[2]

5000283659808: Dupixent 300mg/2ml solution for injection pre-filled syringes (Sanofi Genzyme) 2 pre-filled disposable injectionDupixent
5000283659839: Dupixent 300mg/2ml solution for injection pre-filled syringes (Sanofi Genzyme) 6 pre-filled disposable injectionDupixent
5000283661351: Dupixent 200mg/1.14ml solution for injection pre-filled syringes (Sanofi Genzyme) 2 pre-filled disposable injection

REFERENCES

1. Pharma Finder. Available at: https://www.pharmafinder.co.uk. Accessed January 2024.
2. Unilexicon for medicines. Available at: https://unilexicon.com/med/. Accessed January 2024.

DUPILUMAB PACK IMAGES

Dupilumab pre-filled syringe for injection

Appendix 1: Relevant Links

UK Summary of Product Characteristics (300 mg syringe). Available at: https://www.medicines.org.uk/emc/product/8553/smpc#

UK Summary of Product Characteristics (200 mg syringe). Available at: https://www.medicines.org.uk/emc/product/10619/smpc#

Ireland Summary of Product Characteristics (300 mg syringe). Available at: https://www.medicines.ie/medicines/dupixent-300mg-solution-for-injection-in-pre-filled-syringe-31943/spc

Ireland Summary of Product Characteristics (200 mg syringe). Available at: https://www.medicines.ie/medicines/dupixent-200-mg-solution-for-injection-in-pre-filled-syringe-34859/spc

NHS England. Commissioning Medicines for Children in Specialised Services. 2017. Available at: https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/?UNLID=511760278202282219511 4

NICE. TA534. Dupilumab for treating moderate-to-severe atopic dermatitis. August 2018. Available at: https://www.nice.org.uk/guidance/ta534/resources/dupilumab-for-treating-moderate-to-severe-atopic-dermatitis-pdf-82606900940485

Appendix 2

Prescribing information: Dupixent (dupilumab) solution for injection in a pre-filled syringe or pen (Atopic Dermatitis and Prurigo Nodularis) – Great Britain

Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentations: Dupixent 200 mg solution for injection in a pre-filled syringe or pen, containing 200 mg of dupilumab in 1.14 ml solution (175 mg/ml) or Dupixent 300 mg solution for injection in a pre-filled syringe or pen, containing 300 mg of dupilumab in 2 ml solution (150 mg/ml).

Indications: Dupixent is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy. Dupixent is indicated for the treatment of severe atopic dermatitis in children 6 months to 11 years old who are candidates for systemic therapy. Dupixent is indicated for the treatment of adults with moderate-to- severe prurigo nodularis (PN) who are candidates for systemic therapy.

Dosage and Administration: Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of conditions for which Dupixent is indicated. Dupixent should be administered as subcutaneous (SC) injection, into the thigh or abdomen, except for the 5 cm around the navel. The upper arm can be used if not self-administered. Dupixent can be used with or without topical corticosteroids. ***Adults:*** the recommended initial dose is 600 mg (two 300 mg injections), followed by 300 mg given every other week (EOW). ***Adolescents (12-17 years) with body weight <60 kg:*** the recommended initial dose is 400 mg (two 200 mg SC injections), followed by 200 mg EOW. ***Adolescents (12-17 years) with body weight ≥60 kg:*** the recommended initial dose is 600 mg (two 300 mg SC injections) followed by 300 mg EOW. ***Children 6 to 11 years of age with body weight 15 kg to <60 kg:*** the recommended initial dose is 300 mg on Day 1, followed by 300 mg on Day 15. Subsequent doses of 300 mg every 4 weeks (Q4W) starting 4 weeks after Day 15 dose. The dose may be increased to 200mg EOW in these patients based on physician's assessment. ***Children 6 years to 11 years of age with body weight ≥ 60 kg:*** the recommended initial dose is 600 mg (two 300 mg injections), followed by 300 mg EOW. ***Children 6 months to 5 years of age with body weight 5 kg to <15 kg:*** the recommended initial dose is 200 mg (one 200 mg injection), followed by 200 every 4 weeks (Q4W). ***Children 6 months with body weight 15 kg to <30 kg:*** the recommended initial dose is 300 mg (one 300 mg injection), followed by 300 mg every 4 weeks (Q4W). ***Missed dose:*** See SmPC for more information on missed dose. **Special populations:** ***Elderly patients (≥65 years):*** No dose adjustment recommended. ***Renal impairment:*** No dose adjustment in patients with mild or moderate renal impairment. Very limited data available in patients with severe renal impairment. ***Hepatic impairment:*** No data available. ***Paediatric population <6 months:*** The safety and efficacy of Dupixent in children below the age of 6 months or a body weight < 5 kg have not been established.

