Product Monograph

Including Patient Medication Information

[Pr]EXDENSUR

Depemokimab Injection

Recombinant humanized (IgG1, kappa) monoclonal antibody produced in Chinese hamster ovary cells by recombinant DNA technology

Solution for subcutaneous injection

100 mg/mL of depemokimab

Interleukin-5 (IL-5) inhibitor

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Canada

Date of Authorization: 2026-06-15

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Recent Major Label Changes

Not applicable

Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

Asthma

EXDENSUR (depemokimab injection) is indicated as an add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma characterized by an eosinophilic phenotype and inadequately controlled by medium- to high-dose inhaled corticosteroids (ICS) plus another asthma controller.

EXDENSUR is not indicated for the relief of acute bronchospasm or status asthmaticus (See 7 Warnings and Precautions).

Chronic rhinosinusitis with nasal polyps

EXDENSUR is indicated as an add-on maintenance treatment with intranasal corticosteroids in adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) inadequately controlled by systemic corticosteroids and/or surgery.

1.1. Pediatrics

Asthma

Pediatrics (≥ 12 and < 18 years of age): Of the 502 subjects with asthma treated with EXDENSUR in the main clinical studies, a total of 15 subjects were 12 to less than 18 years of age. In general, the efficacy and safety in this age group were consistent with the overall study population.

Pediatrics (<12 years of age): No data are available to Health Canada; therefore, the efficacy and safety of EXDENSUR in patients younger than 12 years of age with asthma have not been established.

Chronic Rhinosinusitis with Nasal Polyps

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, the efficacy and safety of EXDENSUR in patients younger than 18 years of age with CRSwNP have not been established.

1.2. Geriatrics

Asthma

Geriatrics (≥65 years of age): Of the 502 subjects with asthma treated with EXDENSUR in the main clinical studies, a total of 133 subjects were 65 years of age and older. In general, the efficacy and safety in this age group were consistent with the overall study population.

Chronic Rhinosinusitis with Nasal Polyps

Geriatrics (≥65 years of age): Of the 272 subjects with CRSwNP treated with EXDENSUR in the main clinical studies, a total of 49 subjects were 65 years of age and older. In general, the efficacy and safety in this age group were consistent with the overall study population.

2. Contraindications

EXDENSUR is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 Dosage Forms, Strengths, Composition, and Packaging.

4. Dosage and Administration

4.1. Dosing Considerations

EXDENSUR must only be administered as a subcutaneous injection.

4.2. Recommended Dose and Dosage Adjustment

Asthma

Adults and Adolescents (≥12 years and older)

The recommended dose of EXDENSUR is 100 mg administered by subcutaneous (SC) injection once every 6 months.

Chronic Rhinosinusitis with Nasal Polyps

Adults

The recommended dose of EXDENSUR is 100 mg administered by subcutaneous (SC) injection once every 6 months.

Geriatrics
No dose adjustment is recommended in patients 65 years or older (see 10.3 Pharmacokinetics).

Hepatic Insufficiency
No dose adjustment is recommended in patients with hepatic impairment (see 10.3 Pharmacokinetics).

Renal Insufficiency
No dose adjustment is recommended in patients with renal impairment (see 10.3 Pharmacokinetics).

4.4. Administration

EXDENSUR may be self-administered by adult or adolescent patients or administered by a caregiver using the pre-filled pen or pre-filled syringe if their healthcare professional determines that it is appropriate, and the patient or caregiver are trained in injection techniques.

Instructions for administration:

1. Remove the pre-filled pen or pre-filled syringe from the refrigerator and allow it to sit at room temperature (≤ 30°C) for 30 minutes prior to injection. Do not warm EXDENSUR in any other way. Do not remove the needle cap until you are ready to inject.

2. Prior to administration, visually inspect the window of the pre-filled pen or the pre-filled syringe for particulate matter. EXDENSUR injection should be colourless to yellow to brown, clear to opalescent in color. Do not use EXDENSUR injection if the product exhibits cloudiness or particulate matter. Do not use the EXDENSUR pre-filled pen or pre-filled syringe if dropped on a hard surface or has been left out of the carton for more than 8 hours.

3. Administer the subcutaneous injection into the upper arm, thigh, or abdomen, avoiding the 5 cm (approximately 2 inches) around the navel.

4. Never give injections into areas where the skin is tender, bruised, red, or hard.

5. Immediately dispose of the pre-filled pen or pre-filled syringe and needle cap in the nearest sharps container.

Refer to the INSTRUCTIONS FOR USE for complete administration instructions of EXDENSUR injection

prior to use.

4.5. Missed Dose

If a dose is missed, administer as soon as possible. If the missed dose is taken 1 month or longer after the scheduled dose, resume the 6 monthly (every 26 weeks) injection schedule from the date of when the missed dose was given.

5. Overdose

There is no clinical experience with an overdose of EXDENSUR.

There is no specific treatment for an overdose with EXDENSUR. If an overdose occurs, the patient should be treated supportively with appropriate monitoring as necessary.

Further management should be as clinically indicated or as recommended by a poison control centre, where applicable.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

To help ensure the traceability of biologic products, healthcare professionals should record both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 1 - Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-Medicinal Ingredients
Subcutaneous injection	Solution for subcutaneous injection. Each single-use pre-filled pen contains 100 mg/mL depemokimab. Each single-use pre-filled syringe contains 100 mg/mL depemokimab.	L-arginine hydrochloride, disodium edetate dihydrate, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, trehalose dihydrate, water for injections.

EXDENSUR is available as a sterile, preservative-free, colourless, yellow to brown, clear to opalescent solution for subcutaneous use. It is supplied in the following formats:

- A single-dose, 1-mL, pre-filled pen (autoinjector) with a fixed 29 gauge, half-inch needle;
- A single-dose, 1-mL, pre-filled syringe with a fixed 29 gauge, half-inch needle with a needle guard.

Each pre-filled pen or pre-filled syringe delivers 100 mg depemokimab in 1 mL (100 mg/mL).

Description

EXDENSUR (depemokimab injection) is a humanized monoclonal antibody (IgG1, kappa) that inhibits human interleukin-5 (IL-5) binding to its cognate receptor. Depemokimab is produced by recombinant DNA technology in Chinese hamster ovary cells. The estimated molecular weight of depemokimab is 149 kDa.

7. Warnings and Precautions

General

Acute asthma symptoms or deteriorating disease

EXDENSUR must not be used to treat acute asthma symptoms or acute exacerbations.

Asthma-related adverse events or exacerbations may occur during treatment with EXDENSUR. It is recommended that patients be instructed to seek medical advice if their asthma remains uncontrolled or worsens after initiation of treatment with EXDENSUR.

Reduction of background medications for asthma

Abrupt discontinuation of background medications (including systemic and inhaled corticosteroids) after initiation of EXDENSUR therapy is not recommended. Reductions in the dosages of background medications, if appropriate, must be gradual and performed under the supervision of a healthcare professional.

Hepatic/Biliary/Pancreatic

Cases of elevated liver enzymes, some with features of autoimmune hepatitis, have occurred following administration of EXDENSUR, although a causal relationship between EXDENSUR and these events has not been established (see 8.2 Clinical Trial Adverse Reactions and 8.3 Less Common Clinical Trial Adverse Reactions).

Immune

Hypersensitivity and administration-related reactions

Hypersensitivity reactions, such as anaphylaxis, have been reported with other monoclonal antibodies that target IL-5 or its receptor and therefore, similar reactions may occur with EXDENSUR.

Administration related systemic non-allergic reactions may occur following the administration of EXDENSUR. These reactions are usually nonserious and generally occur within hours of administration, but some may have a delayed onset (i.e., days).

In the event of a hypersensitivity or other reaction, clinical judgement must be used regarding re-administration of EXDENSUR (see 8.2 Clinical Trial Adverse Reactions).

Parasitic (helminth) infections

Eosinophils may be involved in the immunological response to some helminth infections. Patients with pre-existing helminth infections were excluded from participation in the clinical programme. Patients with pre-existing helminth infections should be treated for their infection prior to EXDENSUR therapy. If patients become infected while receiving treatment with EXDENSUR and do not respond to anti-helminth treatment, consider delaying administration of the next EXDENSUR dose until the infection resolves.

Reproductive Health

- **Fertility**

There are no data from human studies to inform on the potential effects of EXDENSUR on fertility.

7.1. Special Populations

7.1.1. Pregnancy

There are limited data from the use of EXDENSUR in pregnant women. No reproductive or developmental toxicology studies have been conducted in animals to evaluate the potential effects of depemokimab on pregnancy.

Monoclonal antibodies, such as depemokimab, are expected to be transported across the placenta in a linear fashion as pregnancy progresses. The higher affinity of depemokimab to the neonatal Fc receptor (see 10.1 Mechanism of Action and 16 Non-Clinical Toxicology) may lead to increased transfer across the placenta, resulting in prolonged and increased exposure of the infant. The potential risk associated with EXDENSUR transmission to the fetus is unknown.

EXDENSUR should not be used by pregnant women, unless the expected benefit to the mother justifies the potential risk to the fetus. Women should be advised to contact their healthcare professional if they become pregnant while receiving EXDENSUR, or during the 8 months after the treatment is stopped.

7.1.2. Breastfeeding

There are no data regarding the excretion of depemokimab in human or animal milk. However, depemokimab is a humanized monoclonal antibody (immunoglobulin G1 [IgG1] kappa), and immunoglobulin G (IgG) is present in human milk in small amounts.

A decision should be made whether to discontinue breastfeeding or discontinue EXDENSUR, taking into account the importance of breastfeeding to the infant and the importance of the drug to the mother.

7.1.3. Pediatrics

Asthma

Pediatrics (≥ 12 and < 18 years of age): A total of 30 pediatric patients aged 12 to 17 years with asthma were enrolled in the SWIFT trials, of which 15 were randomized to EXDENSUR.

