Dupixent (Dupilumab) Abbreviated Prescribing Information 300 mg

1) Name and Presentation: Dupixent (Dupilumab) 300 mg Solution for injection in pre-filled syringe 2) Therapeutic indications **Atopic Dermatitis**: 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 to 11 years old who are candidates for systemic therapy **Asthma** Dupixent is indicated in adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterized by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment. **Chronic Rhinosinusitis with nasal polyps (CRSwNP)** Dupixent is indicated as an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control. Posology and method of administration Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment of conditions for which dupilumab is indicated**. 3) Posology and method of administration:** Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment for which dupilumab is indicated **Posology Atopic Dermatitis:** 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 administered as subcutaneous injection. *Children and Adolescents (6 to 17 years of age)*

The recommended dose of dupilumab for children and adolescents 6 to 17 years of age is specified in Table 1.

Table 1: Dose of dupilumab for subcutaneous administration for children and adolescents 6 years to 17 years of age with atopic dermatitis Body Weight	**Initial Dose**	**Subsequent Doses**
15 to less than 30 kg	600 mg (two 300 mg injections)	300 mg every 4 weeks (Q4W)
30 to less than 60 kg	400 mg (two 200 mg injections)	200 mg every other week (Q2W)
60 kg or more	600 mg (two 300 mg injections)	300 mg every other week (Q2W)

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, intertriginous and genital areas. 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. **Asthma*:*** The recommended dose of dupilumab for adults and adolescents (12 years of age and older) is: • For patients with severe asthma and who are on oral corticosteroids or for patients with severe asthma and co-morbid moderate-to-severe atopic dermatitis, an initial dose of 600 mg (two 300 mg injections), followed by 300 mg every other week administered as subcutaneous injection. • For all other patients, an initial dose of 400 mg (two 200 mg injections), followed by 200 mg every other week administered as subcutaneous injection. Patients receiving concomitant oral corticosteroids may reduce their steroid dose once clinical improvement with dupilumab has occurred Steroid reductions should be accomplished gradually Dupilumab is intended for long-term treatment. The need for continued therapy should be considered at least on an annual basis as determined by physician assessment of the patient's level of asthma. For patients with ***CRSwNP*** the recommended dose of dupilumab for adult patients is an initial dose of 300 mg followed by 300 mg given every other week. Dupilumab is intended for long-term treatment. Consideration should be given to discontinuing treatment in patients who have shown no response after 24 weeks of treatment for CRSwNP. Some patients with initial partial response may subsequently. **4) Special populations:** For patients 6 to 17 years of age with atopic dermatitis, the recommended dose is 300 mg Q4W (15 kg to <30 kg), 200 mg Q2W (30 kg to <60 kg), and 300 mg Q2W (≥60 kg). The safety and efficacy of dupilumab in children with atopic dermatitis below the age of 6 years have not been established. The safety and efficacy of dupilumab in children with a body weight < 15 kg have not been established. The safety and efficacy of dupilumab in children with severe asthma below the age of 12 years have not been established. No data are available. CRSwNP does not normally occur in children. The safety and efficacy in children with CRSwNP below the age of 18 years have not been established**. 5)) Method of administration**: Dupixent is administered by subcutaneous injection into the thigh or abdomen, except for the 5 cm around the navel. If somebody else administers the injection, the upper arm can also be used. For the initial 600 mg dose, two 300 mg injections should be administered consecutively in different injection sites. 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.**6) Contraindications:** hypersensitivity to the active substance or to any of the excipients. See full SmPC for full list of excipients **7Warnings and precautions :** 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. 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. If systemic hypersensitivity reaction occurs, discontinue administration and initiate appropriate therapy. Patients with comorbid asthma should be monitored carefully following discontinuation of dupilumab. 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. Contains < 1 mmol Na (23 mg) per 300 mg, i.e. essentially" sodium-free (Kindly refer to the full SmPC for this section) **8<u>10) Drug interactions:</u>** The safety and efficacy of concurrent use of Dupixent with live vaccines has not been studied. Immune responses to vaccination were assessed in a study in which patients with atopic dermatitis were treated once weekly for 16 weeks with 300 mg of dupilumab. No adverse interactions between either of the non-live vaccines and dupilumab were noted in the study. Therefore, patients receiving Dupixent may receive concurrent inactivated or non-live vaccinations. In a clinical study of AD patients, the effects of dupilumab on the pharmacokinetics (PK) of CYP substrates were evaluated. The data gathered from this study did not indicate clinically relevant effects of dupilumab on CYP1A2, CYP3A, CYP2C19, CYP2D6, or CYP2C9 activity**. 9) Fertility, pregnancy and lactation**: Dupixent should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is unknown whether dupilumab 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. **10) Effects on ability to drive**: Dupixent has no or negligible influence on the ability to drive or operate machinery. **11) Undesirable effects:** Atopic dermatitis: observed in clinical trials: *Infections/infestations*: common: conjunctivitis, oral herpes. *Blood/lymphatic system disorders*: common: eosinophilia. *Immune system disorders:* very rare: serum sickness/serum sickness-like reactions. *Nervous system disorders*: common: headache. *Eye disorders*: common: allergic conjunctivitis, eye pruritus, blepharitis. Uncommon: Keratitis, Ulcerative keratitis. *Musculoskeletal and connective tissue disorders* Arthralgia. *General disorders/administration site conditions*: very common: injection site reactions. Asthma: *Immune system disorders:* very rare: anaphylactic reaction. *General disorders/administration site conditions*: injection site erythema, injection site edema, injection site pain, injection site pruritus. CRSwNP: *Infections and infestations*: Common: Conjunctivitis. *Blood and lymphatic system disorders*: Common: Eosinophilia. *General disorders and administration site conditions*: Very common: Injection site erythema; Common: Injection site edema, Injection site pain, Injection site pruritis**. 13) Overdose:** There is no specific treatment for Dupixent overdose. In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately**. 14) Special precautions for storage**: Store in a refrigerator (2°C - 8°C). Do not freeze. Store in the original carton to protect from light. **15) Pharmacological properties**: Pharmacotherapeutic group: Other dermatological preparations, agents for dermatitis, excluding corticosteroids: ATC code: D11AH05**. 16) Marketing authorization holder**: Sanofi-Aventis groupe, 54, rue La Boétie, 75008 Paris, France. **Abbreviated Prescribing Information based on the EU SmPC as of January 2021.**