<18 years: The safety and efficacy of dupilumab in children with PN below the age of 18 years have not been established. ***Method of administration:*** The dupilumab pre-filled pen is not intended for use in children below 12 years of age.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Warnings and Precautions: ***Corticosteroids:*** Systemic, topical, or inhaled corticosteroids should not be discontinued abruptly upon initiation of therapy with dupilumab. Reductions in corticosteroid dose, if appropriate, should be gradual and performed under the direct supervision of a physician. Reduction in corticosteroid dose may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy. ***Hypersensitivity:*** If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of Dupixent should be discontinued immediately and appropriate therapy initiated. Anaphylactic reactions and angioedema have occurred from minutes up to seven days post injection. ***Helminth infection:*** Patients with pre-existing helminth infections should be treated before initiating Dupixent. If patients become infected while receiving treatment with Dupixent and do not respond to anti-helminth treatment, treatment with Dupixent should be discontinued until infection resolves. ***Conjunctivitis, dry eye and keratitis related events:*** Patients should be advised to promptly report new onset or worsening eye symptoms to their healthcare provider. Sudden changes in vision or significant eye pain that does not settle warrant urgent review. Patients treated with Dupixent who develop conjunctivitis or dry eye that does not resolve following standard treatment or signs and symptoms suggestive of keratitis should undergo ophthalmological examination, as appropriate. ***Comorbid asthma:*** Patients with comorbid asthma should not adjust or stop their asthma treatments without consultation with their physicians. Patients with comorbid asthma should be monitored carefully following discontinuation of Dupixent. ***Vaccinations:*** Concurrent use of live and live attenuated vaccines with dupilumab should be avoided as clinical safety and efficacy have not been established. ***Interactions:*** Patients receiving Dupixent may receive concurrent inactive or non-live vaccinations.

Fertility, pregnancy and lactation: Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. There are limited data from the use of Dupixent in pregnant women. Dupixent should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. It is unknown whether Dupixent is excreted in human milk or absorbed systemically after ingestion.

Adverse effects: ***Common (≥1/100 to <1/10):*** Arthralgia, conjunctivitis, conjunctivitis allergic, eosinophilia, injection site reactions (erythema, oedema, pruritis, pain, swelling and bruising), oral herpes. ***Uncommon (≥ 1/1,000 to < 1/100):*** Angioedema, blepharitis, dry eye, eye pruritis, facial rash, keratitis. ***Rare (≥ 1/10,000 to < 1/1,000):*** Anaphylactic reaction, serum sickness reaction, serum sickness-like reaction, ulcerative keratitis. Eye disorders and oral herpes occurred predominately in atopic dermatitis studies. The frequencies for eye pruritus, blepharitis, and dry eye were common and ulcerative keratitis was uncommon

in atopic dermatitis studies. ***Serious adverse reactions:*** eczema herpeticum, infections and immunogenicity have also been reported. Prescribers should consult the SmPC in relation to other adverse reactions.

Legal Classification: POM. **List Price:** pack containing 2 x pre- filled syringes or pens: £1,264.89. **Marketing Authorisation Holder:** Sanofi Genzyme, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. **Marketing Authorisation Numbers**: 2 x 200 mg pre-filled syringe: PLGB 04425/0874; 2 x 300 mg pre-filled syringe: PLGB 04425/0820. 2 x 200 mg pre-filled pen: PLGB 04425/0875; 2 x 300 mg pre-filled pen: PLGB 04425/0771. **Further information is available from:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com. **Date of preparation**: November 2023.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com

Appendix 3:

Prescribing Information: Dupixent (dupilumab) solution for injection in a pre-filled syringe or pen (Atopic Dermatitis and Prurigo Nodularis) – Northern Ireland and Republic of Ireland

Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentations: Dupixent 200 mg solution for injection in a pre- filled syringe or pen, containing 200 mg of dupilumab in 1.14 ml solution (175 mg/ml) or Dupixent 300 mg solution for injection in a pre-filled syringe or pen, containing 300 mg of dupilumab in 2 ml solution (150 mg/ml).

Indications: Dupixent is indicated for the treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy. Dupixent is indicated for the treatment of severe atopic dermatitis in children 6 months to 11 years old who are candidates for systemic therapy. Dupixent is indicated for the treatment of adults with moderate-to-severe prurigo nodularis (PN) who are candidates for systemic therapy.