Pediatrics (<12 years of age): The safety and effectiveness of EXDENSUR in patients younger than 12 years with asthma have not been established.

Chronic Rhinosinusitis with Nasal Polyps

Pediatrics (<18 years of age): The safety and effectiveness of EXDENSUR in patients aged younger than 18 years with CRSwNP have not been established.

7.1.4. Geriatrics

Geriatrics (≥65 years of age): Of the 773 patients that received EXDENSUR 100 mg, 182 (24%) were 65 years of age and older and 33 (4%) were 75 years of age and older. No overall differences in safety or efficacy were observed between these subjects and younger subjects.

8. Adverse Reactions

8.1. Adverse Reaction Overview

In clinical studies of adult and adolescent patients with severe asthma characterized by an eosinophilic phenotype, the most common adverse events considered to be possibly related to treatment with depemokimab were pruritus (<1%), administration-related systemic reactions (2%) and injection site reactions (1%).

In clinical studies of adult patients with CRSwNP, the most common adverse events considered to be possibly related to treatment with depemokimab were pruritus (1%), administration-related systemic reactions (<1%), and injection site reactions (1%).

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

Asthma

The safety of EXDENSUR in pediatric (age ≥ 12 years) and adult patients with severe asthma characterized by an eosinophilic phenotype has been studied in two 52-week, randomized, placebo-controlled, multicentre trials (SWIFT-1 and SWIFT-2). In SWIFT-1 and SWIFT-2, patients received either EXDENSUR 100 mg or placebo SC once every 6 months in addition to their existing background medications (see 14 Clinical Trials). A total of 501 patients received at least 1 dose of EXDENSUR in these trials. Less than 1% of the patients who received either EXDENSUR or placebo discontinued treatment due to adverse events.

Adverse events that occurred more commonly in EXDENSUR-exposed versus placebo-exposed patients are shown in Table 2.

Other phase 3 clinical trials include an ongoing open-label 52-week extension study (AGILE) involving asthma patients who had previously completed either of SWIFT-1 or SWIFT-2. This study has enrolled 629 patients (419 previously exposed to EXDENSUR, 210 previously exposed to placebo in the SWIFT studies). Based on the interim analysis, the safety profile of EXDENSUR was consistent with that observed in the placebo-controlled studies.

Table 2 – On- and post-treatment adverse events with ≥1% incidence in EXDENSUR and ≥1% more common with EXDENSUR than placebo in adult and pediatric (age ≥ 12 years) patients with severe asthma characterized by an eosinophilic phenotype from placebo-controlled studies (SWIFT-1 and SWIFT-2), regardless of causality

System organ class/ preferred term	EXDENSUR 100 mg SC (N=501) n (%)	Placebo (N=261) n (%)
Infections and infestations		
Upper respiratory tract infection	47 (9%)	20 (8%)
Pharyngitis	18 (4%)	3 (1%)
Respiratory, thoracic and mediastinal disorders		
Rhinitis allergic	30 (6%)	7 (3%)
Nervous system disorders		
Dizziness	10 (2%)	2 (1%)
General disorders and administration site conditions		
Influenza like illness	9 (2%)	1 (< 1%)
Musculoskeletal and connective tissue disorders		
Pain in extremity	9 (2%)	1 (< 1%)
Injury, poisoning and procedural complications		
Ligament sprain	6 (1%)	0

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

The safety of EXDENSUR in adult patients with CRSwNP has been studied in two 52-week, randomized, placebo-controlled, multicenter trials (ANCHOR-1 and ANCHOR-2). In ANCHOR-1 and ANCHOR-2, patients received either EXDENSUR 100 mg or placebo SC once every 6 months in addition to their existing background medications (see 14 Clinical Trials). A total of 272 patients received at least 1 dose of EXDENSUR in these trials. Less than 1% of the patients who received EXDENSUR discontinued treatment due to adverse events compared with 1% of patients receiving placebo.

Adverse events that occurred more commonly in EXDENSUR-exposed versus placebo-exposed patients are shown in Table 3.

Table 3 – On- and post-treatment adverse events with ≥1% Incidence in EXDENSUR and ≥1% more common with EXDENSUR than placebo in adult subjects with CRSwNP from placebo-controlled studies (ANCHOR-1 and ANCHOR-2), regardless of causality

System organ class/ preferred term	EXDENSUR 100 mg SC (N=272) n (%)	Placebo (N=256) n (%)
Infections and infestations		
Nasopharyngitis	49 (18%)	39 (15%)
Respiratory, thoracic and mediastinal disorders		
Epistaxis	13 (5%)	5 (2%)
Catarrh	4 (1%)	1 (< 1%)
Gastrointestinal disorders		

System organ class/ preferred term	EXDENSUR 100 mg SC (N=272) n (%)	Placebo (N=256) n (%)
Diarrhoea	8 (3%)	3 (1%)
Abdominal pain upper	4 (1%)	1 (< 1%)
Skin and subcutaneous tissue		
Eczema	4 (1%)	0
Pruritus	4 (1%)	0

Hepatic/Biliary/Pancreatic

In the placebo-controlled asthma and CRSwNP populations (SWIFT and ANCHOR studies), liver-related adverse events and/or abnormal liver tests requiring treatment discontinuation or increased laboratory monitoring were reported in 2% of patients receiving depemokimab compared to 1% of patients who received placebo.

Administration-related reactions

In the placebo-controlled asthma and CRSwNP populations (SWIFT and ANCHOR studies), acute and delayed systemic non-allergic reactions (e.g., headache, fatigue, rash) were reported in 1% of patients receiving depemokimab compared to < 1% of patients who received placebo. All of these events were nonserious and from their onset, 85% resolved in ≤ 7 days and 57% in ≤ 2 days.

Local injection site reactions

In the placebo-controlled asthma and CRSwNP populations (SWIFT and ANCHOR studies), local injection site reactions (e.g., pain, erythema, swelling, itching) were reported in 1% of patients receiving depemokimab compared to < 1% of patients who received placebo. The reactions reported with depemokimab were mild in intensity and were transient (67% resolved in ≤ 7 days, with 50% resolving in ≤ 2 days from their onset).

8.2.1. Clinical Trial Adverse Reactions – Pediatrics

Fifteen adolescents (aged 12-17) received EXDENSUR in two placebo-controlled studies for asthma (SWIFT-1 and SWIFT-2) of 52 weeks duration. The safety profile was generally similar to that seen in adults. No additional adverse reactions were identified.

8.3. Less Common Clinical Trial Adverse Reactions

Hepatobiliary disorders: autoimmune hepatitis (see 7 Warnings and Precautions).

9. Drug Interactions

9.2. Drug Interactions Overview

EXDENSUR has a low potential for drug-drug interactions, based on its route of metabolism and mechanism of action.

9.3. Drug-Behaviour Interactions

Drug-behavioural interactions have not been established.

9.4. Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10. Clinical Pharmacology

10.1. Mechanism of Action

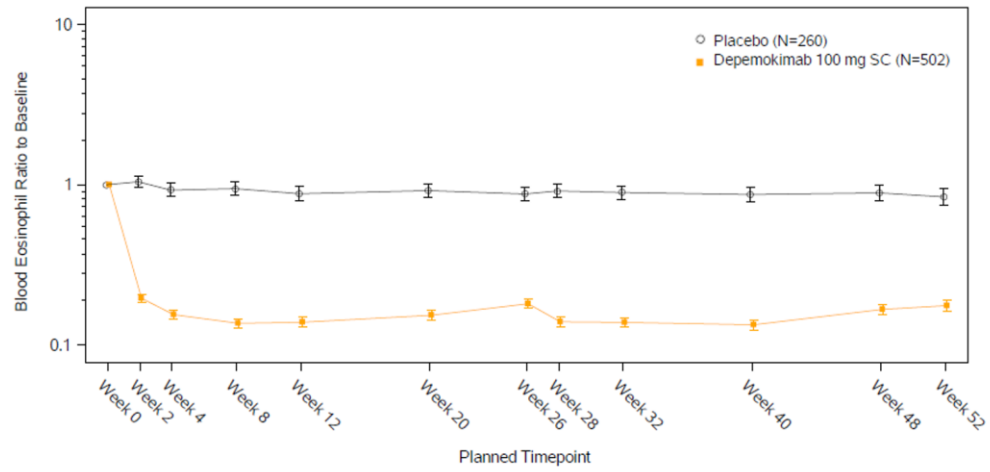
Depemokimab is a long-acting monoclonal antibody that targets human IL-5 with high binding affinity and specificity. Depemokimab contains a triple amino acid substitution (YTE) in the fragment crystallisable (Fc) region which increases binding to the neonatal Fc receptor (FcRn) and thereby extends the elimination half-life. These modifications allow for dosing every 6 months.

IL-5 is a key cytokine involved in eosinophilic inflammation and is responsible for the growth, differentiation, recruitment, activation, and survival of eosinophils. Depemokimab may exert its therapeutic effect in the treatment of asthma and CRSwNP by blocking IL-5 signaling to reduce the production and survival of eosinophils; however, the exact mechanism of action in these diseases has not been definitively established.

10.2. Pharmacodynamics

In placebo-controlled studies involving adult and adolescent patients aged 12 years and older with asthma, a 100 mg dose of depemokimab administered SC every 6 months for 52 weeks reduced blood eosinophils to a geometric mean count of 57 cells/mcL at Week 52 corresponding to a geometric mean reduction of 79% (95% CI: 75.8, 81.8) compared to placebo. This magnitude of blood eosinophil reduction was observed within 2 weeks of treatment (at the first assessment) and was maintained throughout the treatment period (Figure 1).