Dupixent (Dupilumab) Abbreviated Prescribing Information 200 mg

1) Name and Presentation: Dupixent (Dupilumab) 200 mg Solution for injection in pre-filled syringe. 2) Therapeutic indications<u>: Atopic Dermatitis</u>: 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 to 11 years old who are candidates for systemic therapy. **<u>Asthma</u>** Dupixent is indicated in adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterized by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment.**3) Posology and method of administration:** Treatment should be initiated by healthcare professionals experienced in the diagnosis and treatment for which dupilumab is indicated **Posology Atopic Dermatitis:** 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 administered as subcutaneous injection. *Children and Adolescents (6 to 17 years of age)*

The recommended dose of dupilumab for children and adolescents 6 to 17 years of age is specified in Table 1.

Table 1: Dose of dupilumab for subcutaneous administration for children and adolescents 6 years to 17 years of age with atopic dermatitis Body Weight	**Initial Dose**	**Subsequent Doses**
15 to less than 30 kg	600 mg (two 300 mg injections)	300 mg every 4 weeks (Q4W)
30 to less than 60 kg	400 mg (two 200 mg injections)	200 mg every other week (Q2W)
60 kg or more	600 mg (two 300 mg injections)	300 mg every other week (Q2W)

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, intertriginous and genital areas. 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. **Asthma*:*** The recommended dose of dupilumab for adults and adolescents (12 years of age and older) is: • For patients with severe asthma and who are on oral corticosteroids or for patients with severe asthma and co-morbid moderate-to-severe atopic dermatitis, an initial dose of 600 mg (two 300 mg injections), followed by 300 mg every other week administered as subcutaneous injection. • For all other patients, an initial dose of 400 mg (two 200 mg injections), followed by 200 mg every other week administered as subcutaneous injection. Patients receiving concomitant oral corticosteroids may reduce their steroid dose once clinical improvement with dupilumab has occurred Steroid reductions should be accomplished gradually Dupilumab is intended for long-term treatment. The need for continued therapy should be considered at least on an annual basis as determined by physician assessment of the patient's level of asthma. **Missed dose**: If a dose is missed, administer the dose as soon as possible. Thereafter, resume dosing at the regular scheduled time**4) Special populations:** For patients 6 to 17 years of age with atopic dermatitis, the recommended dose is 300 mg Q4W (15 kg to <30 kg), 200 mg Q2W (30 kg to <60 kg), and 300 mg Q2W (≥60 kg)..The safety and efficacy of dupilumab in children with atopic dermatitis below the age of 6 years have not been established. No data are available. The safety and efficacy of dupilumab in children with severe asthma below the age of 12 years have not been established. No data are available. The safety and efficacy of dupilumab in children with severe asthma below the age of 12 years have not been established. No data are available. CRSwNP does not normally occur in children. The safety and efficacy in children with CRSwNP below the age of 18 years have not been established**. 5)) Method of administration**: Dupixent is administered by subcutaneous injection into the thigh or abdomen, except for the 5 cm around the navel. If somebody else administers the injection, the upper arm can also be used. For the initial 400 mg dose, two 200 mg injections should be administered consecutively in different injection sites. 