Dosage and Administration: Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of atopic dermatitis. Dupixent should be administered as subcutaneous (SC) injection, into the thigh or abdomen, except for the 5 cm around the navel. The upper arm can be used if not self-administered. Dupixent can be used with or without topical corticosteroids. Topical calcineurin inhibitors should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas. ***Adults (with Atopic Dermatis):*** the recommended initial dose of Dupixent is 600 mg (two 300 mg injections), followed by 300 mg given every other week (EOW). ***Adolescents (12-17 years) with body weight <60 kg:*** the recommended initial dose of Dupixent is 400 mg (two 200 mg injections), followed by 200 mg EOW. ***Adolescents (12-17 years) with body weight ≥60 kg:*** the recommended initial dose of Dupixent is 600 mg (two 300 mg injections) followed by 300 mg EOW. ***Children 6 to 11 years of age with body weight 15 kg to <60 kg:*** the recommended initial dose of Dupixent is 300 mg (one 300 mg injection) on Day 1, followed by 300 mg on Day 15. Subsequent doses of 300 mg every 4 weeks (Q4W) starting 4 weeks after Day 15 dose. The dose may be increased to 200mg EOW in these patients based on physician's assessment. ***Children 6 to 11 years of age with body weight ≥ 60 kg:*** the recommended initial dose of Dupixent is 600 mg (two 300 mg injections), followed by 300 mg EOW. ***Children 6 months to 5 years of age with body weight of 5 kg to <15 kg:*** the recommended initial dose of Dupixent is 200 mg (one 200 mg injection). Followed by subsequent doses 200mg every 4 weeks (Q4W). ***Children 6 months to 5 years of age with body weight of 15kg to less than 30kg:*** the recommended initial dose of Dupixent is 300mg (one 300 mg injection). Followed by subsequent doses of 300 mg every 4 weeks (Q4W).

Adults (with Prurigo Nodularis): The recommended dose of dupilumab for adult patients is an initial dose of 600 mg (two 300 mg injections), followed by 300 mg given every other week. Dupilumab can be used with or without topical corticosteroids. ***Missed dose***: If an every other week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, wait until the next dose on the original schedule. If an every 4 week dose is missed, administer the injection within 7 days from the missed dose and then resume the patient's original schedule. If the missed dose is not administered within 7 days, administer the dose, starting a new schedule based on this date. ***No or partial response:*** Consideration should be given to discontinuing treatment in patients who have shown no response after 16 weeks of treatment for atopic dermatitis. Some patients with initial partial response may subsequently improve with continued treatment beyond 16 weeks. If Dupixent treatment interruption becomes necessary, patients can still be successfully re-treated. Proper training should be provided to patients and/or caregivers on the preparation and administration of Dupixent prior to use according to the Instructions for Use (IFU) section in the package leaflet. **Special populations:** ***Elderly patients (≥65 years):*** No dose adjustment recommended. ***Renal impairment:*** No dose adjustment in patients with mild or moderate renal impairment. Very limited data available in patients with severe renal impairment. ***Hepatic impairment:*** No data available. ***Paediatric patients <6 years:*** No data available. ***Method of administration:*** The dupilumab pre-filled pen is not intended for use in children below 12 years of age. For children 6 to 11 years of age with severe atopic dermatitis, the dupilumab pre-filled syringe is the presentation appropriate for administration to this population. Each pre-filled syringe or pre-filled pen is for single use only.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Warnings and Precautions: ***Traceability:*** In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. ***Hypersensitivity:*** If a systemic hypersensitivity reaction (immediate or delayed) occurs, administration of Dupixent should be discontinued immediately and appropriate therapy initiated. Anaphylactic reactions and angioedema have occurred from minutes up to seven days post injection. ***Helminth infection:*** Patients with known helminth infection were excluded from the clinical trials. Dupixent may influence the immune response against helminth infections by inhibiting IL-4/IL-13 signaling. Patients with pre-existing helminth infections should be treated before initiating Dupixent. If patients become infected while receiving treatment with Dupixent and do not respond to anti-helminth treatment, treatment with Dupixent should be discontinued until infection resolves. Cases of enterobiasis were reported in children 6 to 11 years old who participated in the paediatric asthma development program. ***Conjunctivitis and keratitis related events:*** Conjunctivitis and keratitis related events