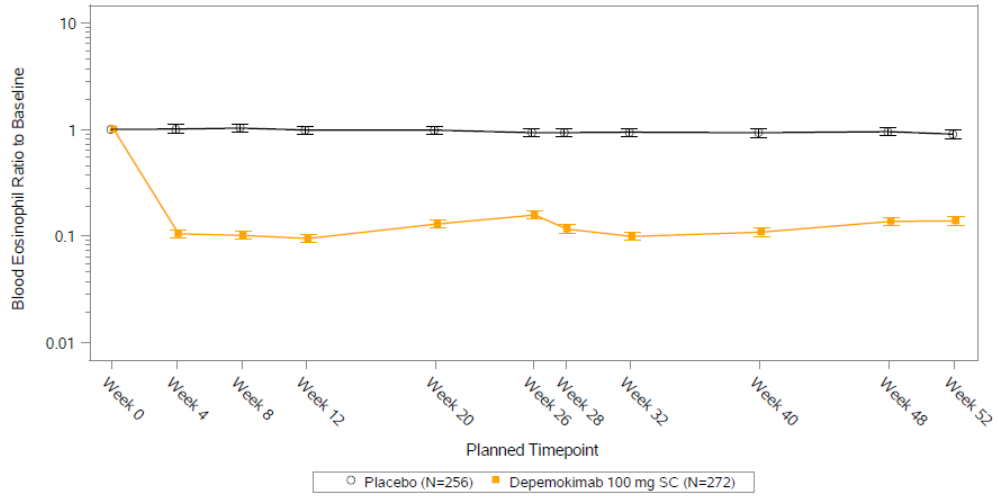
Figure 1 - Reduction in blood eosinophils from baseline over 52 weeks (SWIFT-1 and SWIFT-2 Pooled FAS Population)



FAS = Full Analysis Set

In placebo-controlled studies involving adult patients with CRSwNP a 100 mg dose of depemokimab administered SC every 6 months for 52 weeks reduced blood eosinophils to a geometric mean count of 48 cells/mcL at Week 52, corresponding to a geometric mean reduction of 85% (95% CI: 82.4, 86.7) compared to placebo. This magnitude of blood eosinophil reduction was observed within 4 weeks of treatment (at the first assessment) and was maintained throughout the treatment period Figure 2.

Figure 2 - Reduction in blood eosinophils from baseline over 52 weeks (ANCHOR-1 and ANCHOR-2 Pooled FAS Population)



FAS = Full Analysis Set

10.3. Pharmacokinetics

Depemokimab exhibited approximately dose-proportional pharmacokinetics over a dose range of 10 to 300 mg in patients with asthma following SC administration. Depemokimab pharmacokinetics were

similar in patients with asthma and CRSwNP after SC administration of 100 mg depemokimab every 6 months.

Absorption

Following single SC administration (doses ranging from 2 to 300 mg), maximum observed plasma concentrations (C_{max}) were achieved at a median time ranging from 8 to 14 days. There was no accumulation following repeat SC administration once every 6 months.

Distribution

Following single SC administration of depemokimab, the volume of distribution was estimated to be 6.3 L based on population pharmacokinetic analysis.

Metabolism

Depemokimab is a monoclonal antibody which is catabolized into small peptides and amino acids by ubiquitous proteolytic enzymes not restricted to hepatic tissue.

Elimination

Following single SC administration of depemokimab, the estimated apparent clearance (CL/F) was 0.092 L/day, based on population pharmacokinetic analysis. The estimated terminal elimination half-life was 48 days.

Special populations and conditions

Population pharmacokinetic analyses did not suggest clinically relevant effect of age, race or gender on depemokimab pharmacokinetics.

- **Pediatrics:** There are limited pharmacokinetic data available in the pediatric population (N = 15). The pharmacokinetics of depemokimab in adolescents aged 12 to 17 years were consistent with adults. The pharmacokinetics of depemokimab have not been studied in pediatric patients aged less than 12 years.
- **Geriatrics:** There are limited pharmacokinetic data available in elderly patients (≥65 years old) across all clinical studies (N = 175). The pharmacokinetics of depemokimab in patients aged 65 to 93 years were consistent with adults.
- **Hepatic Insufficiency:** No formal studies have been conducted to investigate the effect of hepatic impairment on the pharmacokinetics of depemokimab. Based on population pharmacokinetic analyses, baseline hepatic function biomarkers (alanine aminotransferase [ALT: 5 to 153 IU/L], aspartate aminotransferase [AST: 9 to 115 IU/L], and bilirubin (1.7 to 42 micromol/L) had no clinically relevant effect on depemokimab apparent clearance.

  Hepatic impairment is not expected to have significant impact on metabolism as depemokimab metabolism is not restricted to proteolytic enzymes in hepatic tissue.
- **Renal Insufficiency:** No formal studies have been conducted to investigate the effect of renal impairment on the pharmacokinetics of depemokimab. Based on population pharmacokinetic analyses, patients with an estimated glomerular filtration rate [eGFR] <60 mL/min/1.73m^2 had no clinically relevant effect on depemokimab apparent clearance.

  Renal impairment is not expected to have a significant impact on clearance as depemokimab is not cleared renally.

10.4. Immunogenicity

The observed incidence of anti-drug antibodies (ADA) is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of ADA in the studies described below with the incidence of ADA in other studies.

In patients who received at least one 100 mg dose of depemokimab administered SC every 6 months, 9% (44/499) of patients with asthma (SWIFT-1 and SWIFT-2) and 8% (21/272) of patients with CRSwNP (ANCHOR-1 and ANCHOR-2) were positive for anti-depemokimab antibodies during the 52-week studies.

The percentage of patients who were positive for ADA was 7% (43/588) in an ongoing 52-week open-label extension asthma study (AGILE; n = 214 with data collected for 104 weeks). Among ADA-positive patients during the placebo-controlled studies for asthma and CRSwNP indications, 8% (5/65) of the patients were positive for neutralizing antibodies.

There was no identified clinically significant effect of ADA on the pharmacokinetics, pharmacodynamics, efficacy, or safety of EXDENSUR.

11. Storage, Stability, and Disposal

The recommended storage condition is 2°C to 8°C, protected from light.

Do not freeze.

The pre-filled pen and pre-filled syringe can be removed from the refrigerator and kept in the unopened carton for up to 7 days at room temperature (up to 30°C), when protected from light. Discard if left out of the refrigerator for more than 7 days.

The pre-filled pen or pre-filled syringe must be administered within 8 hours once the carton is opened. Discard if not administered within 8 hours.

12. Special Handling Instructions

Any unused medicinal product or waste material must be disposed of in accordance with local requirements.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Non-proprietary name of the drug substance: depemokimab

Chemical name: Not applicable. Depemokimab is not a chemical. It is an immunoglobulin (recombinant humanized (IgG1, kappa) monoclonal antibody).

Molecular formula and molecular mass: The estimated molecular weight of depemokimab is 149 kDa.

Structural formula: Depemokimab is a recombinant fucosylated humanized IgG1κ monoclonal antibody that consists of two kappa light chains and two IgG1 heavy chains. The light chain is attached to a heavy chain by a single interchain disulfide bond. The heavy chains are also covalently linked to each other by disulfide bonds. Depemokimab is N-linked glycosylated on each heavy chain with fucosylated complex bi-antennary oligosaccharides. The antibody molecular mass is 146 kDa and the carbohydrate molecular mass is approximately 3 kDa resulting in a total estimated molecular mass of 149 kDa for depemokimab.

Physicochemical properties: Depemokimab is a colourless, yellow to brown, clear to opalescent solution.

Product Characteristics:

Depemokimab is a recombinant humanized (IgG1, kappa) monoclonal antibody specific for human interleukin-5 (IL-5) produced in Chinese hamster ovary cells by recombinant DNA technology.

14. Clinical Trials

14.1. Clinical Trials by Indication

14.1.1. Asthma

Trial Design and Study Demographics

The efficacy and safety of EXDENSUR for the add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype was evaluated in two replicate, randomized, double-blind, placebo-controlled, parallel-group, multicentre, phase 3 clinical studies of 52 weeks treatment duration (SWIFT-1 and SWIFT-2) in adult and adolescent subjects (Table 4).

The Full Analysis set (FAS) population in studies SWIFT-1 and SWIFT-2 consisted of a total of 382 and 380 subjects, respectively, randomized 2:1 to receive either 100 mg EXDENSUR administered by subcutaneous injection (SC) plus standard of care (SoC) or placebo SC plus SoC once every 26 weeks (Q26W). SoC treatment included medium- to high-dose inhaled corticosteroids (ICS) (Medium ICS dose = 500 mcg Fluticasone Propionate (FP) daily metered dose or equivalent; High ICS dose >500 mcg Fluticasone Propionate (FP) daily metered dose or equivalent) plus at least one additional controller, excluding biologics. Randomization was stratified by baseline ICS dose (medium-dose; high-dose) with the aim of randomizing approximately 50% of subjects per dose. Subjects were to remain on their existing stable maintenance asthma therapy throughout the study.

Subjects were required to have a confirmed history of ≥2 asthma exacerbations that required treatment with systemic CS (i.e., intramuscular, intravenous, or oral) in the 12 months prior to

screening, despite the use of medium- to high-dose ICS and/or required a two-fold increase in oral CS dose if receiving maintenance oral CS; elevated peripheral blood eosinophil counts of ≥150 cells/mcL at screening or ≥300 cells/mcL in the 12 months prior to screening; a pre-bronchodilator forced expiratory volume in 1 sec (FEV_1) <80% predicted at screening (subjects ≥18 years of age) or <90% predicted at screening or an FEV_1: Forced vital capacity (FVC) ratio <0.8 (subjects ≥12 to <18 years of age) at screening, with evidence of airway reversibility (FEV_1≥12% and 200 ml); and received medium- to high-dose ICS in the 12 months prior to screening and currently receiving treatment with at least one controller medication in addition to inhaled CS for at least 3 months.