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. A patient may self-inject dupilumab or the patient's caregiver may administer dupilumab if their healthcare professional determines that this is appropriate. Proper training should be provided to patients and/or caregivers on the preparation and administration of dupilumab prior to use according to the Instructions for Use (IFU) section in the package leaflet. **6) Contraindications:** hypersensitivity to the active substance or to any of the excipients. See full SmPC for full list of excipients **7)Warnings and precautions :** 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. 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. If systemic hypersensitivity reaction occurs, discontinue administration and initiate appropriate therapy. Patients with comorbid asthma should be monitored carefully following discontinuation of dupilumab. 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. Contains < 1 mmol Na (23 mg) per 300 mg, i.e. essentially" sodium-free (Kindly refer to the full SmPC for this section) **8) Drug interactions:** The safety and efficacy of concurrent use of Dupixent with live vaccines has not been studied. Immune responses to vaccination were assessed in a study in which patients with atopic dermatitis were treated once weekly for 16 weeks with 300 mg of dupilumab. No adverse interactions between either of the non-live vaccines and dupilumab were noted in the study. Therefore, patients receiving Dupixent may receive concurrent inactivated or non-live vaccinations. In a clinical study of AD patients, the effects of dupilumab on the pharmacokinetics (PK) of CYP substrates were evaluated. The data gathered from this study did not indicate clinically relevant effects of dupilumab on CYP1A2, CYP3A, CYP2C19, CYP2D6, or CYP2C9 activity**. 9) Fertility, pregnancy and lactation**: Dupixent should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is unknown whether dupilumab 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. Fertility animal studies showed no impairment of fertility **10) Effects on ability to drive**: Dupixent has no or negligible influence on the ability to drive

or operate machinery. **11) Undesirable effects:** Atopic dermatitis: observed in clinical trials: *Infections/infestations*: common: conjunctivitis, oral herpes. *Blood/lymphatic system disorders*: common: eosinophilia. *Immune system disorders:* very rare: serum sickness/serum sickness-like reactions. *Nervous system disorders*: common: headache. *Eye disorders*: common: allergic conjunctivitis, eye pruritus, blepharitis. Uncommon: Keratitis, Ulcerative keratitis. *Musculoskeletal and connective tissue disorders* Arthralgia. *General disorders/administration site conditions*: very common: injection site reactions. Asthma: *Immune system disorders:* very rare: anaphylactic reaction. *General disorders/administration site conditions*: injection site erythema, injection site edema, injection site pain, injection site pruritus. CRSwNP: *Infections and infestations*: Common: Conjunctivitis. *Blood and lymphatic system disorders*: Common: Eosinophilia. *General disorders and administration site conditions*: Very common: Injection site erythema; Common: Injection site edema, Injection site pain, Injection site pruritis**. 13) Overdose:** There is no specific treatment for Dupixent overdose. In the event of overdosage, monitor the patient for any signs or symptoms of adverse reactions and institute appropriate symptomatic treatment immediately**. 14) Special precautions for storage**: Store in a refrigerator (2°C - 8°C). Do not freeze. Store in the original carton to protect from light. **15) Pharmacological properties**: Pharmacotherapeutic group: Other dermatological preparations, agents for dermatitis, excluding corticosteroids: ATC code: D11AH05**. 16) Marketing authorization holder**: Sanofi-Aventis groupe, 54, rue La Boétie, 75008 Paris, France

Abbreviated Prescribing Information based on the EU SmPC as of January 2021 for 200 mg.