have been reported with dupilumab, predominantly in atopic dermatitis patients. Some patients reported visual disturbances (e.g. blurred vision) associated with conjunctivitis or keratitis. Patients should be advised to report new onset or worsening eye symptoms to their healthcare provider. Patients treated with Dupixent who develop conjunctivitis that does not resolve following standard treatment or signs and symptoms suggestive of keratitis should undergo ophthalmological examination, as appropriate. ***Comorbid asthma:*** Patients with comorbid asthma should not adjust or stop their asthma treatments without consultation with their physicians. Patients with comorbid asthma should be monitored carefully following discontinuation of Dupixent. ***Vaccinations:*** Concurrent use of live and live attenuated vaccines with dupilumab should be avoided as clinical safety and efficacy have not been established. It is recommended that patients should be brought up to date with live and live attenuated immunisations in agreement with current immunisation guidelines prior to treatment with dupilumab. Clinical data are not available to support more specific guidance for live or live attenuated vaccines administration in patients treated with dupilumab. Immune responses to TdaP vaccine and meningococcal polysaccharide vaccine were assessed. ***Sodium content:*** This medicinal product contains less than 1 mmol sodium (23 mg) per 300 mg dose, that is to say essentially "sodium-free". ***Interactions:*** Patients receiving Dupixent may receive concurrent inactive or non-live vaccinations. One study evaluating the pharmacokinetic effects of Dupixent on CYP substrates did not indicate clinically relevant effects of Dupixent on CYP1A2, CYP3A, CYP2C19, CYP2D6 or CYP2C9 activity.

Fertility, pregnancy and lactation: Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. There are limited data from the use of Dupixent in pregnant women. Animal studies do not indicate harmful effects. Dupixent should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus. It is unknown whether Dupixent is excreted in human milk or absorbed systemically after ingestion. A decision must be made whether to discontinue breast-feeding or to discontinue Dupixent therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Adverse effects: ***Common (≥1/100 to <1/10):*** Arthralgia[#], conjunctivitis*, conjunctivitis allergic*, eosinophilia, injection site reactions (erythema, oedema, pruritis, pain, swelling, and bruising), oral herpes*. ***Uncommon (≥ 1/1,000 to < 1/100):*** Angioedema[#], blepharitis*[†], dry eye*[†], eye pruritis*[†], facial rash[#], keratitis*[#]. ***Rare (≥ 1/10,000 to < 1/1,000):*** Anaphylactic reaction, serum sickness reaction, serum sickness-like reaction, ulcerative keratitis*[†#]. *Eye disorders and oral herpes occurred predominately in atopic dermatitis studies. [†]The frequencies for eye pruritus, blepharitis, and dry eye were common and ulcerative keratitis was uncommon in atopic dermatitis studies. [#]From postmarketing reporting. ***Serious adverse reactions:*** eczema herpeticum, infections and immunogenicity have also been reported. ***Adolescents (12-17 years) and children (6-11 years):*** The long-term safety profile of Dupixent observed in patients 6-17 years of age was consistent with that seen in adults with atopic dermatitis.

Legal Classification: POM. **List Price:** ***NI*:** Pack containing 2 x pre-filled syringes or pens: £1,264.89. ***IE:*** Price on application. **Marketing Authorisation Holder:** Sanofi Winthrop Industrie, 82 avenue Raspail, 94250 Gentilly, France. **Marketing Authorisation Numbers**: 2 x 200 mg pre-filled syringe: EU/1/17/1229/010; 2 x 300 mg pre-filled syringe: EU/1/17/1229/006. 2 x 200 mg pre-filled pen: EU/1/17/1229/014; 2 x 300 mg pre-filled pen: EU/1/17/1229/018. **Further information is available from: *NI*:** Medical Information, Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com. ***IE:*** Sanofi, 18 Riverwalk, Citywest Business Campus, Dublin 24 or contact IEmedinfo@sanofi.com. **SmPC Date:** 15 March 2023. **Date of preparation**: March 2023.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com
In Ireland: www.hpra.ie email: medsafety@hpra.ie Adverse events should also be reported to Sanofi Ireland Ltd. Tel: 01 403 5600. Alternatively, send via email to IEPharmacovigilance@sanofi.com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CERTIFICATE FOR PROMOTIONAL ITEMS (PMCPA)

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Document Name: Infant AD Formulary pack Jan 2024

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Additional Audience:

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Method of Dissemination: Digital Oral Pro-active

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Role	Signature
Jeet Mehta - Medical	Date: 06-Feb-2024 15:02:50 GMT+0000