In both studies, the primary efficacy endpoint was the annualized rate of clinically significant exacerbations over 52 weeks. A clinically significant exacerbation was defined as a worsening of asthma that led to: 1) use of systemic CS or a temporary increase in the systemic CS dose for at least 3 days to treat the symptoms; 2) an emergency department/urgent care visit resulting from asthma that led to treatment with a systemic CS in addition to their regular maintenance medications; or 3) an inpatient hospitalization due to asthma.

Key secondary efficacy endpoints included the change from baseline at Week 52 in: 1) the St. George's Respiratory Questionnaire (SGRQ) total score; 2) the Asthma Control Questionnaire-5 (ACQ-5) score; and 3) pre-bronchodilator forced expiratory volume in one second (FEV_1).

The SGRQ is a patient-reported tool that assesses the health-related quality of life of individuals with airway obstruction, including asthma. It contains 50 items comprising three domains of symptoms, activity, and impacts that are graded on various scales and is scored out of 100. The ACQ-5 assesses asthma control based on recall of the previous 7 days of breathlessness, nocturnal waking, symptoms on waking, activity limitations, wheeze, and frequency of short-acting beta agonists use. All items are assessed on a 7-point scale (0=no impairment, through 6=maximum impairment for symptoms and rescue use).

Table 4 - Summary of Trial Design for Clinical Trials in Asthma

Study #	Study design	Dosage, route of administration and duration	Study subjects	Mean age (min, max)	Sex n (%)
206713 (SWIFT-1)	Phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group	EXDENSUR 100 mg SC at week 0 and week 26 Placebo at week 0 and week 26 Duration: 52 weeks	N=250 N=132 Total: 382[a]	54 years (14, 78)	Female: 223 (58%) Male: 159 (42%)
213744 (SWIFT-2)	Phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group	EXDENSUR 100 mg SC at week 0 and week 26 Placebo at week 0 and week 26 Duration: 52 weeks	N=252 N=128 Total: 380[a]	53 years (12, 82)	Female: 241 (63%) Male: 139 (37%)

[a] Full Analysis Set (FAS) population who were randomized and received at least 1 dose of EXDENSUR or placebo.

SC = subcutaneous.

The demographics and baseline disease characteristics of the subjects in SWIFT-1 and SWIFT-2 are generally consistent between groups (Table 5).

Table 5 - Demographics and Baseline Disease Characteristics (FAS Population) of Subjects in SWIFT-1 and SWIFT-2

Parameter	SWIFT-1 N = 382	SWIFT-2 N = 380
Age (years) of subjects, mean (SD)	54 (14.2)	53 (16.2)
Female, n (%)	223 (58)	241 (63)
White, n (%)	316 (83)	272 (72)
Body Mass Index (kg/m^2), mean (SD)	28.03 (5.930)	28.73 (6.310)
Never smoked, n (%)	288 (75)	294 (77)
Duration of asthma, years, mean (SD)	22 (16.2)	25 (18.5)
Pre-bronchodilator % predicted FEV_1, mean (SD)	62 (15.2)	62 (15.9)
% reversibility, mean (SD)	17 (15.3)	18 (17.4)
Eosinophil count, cells/mcL, median (min, max)	310 (20, 2360)	340 (10, 4440)
Total IgE, U/mcL, median (min, max)	185 (1.9, 12142)	180 (2.2, 16198)
Number of exacerbations in previous year, mean (SD)	2.2 (0.69)	2.7 (1.92)
SGRQ total score, mean (SD)	44.3 (20.70)	44.5 (18.69)
Subjects with ACQ-5 ≥1.5 at baseline (%)	280 (75)	279 (75)
High-dose ICS use (%)[a]	203 (53)	226 (59)
ICS + LABA + LAMA use (%)	95 (25)	127 (33)
Maintenance OCS use (%)	21 (5)	19 (5)

ACQ-5 = Asthma Control Questionnaire, FEV_1 = forced expiratory volume in 1 second, OCS = Oral corticosteroid; IgE = immunoglobulin E; ICS = inhaled corticosteroid; LABA =Long acting β-agonist; LAMA =Long-acting muscarinic antagonist; OCS = Oral corticosteroid; SD = Standard deviation; SGRQ = St. George's Respiratory Questionnaire.
[a] High ICS dose >500 mcg Fluticasone Propionate (FP) daily metered dose or equivalent.

Study Results

The key efficacy results of the SWIFT-1 and SWIFT-2 studies evaluating the efficacy of EXDENSUR at Week 52 in subjects with severe asthma are presented in Table 6.

Table 6 - Results of Primary Efficacy Endpoint in Subjects with Severe Asthma over 52 Weeks in SWIFT-1 and SWIFT-2 (FAS Population)

	SWIFT-1		SWIFT-2	
	EXDENSUR N = 250	**Placebo N = 132**	**EXDENSUR N = 252**	**Placebo N = 128**
Annualized Asthma Exacerbation Rate[a]	0.46	1.11	0.56	1.08
Rate ratio (95% CI)	0.42* (0.30, 0.59)		0.52* (0.36, 0.73)	

FAS = Full Analysis Set, CI = Confidence Interval

[a] Results obtained from a negative binomial model with an offset term to adjust for different follow-up durations and fixed effects for treatment group, asthma exacerbation history, baseline ICS dose, geographical region, and baseline pre-bronchodilator % predicted FEV_1.

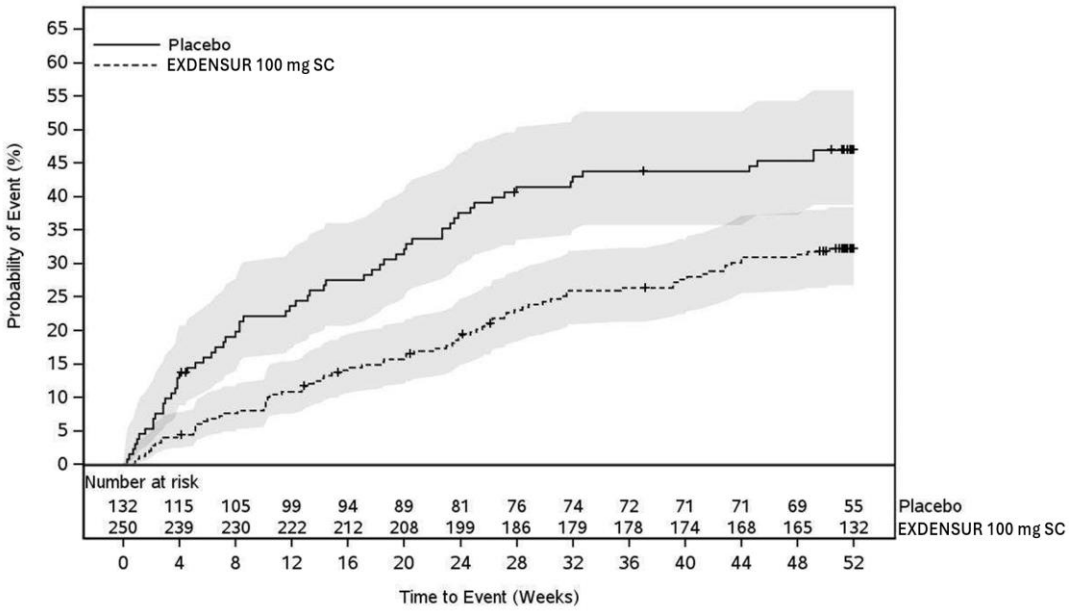
* Statistically significant at the prespecified level of 5%.

In SWIFT-1 and SWIFT-2, the percentage of subjects experiencing a clinically significant exacerbation during the 52-week treatment period was 32% and 32%, respectively for EXDENSUR and 46% and 50%, respectively for placebo.

In SWIFT-1 and SWIFT-2, the percentage of subjects with exacerbations requiring hospitalization and/or Emergency Department visit was 1% and 4%, respectively for EXDENSUR and 8% and 10%, respectively for placebo.

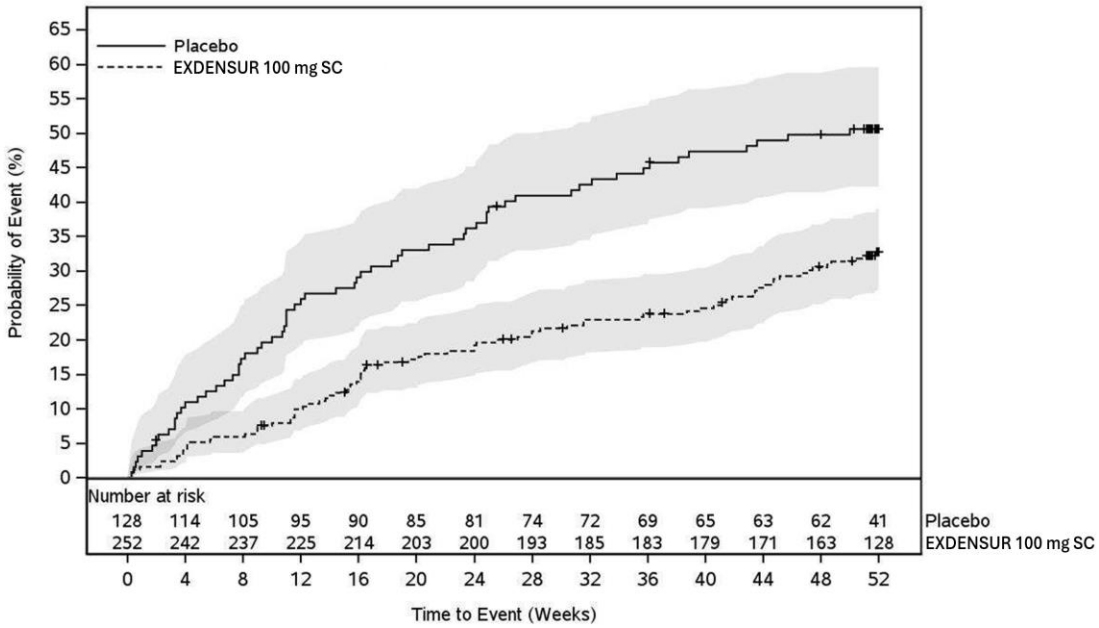
In SWIFT-1 and SWIFT-2, the time to first clinically significant exacerbation was numerically longer for EXDENSUR than placebo (hazard ratio [HR]: 0.56 (95% CI; 0.40, 0.79); and 0.53 (95% CI; 0.38, 0.74), respectively) (Figure 3A and Figure 3B).

Figure 3A - Kaplan Meier Curve for Time to First Clinically Significant Exacerbation in Subjects with Severe Asthma in SWIFT-1 (FAS Population)



FAS = Full Analysis Set, SC = Subcutaneous

Figure 3B: Kaplan Meier Curve for Time to First Clinically Significant Exacerbation in Subjects with Severe Asthma in SWIFT-2 (FAS Population)



FAS = Full Analysis Set, SC = Subcutaneous

In SWIFT-1 and SWIFT-2, the LS mean change from baseline in SGRQ Total score at Week 52 was -13.0 and -14.8, respectively for EXDENSUR and -9.7 and -12.5, respectively for placebo (Adjusted difference:

-3.4 (95%CI; -7.1, 0.4) and -2.3 (95% CI; -5.8, 1.2)). The percentage of subjects achieving a ≥4-point decrease (improvement) from baseline in SGRQ at Week 52 was 63% and 66%, respectively for EXDENSUR and 57% and 65%, respectively for placebo.

In SWIFT-1 and SWIFT-2, the LS mean change from baseline in ACQ-5 total score at Week 52 was -0.82 and -0.81, respectively for EXDENSUR and -0.77 and -0.70, respectively for placebo (Adjusted difference: -0.04 (95%CI; -0.27, 0.18) and -0.11 (95% CI; -0.33, 0.11)). The percentage of subjects achieving a ≥0.5-point decrease (improvement) from baseline in ACQ-5 at Week 52 was 54% and 54%, respectively for EXDENSUR and 55% and 53%, respectively for placebo.

In SWIFT-1 and SWIFT-2, the LS mean change from baseline in pre-bronchodilator FEV_1 at Week 52 was 0.160 L and 0.240 L, respectively for EXDENSUR and 0.160 L and 0.184 L, respectively for placebo (Adjusted difference: -0.001 (95%CI; -0.089, 0.088) and 0.056 (95% CI; -0.043, 0.154)).

14.1.2. Chronic Rhinosinusitis with Nasal Polyps

Trial Design and Study Demographics

The efficacy and safety of EXDENSUR was evaluated in two replicate, randomized, double-blind, placebo-controlled, parallel-group, multicentre phase 3 clinical studies of 52 weeks treatment duration (ANCHOR-1 and ANCHOR-2) in adult subjects with severe chronic rhinosinusitis with nasal polyps (CRSwNP) (Table 7).

The Full Analysis Set (FAS) population in studies ANCHOR-1 and ANCHOR-2 consisted of a total of 271 and 257 subjects, respectively randomized 1:1 to receive either 100 mg depemokimab administered by subcutaneous injection (SC) once every 26 weeks (Q26W) plus standard of care (SoC) or placebo SC + SoC. SoC treatment included intranasal corticosteroids (CS), saline nasal douching, inhaled corticosteroids exhalation through nose (ICS/ETN), occasional short courses of systemic CS (except during the run-in period), and/or antibiotics; short courses of systemic CS for treatment of CRSwNP were allowed as rescue medication. Subjects were to remain on their existing stable SoC therapy throughout the study.

Subjects were required to have a bilateral endoscopic nasal polyp (NP) score of at least 5 (with a minimum score of 2 in each nasal cavity); a history of nasal surgery for the removal of NP and/or uses of systemic CS for the treatment of NP for at least 3 consecutive days in the previous 2 years (or were unsuitable/intolerant to systemic CS); presence of moderate-to-severe intensity symptoms of CRS characterized by either nasal blockage/obstruction/congestion or nasal discharge (i.e., anterior/posterior nasal drip) and facial pain/pressure or reduction/loss of smell; and been receiving daily intranasal CS for at least 8 weeks immediately prior to screening At randomization, subjects were required to have had a nasal obstruction verbal response scale (VRS) mean score of 2 or greater over the previous 7 days.

In both studies, the co-primary efficacy endpoints were 1) a change from baseline in bilateral endoscopic NP score at Week 52 (centrally read); and 2) a change from baseline in nasal obstruction VRS mean score over Weeks 49 to 52. Key secondary efficacy endpoints included 1) a change from baseline in rhinorrhea VRS mean score over Weeks 49 to 52; 2) a change from baseline in loss of smell VRS score over Weeks 49 to 52; 3) a change from baseline in Lund-Mackay computed tomography (LMK CT) score at Week 52; and 4) a change from baseline in sino-nasal outcome test total score (SNOT-22) at Week 52.

The NP score is the sum of scores from both nostrils where each nostril was graded on a 4-point categorical scale (0 = no polyps through 4 = large polyps causing almost complete

congestion/obstruction of the inferior meatus). The VRS score graded daily symptoms on a 4-point categorical scale (0 = no symptoms through 3 = severe symptoms). The LMK sinus CT scan score evaluated the opacification of each sinus using a 3-point categorical scale (0 = normal; 1 = partial opacification; 2 = total opacification) with a possible overall maximum score of 24. SNOT-22 assessed the symptoms and symptom impact associated with CRSwNP based on 22 items with each item scored on a 6-point categorical scale (0 = not present/no problem through 5 = problem as "bad as it can be") with a possible overall maximum score of 110; SNOT-22 had a 2 week recall period.

Table 7 - Summary of Trial Design for Clinical Trials in Chronic Rhinosinusitis with Nasal Polyps

Study #	**Study design**	**Dosage, route of administration and duration**	**Study subjects**	**Mean age (min, max)**	**Sex n (%)**
217095 (ANCHOR-1)	Phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group	EXDENSUR 100 mg SC at week 0 and week 26 Placebo at week 0 and week 26 Duration: 52 weeks	N=143 N=128 Total: 271[a]	54 years (19, 93)	Female: 83 (31%) Male: 188 (69%)
210879 (ANCHOR-2)	Phase 3, multicentre, randomized, double-blind, placebo-controlled, parallel-group	EXDENSUR 100 mg SC at week 0 and week 26 Placebo at week 0 and week 26 Duration: 52 weeks	N=129 N=128 Total: 257[a]	50 years (20, 82)	Female: 80 (31%) Male: 177 (69%)

[a] Full Analysis Set (FAS) population who were randomized and received at least 1 dose of EXDENSUR or placebo

The demographics and baseline disease characteristics of subjects in ANCHOR-1 and ANCHOR-2 are generally consistent between groups (Table 8).

Table 8 - Demographics and Baseline Disease Characteristics (FAS Population) of Subjects in ANCHOR-1 and ANCHOR-2

Parameter	ANCHOR-1 (N = 271)	ANCHOR-2 (N = 257)
Age (years) of subjects, mean (SD)	54 (13.4)	50 (12.9)
Male, n (%)	188 (69)	177 (69)
White, n (%)	185 (70)	197 (77)
Asian/Other, n (%)	72 (27)	55 (21)
Body Mass Index (kg/m^2), mean (SD)	26.91 (4.667)	26.79 (4.726)
Duration (years) of CRSwNP, mean (SD)	13 (11.2)	11 (8.7)
Subjects with ≥1 previous NP surgery, n (%)	171 (63)	162 (63)
Systemic CS use for NP in past 12 months, n (%)	190 (70)	172 (67)
Asthma, n (%)	161 (59)	131 (51)
AERD, n (%)	43 (16)	42 (16)
Blood eosinophil count, cells/mcL, median (min, max)	360 (10, 10,550)	360 (30, 1,670)
Bilateral endoscopic NP score[a, b, c], mean (SD)	6.0 (1.35)	5.9 (1.29)
Nasal obstruction VRS mean score[a, d], mean (SD)	2.5 (0.48)	2.6 (0.42)
Rhinorrhoea VRS mean score[a, d], mean (SD)	2.2 (0.70)	2.3 (0.67)
Loss of smell VRS mean score[a, d], mean (SD)	2.7 (0.55)	2.8 (0.41)
LMK CT score[a, b], mean (SD)	18.7 (4.08)	18.9 (4.19)
SNOT-22 total score[a, e], mean (SD)	57.4 (22.15)	60.1 (19.95)
Subjects with SNOT-22 total score ≥40, n (%)	204 (75)	207 (81)

AERD = aspirin-exacerbated respiratory disease; CRSwNP = chronic rhinosinusitis with nasal polyps, FAS = full analysis set, LMK CT = Lund-MacKay Computed Tomography, NP = nasal polyps, CS = corticosteroid, SNOT-22 = Sino-Nasal Outcome Test, VRS = verbal response scale.

[a] Higher scores indicate greater disease severity.

[b] As graded by independent blinded assessors.

[c] NP score is the sum of scores from both nostrils where each nostril was graded on 4-point categorical scale (0 = no polyps; 1 = small polyps in the middle meatus not reaching below the inferior border of the middle concha; 2 = polyps reaching below the lower border of the middle turbinate; 3 = large polyps reaching the lower border of the inferior turbinate or polyps medial to the middle concha; 4 = large polyps causing almost complete congestion/obstruction of the inferior meatus).

[d] Collected daily by subjects on a 4-point categorical scale (0 = no symptoms, 1 = mild symptoms, 2 = moderate symptoms, 3 = severe symptoms).

[e] SNOT-22 is a health-related quality of life assessment tool and includes 22-items in 6 domains of symptoms and impact associated with CRSwNP (nasal, non-nasal, ear/facial, sleep, fatigue, emotional consequences). These symptoms are rated via a 6-point scale (0 = not present/no problem; 1 = very mild problem; 2 = mild or slight problem; 3 = moderate problem; 4 = severe problem; 5 = problem as "bad as it can be"). The maximum score is 110.

Study Results

The key efficacy results from ANCHOR-1 and ANCHOR-2 evaluating the efficacy of EXDENSUR at Week 52 in subjects with severe CRSwNP are presented in Table 9 and Figure 4 and Figure 5.

Table 9 - Results of Co-Primary Efficacy Endpoints in Subjects with Severe CRSwNP at Week 52 in ANCHOR-1 and ANCHOR-2 (FAS Population)

	ANCHOR-1		ANCHOR-2	
	EXDENSUR N = 143	**Placebo N = 128**	**EXDENSUR N = 129**	**Placebo N = 128**
Total Endoscopic NP Score at Week 52[a, b]				
n[c]	128	120	120	115
LS Mean (SE)	5.4 (0.14)	6.2 (0.15)	5.4 (0.14)	6.0 (0.15)
LS Mean change from baseline (SE)	-0.6 (0.14)	0.2 (0.15)	-0.5 (0.14)	0.1 (0.15)
Adjusted difference (95% CI)	-0.7 (-1.1, -0.3) *		-0.6 (-1.0, -0.2) *	
Nasal Obstruction VRS Mean Score over Weeks 49 to 52[a, b]				
n[c]	125	116	119	111
LS Mean (SE)	1.77 (0.079)	2.00 (0.083)	1.83 (0.076)	2.07 (0.078)
LS Mean change from baseline (SE)	-0.76 (0.079)	-0.53 (0.083)	-0.77 (0.076)	-0.53 (0.078)
Adjusted difference (95% CI)	-0.23 (-0.46, 0.00)*		-0.25 (-0.46, -0.03)*	

FAS = Full Analysis Set; LS = Least Squares, NP = Nasal Polyps; VRS = Verbal Response Scale.

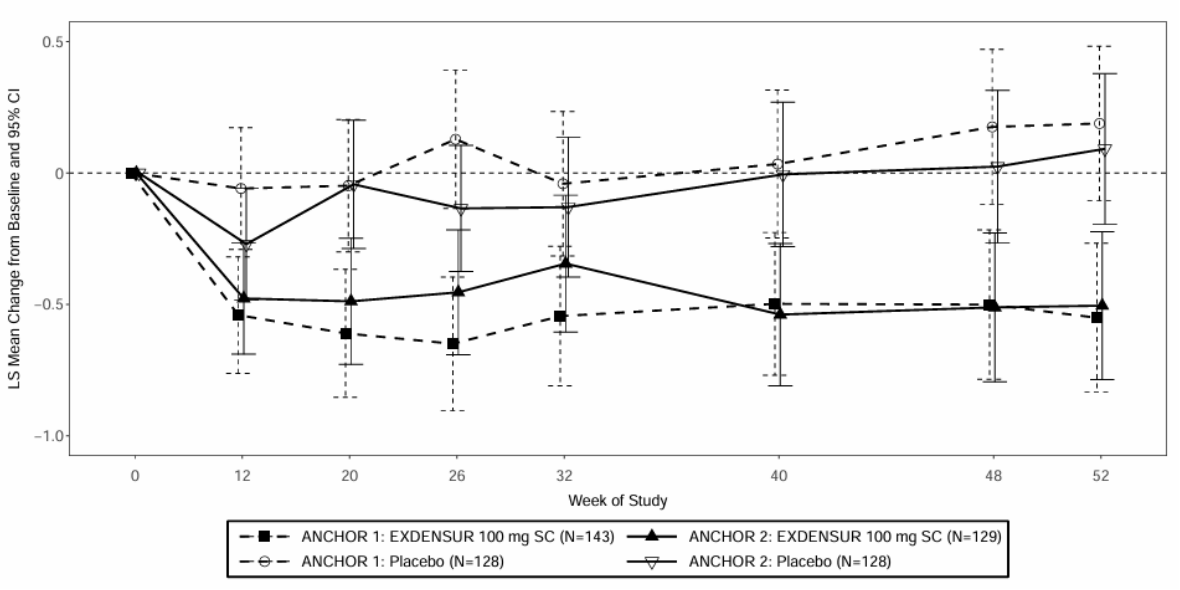
[a] Subjects who had nasal surgery or used disease-modulating medication for CRSwNP prior to the timepoint of interest were assigned the worst possible value of the relevant score for all assessments following surgery or initiation of disease-modulating medication.

[b] Based on Mixed Model Repeat Measures (MMRM) analyses with covariates of treatment, baseline score, log(e) baseline blood eosinophil count, region, previous surgery for nasal polyps, and visit, with interaction terms for visit by baseline and visit by treatment.

[c] Number of subjects with analysable data at the given timepoint.

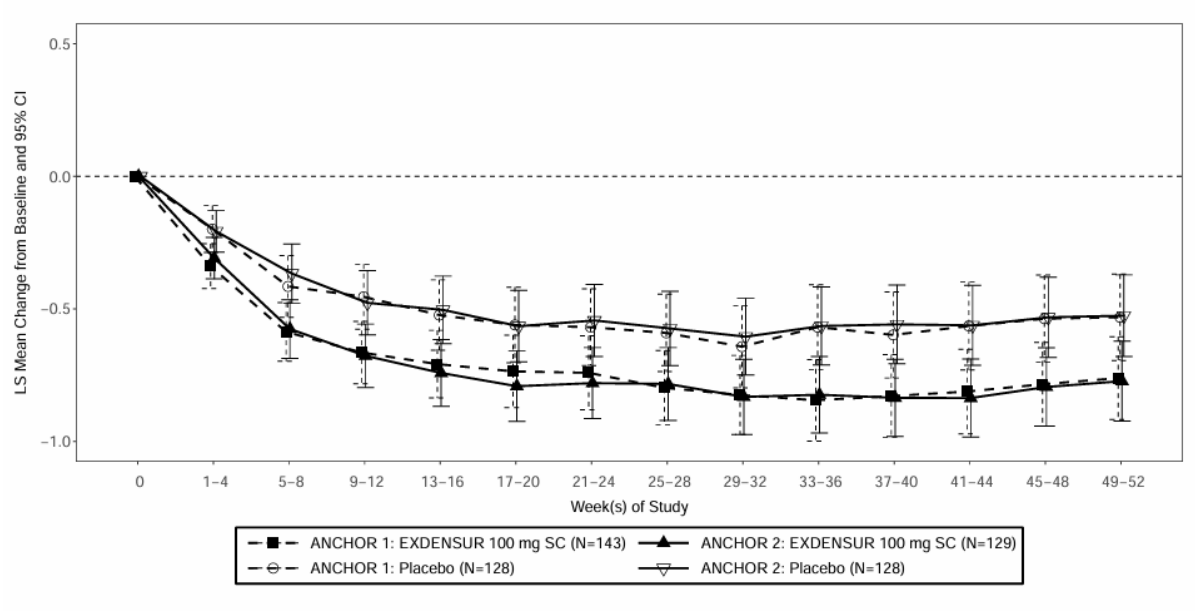
* Statistically significant at the prespecified level of 5%.

Figure 4 – LS Mean Change from Baseline in Total Endoscopic NP Score (ANCHOR-1 and ANCHOR-2)



LS= Least Squares; NP= nasal polyp; FAS= Full Analysis Set

Figure 5 – LS Mean Change from Baseline in Mean Nasal Obstruction VRS Score (ANCHOR-1 and ANCHOR-2)



LS= Least Squares; VRS= Verbal Response Scale; FAS= Full Analysis Set

In ANCHOR-1 and ANCHOR-2, the percentage of subjects achieving a ≥1-point decrease from baseline in total endoscopic bilateral NP score at Week 52 was 44% and 41%, respectively for EXDENSUR and 24% and 24%, respectively for placebo. Additionally, the percentage of subjects achieving a ≥1-point decrease from baseline in nasal obstruction VRS mean score over Weeks 49 to 52 was 36% and 46%, respectively for EXDENSUR and 30% and 29%, respectively for placebo.

In ANCHOR-1 and ANCHOR-2, the LS mean change from baseline in rhinorrhoea VRS mean score over Weeks 49 to 52 was -0.71 and -0.72, respectively for EXDENSUR and -0.49 and -0.54, respectively for placebo (Adjusted difference: -0.22 (95%CI; -0.46, 0.02) and -0.18 (95% CI; -0.40, 0.05)). In ANCHOR-1 and ANCHOR-2, the LS mean change from baseline in loss of smell VRS mean score over Weeks 49 to 52 was -0.48 and -0.56, respectively for EXDENSUR and -0.29 and -0.30, respectively for placebo (Adjusted difference: -0.19 (95%CI; -0.39, 0.00) and -0.26 (95% CI; -0.45, -0.07)).

In ANCHOR-1 and ANCHOR-2, the LS mean change from baseline in LMK CT score at Week 52 was -2.8 and -3.5, respectively for EXDENSUR and -0.8 and -0.3, respectively for placebo (Adjusted difference: -2.0 (95%CI; -3.3, -0.8) and -3.2 (95% CI; -4.4, -2.0)). In ANCHOR-1 and ANCHOR-2, the LS mean change from baseline in SNOT-22 Total score at Week 52 was -13.3 and -15.9, respectively for EXDENSUR and -6.5 and -6.0, respectively for placebo (Adjusted difference: -6.8 (95%CI; -15.2, 1.6) and -9.9 (95% CI; -17.9, -2.0)).

In a pre-specified pooled analysis of ANCHOR-1 and ANCHOR-2, the percentage of subjects that required systemic corticosteroids or sino-nasal surgery (actual) or disease-modulating medications for CRSwNP, up to Week 52 was 26% (72/272) for EXDENSUR and 36% (92/256) for placebo.

In the subgroup of subjects with CRSwNP and comorbid asthma enrolled in ANCHOR-1 and ANCHOR-2 (n=292), changes in total endoscopic nasal polyp score and nasal obstruction VRS score favoured EXDENSUR, consistent with the overall study population.

16. Non-Clinical Toxicology

General Toxicology:

In monkeys administered depemokimab as a single subcutaneous dose of 10 or 100 mg/kg (equal to 2- or 21-times the exposure in asthma patients given the recommended human dose [100 mg SC every 6 months] based on AUC) and observed for 4 weeks, adverse vascular inflammation within the kidney, heart, pancreas, spleen, liver and/or lung was present in one low-dose and one high-dose monkey given. A NOAEL was not determined due to the vasculitis observed at both doses. The relationship between depemokimab administration and vasculitis is unclear.

In the 26-week repeat-dose (10 and 100 mg/kg administered by subcutaneous injection on Day 1 and Week 14) toxicity study, with a 30 week off-dose period, high-dose monkeys developed reversible (within the 24 hour recording period) increases in QTc following the Week 14 dose (18 milliseconds or 7% of mean absolute vehicle control or baseline values). The toxicological significance of this finding is unclear. The NOAEL was determined to be 10 mg/kg (8-times the exposure in asthma patients given the recommended human dose based on AUC).

Genotoxicity: No genotoxicity studies have been conducted with depemokimab.

Carcinogenicity: No carcinogenicity studies have been conducted with depemokimab.

Reproductive and developmental toxicology:

No reproductive or developmental toxicology studies have been conducted with depemokimab. However, there were no adverse histopathological findings in the reproductive organs from sexually mature cynomolgus monkeys receiving SC dosages up to 100 mg/kg depemokimab for 6 months.

Data from pregnant monkeys demonstrate that mepolizumab, a related biologic product without the YTE modification, crosses the placenta. Concentrations of mepolizumab were approximately 2.4-times higher in infants than in maternal monkeys for several months post-partum. Mepolizumab was excreted into the milk of cynomolgus monkeys at concentrations that were less than 0.5% of those

detected in maternal plasma. Depemokimab has greater binding affinity for FcRn and may be transferred to fetal blood at concentrations that exceed those of mepolizumab. *In silico* analysis estimates that concentrations of depemokimab will be 3.2-times higher in infants than in maternal monkeys. A more prolonged exposure in the infant is expected due to the extended elimination half-life of depemokimab when compared to mepolizumab.

Juvenile Toxicity: No juvenile toxicity studies have been conducted with depemokimab.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]EXDENSUR

Depemokimab Injection

This Patient Medication Information is written for the person who will be taking **EXDENSUR**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **EXDENSUR**, talk to a healthcare professional.

What EXDENSUR is used for:

- EXDENSUR is used with other asthma medicines for the maintenance treatment of adults and adolescents 12 years of age and older with severe eosinophilic asthma that is not controlled with their current asthma medicine. Asthma is a chronic inflammatory disease of the lungs and airways that causes symptoms like shortness of breath, chest tightness, coughing and wheezing. Severe eosinophilic asthma is a type of asthma where patients have increased eosinophils in their lungs and airways. Eosinophils are a type of white blood cell that are associated with inflammation of the lungs and airways that can cause your asthma to get worse.

  EXDENSUR is not used to treat asthma attacks (sudden difficulty breathing).

- EXDENSUR is used to treat Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) in adults. CRSwNP is a chronic inflammatory disease of your nose and sinuses that can cause symptoms such as a blocked nose and loss of smell, and soft jelly-like growths (called nasal polyps) to form inside the nose.

How EXDENSUR works:

EXDENSUR contains the active substance depemokimab.

Depemokimab is a monoclonal antibody (a type of specialized protein) that blocks the action of an inflammatory protein called interleukin (IL)-5 that plays a critical role in eosinophil inflammation. EXDENSUR reduces inflammation that plays a major role in asthma and CRSwNP.

Asthma

EXDENSUR helps prevent severe asthma attacks (exacerbations).

Chronic Rhinosinusitis with Nasal Polyps (CRSwNP)

EXDENSUR helps reduce symptoms of CRSwNP, including nasal congestion, and reduces the size of your nasal polyps.

The ingredients in EXDENSUR are:

Medicinal ingredients: depemokimab.

Non-medicinal ingredients: L-arginine hydrochloride, disodium edetate dihydrate, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, trehalose dihydrate, water for injections.

EXDENSUR comes in the following dosage forms:

A solution for subcutaneous injection in pre-filled pen or pre-filled syringe. Each pre-filled pen or pre-filled syringe contains 100 mg/mL of depemokimab.

Do not use EXDENSUR if:

- you are allergic to depemokimab or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take EXDENSUR.

- Medicines of this type (monoclonal antibodies) can cause severe allergic reactions such as anaphylaxis (skin rash (hives) or redness, swelling of the face or mouth (angioedema), becoming very wheezy, coughing or having difficulty breathing, suddenly feeling weak or light headed (may lead to collapse or loss of consciousness)) when injected into the body. If you have had a similar reaction before, tell your healthcare professional before you are given EXDENSUR.
- EXDENSUR must not be used to treat sudden breathing problems that may occur with asthma. Some people get asthma-related side effects, or their asthma may become worse, during treatment with EXDENSUR. Talk to your healthcare professional if your asthma remains uncontrolled, or gets worse, after you start EXDENSUR treatment.
- Talk to your healthcare professional if you are taking, have recently taken, or might take any other medicines. Don't suddenly stop taking your medicines for your asthma or CRSwNP once you have started EXDENSUR. These medicines (especially ones called corticosteroids) must be stopped gradually, under the direct supervision of your healthcare professional.

Talk about any health conditions or problems you may have, including if you:

- have an existing parasitic infection, live in a region where infections caused by parasites are common, or if you are travelling to such a region. EXDENSUR may weaken your resistance to such infections. Parasitic infections should be treated prior to starting treatment with EXDENSUR.

Pregnancy and breastfeeding:

- If you are pregnant, if you think you may be pregnant, or if you are planning to become pregnant, ask your healthcare professional about the risks of EXDENSUR before using this medicine.
- It is not known whether the ingredients of EXDENSUR can pass into breast milk. If you are breastfeeding, check with your healthcare professional before you use EXDENSUR.

Other warnings you should know about:

- EXDENSUR should not be given to children under 12 years of age for the treatment of severe asthma and should not be given to children and adolescents under 18 years of age for the treatment of CRSwNP.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

How to take EXDENSUR:

- EXDENSUR is given by injection under the skin.
- EXDENSUR can be given either by you, your caregiver, or a healthcare professional.
- Your healthcare professional will decide if you can inject yourself, or if your caregiver can inject you, with EXDENSUR. If appropriate, your healthcare professional will provide training to show you or your caregiver the correct way to use EXDENSUR.
- You can inject EXDENSUR under your skin in your stomach area (abdomen) or upper leg (thigh). Your caregiver can also inject EXDENSUR into the back of your upper arm. Injections must not be given into areas where the skin is tender, bruised, red, or hard.
- Speak to your healthcare professional if you experience difficulties with injections given by yourself or your caregiver including if you have concerns regarding an incomplete injection.

Usual dose:

Asthma

Adults and adolescents aged 12 years and over

The recommended dose for adults and adolescents aged 12 years and over is 100 mg. You will be given one (1) injection once every 6 months under the skin (subcutaneous).

CRSwNP

The recommended dose for adults is 100 mg. You will be given one (1) injection once every 6 months under the skin.

Overdose:

If you think you, or a person you are caring for, have taken too much EXDENSUR, contact a healthcare professional, hospital emergency department, regional poison control centre, or Health Canada's toll-free number at 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed Dose:

If your healthcare professional gives you your injection of EXDENSUR and you miss a planned dose, contact your healthcare professional as soon as possible to re-schedule your appointment.

If you or your caregiver forget to give the injection of EXDENSUR:

- If you miss a dose, inject a dose of EXDENSUR as soon as possible. After that, continue EXDENSUR on your usual injection day as planned.
- If you miss a dose by 1 month or more, inject a dose of EXDENSUR and restart your 6 month injection schedule from the day you take the missed dose. If you are not sure what to do, ask your healthcare professional.

Do not stop injections of EXDENSUR unless your healthcare professional advises you to do so. Interrupting or stopping treatment with EXDENSUR may cause your symptoms to come back or become worse. **If your symptoms get worse while receiving injections of** EXDENSUR **call your healthcare professional.** If you have any further questions on the use of this medicine, ask your healthcare professional.

Possible side effects from using EXDENSUR:

These are not all the possible side effects you may have when taking EXDENSUR. If you experience any side effects not listed here, tell your healthcare professional.

Common side effects (may affect up to 1 in 10 people):

- Itching
- Headache, tiredness, or rash around the time of injection
- Injection site reactions (e.g. pain, redness, swelling, or itching at the site of the injection)

Tell your healthcare professional immediately if you get any of these symptoms, or if you notice any side effects not listed in this leaflet.

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Unknown			
Anaphylaxis (Sudden, severe allergic reaction): • skin rash (hives) or redness • swelling, sometimes of the face or mouth (angioedema) • becoming very wheezy, coughing or having difficulty breathing • suddenly feeling weak or light headed (may lead to collapse or loss of consciousness)			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of reach and sight of children.
- Do not use EXDENSUR after the expiry date stated on the label and carton. The expiry date is the last day of that month noted after the text EXP:.
- Store EXDENSUR in a refrigerator between 2°C to 8°C in the original carton until you are ready to use it.
- Do not freeze.
- Store in the original carton to protect from light.
- The pre-filled pen and pre-filled syringe can be removed from the refrigerator and kept in its unopened carton for up to 7 days at room temperature (up to 30°C) when protected from light. Discard if left out of the refrigerator for more than 7 days.
- The pre-filled pen and pre-filled syringe must be used within 8 hours once the carton is opened. Discard if not used within 8 hours.
- Any unused medicinal product or waste material must be disposed of in accordance with local requirements.

If you want more information about EXDENSUR:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (Drug Product Database: Access the database); the manufacturer's website www.gsk.ca, or by calling 1-800-387-7374.

This leaflet was prepared by GlaxoSmithKline Inc.

Date of Authorization: 2026-06-15

Instructions For Use – Pre-Filled Pen

INSTRUCTIONS FOR USE

EXDENSUR [ex-DEN-shur]

(depemokimab)

injection, for subcutaneous use

100 mg/mL

This Instructions for Use contains information on how to inject EXDENSUR.

Read These Sections First

Before using your EXDENSUR pen, it is important that your healthcare provider explain your EXDENSUR dosing instructions, and show you (or your caregiver) how to use the pen the right way.

Important Information

Read all of these instructions before using your pen. If you do not follow these instructions, you may not get all your medicine.

Do not use EXDENSUR pen if:

- It has been frozen
- It has been dropped or damaged
- The security seal on the carton has been broken
- The expiration date (EXP) has passed

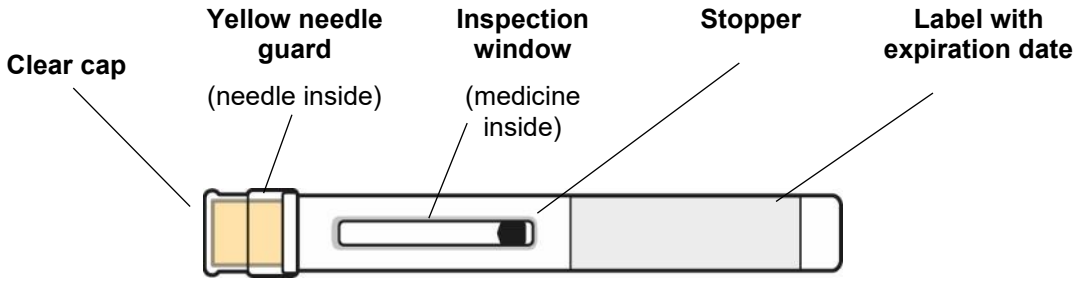
Do not:

- Shake EXDENSUR pen
- Share or reuse your pen
- Expose your pen to heat

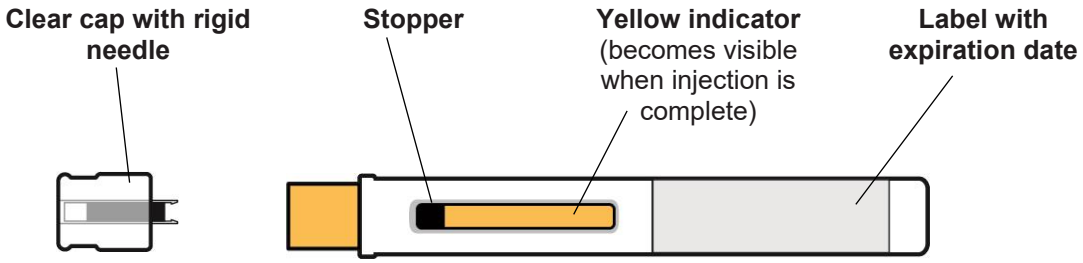
If any of these happen, dispose of the EXDENSUR pen according to local health and safety laws and use a new EXDENSUR pen. **Keep out of reach of children. Contains small parts.**

Get to Know the EXDENSUR Pen

Before Use



After Use



Storage

Pen Stored in Carton

Store EXDENSUR in a refrigerator between 2°C to 8°C in the original carton until you are ready to use it. **Do not** freeze.

An unopened carton of EXDENSUR pen may be kept at room temperature up to 30°C for a maximum of 7 days. After being brought to room temperature, EXDENSUR must be used within 7 days or dispose of the pen according to local health and safety laws.

Pen Removed From Carton
After the EXDENSUR pen is out of the carton, it must be used within 8 hours or dispose of the pen according to local health and safety laws. **Do not** place back in the refrigerator.

Keep out of reach of children. Contains small parts.

A. Prepare

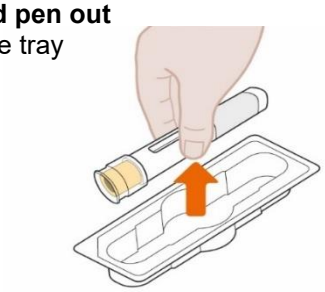
A1

Gather Supplies

Supplied	Not Supplied
• EXDENSUR pen	• Alcohol swab • Cotton ball or gauze • Adhesive bandage • Sharps disposal container (See Section C for disposal instructions)

A2

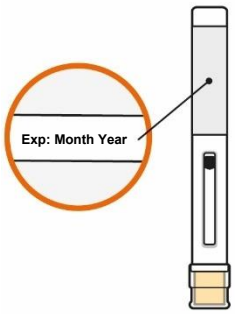
Take the **pre-filled pen out** of the tray



Take The Carton Containing Your Pen Out of the Refrigerator

- Holding the middle of the pen (near the inspection window), carefully take the pen out of the tray.
- **Do not** remove the clear needle cap at this step.

A3

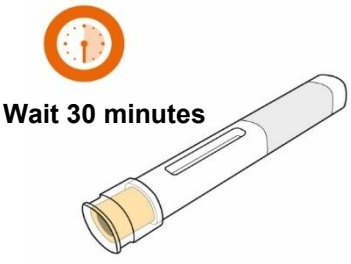


Check the **expiration date** and the **medicine**

Check Your Pen

- Check the expiration date. **Do not** use if the expiration date has passed.
- Look at the medicine in the EXDENSUR pen through the inspection window. The medicine should be clear and colourless to slightly yellow.
- **Do not** inject if EXDENSUR is cloudy or has particles.
- It is normal to see air bubbles. You **do not** need to do anything about it.
- **Do not** shake the pen.

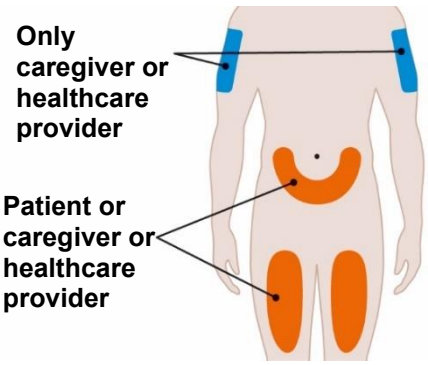
A4



Wait 30 minutes

- **Do not** remove the clear cap.
- Place the pen on a clean, flat surface away from direct sunlight and out of the reach of children.
- **Wait 30 minutes** to bring to room temperature before you inject. Cold medicine is more painful to inject.
- **Do not** warm EXDENSUR pen in a microwave, hot water, or direct sunlight.
- **Do not** use the EXDENSUR pen if it has been left out of the carton for more than 8 hours.

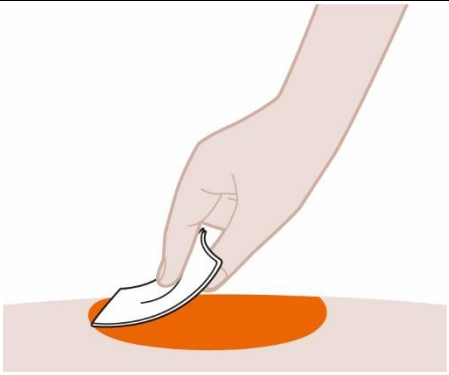
A5



Choose Your Injection Site

- If you are giving yourself the injection, you can inject into your thighs or stomach (abdomen).
- A caregiver can inject into the upper arm, thigh, or abdomen.
- **Do not** inject yourself in the upper arm, as it is more difficult to avoid pen movement during the injection.
- **Do not** inject where the skin is bruised, tender, red, or hard.
- **Do not** inject within 2 inches (5 cm) of your belly button.

A6



Clean the Injection Site

- Wash your hands with soap and water.
- Clean the injection site with an alcohol swab. Allow skin to air dry.
- **Do not** fan or blow on the cleaned injection site.
- **Do not** touch the cleaned injection site again until you have finished your injection.

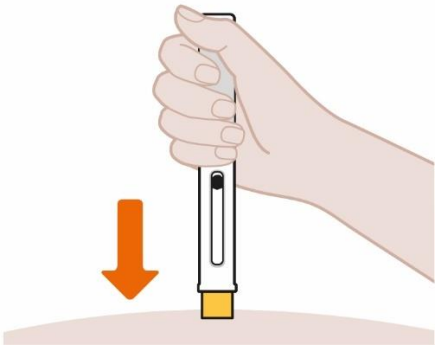
B. Inject

B1

Pull Off the Clear Cap

- Remove the clear cap by pulling it straight off, away from the yellow needle guard. It may take some force to remove the clear cap.
- **Do not** press the yellow needle guard. **Do not** put the cap back on the pen. This could accidentally start the injection.
- You may see a drop of medicine at the end of the needle. This is normal.
- Inject within 5 minutes after you remove the clear cap.

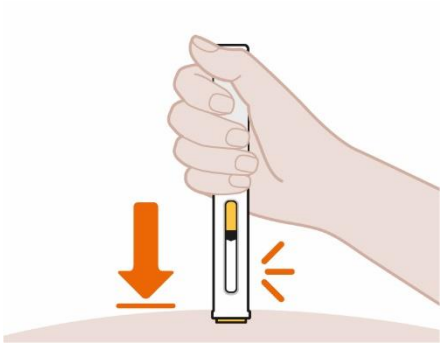
B2



Position the Pen at the Injection Site

- Place the yellow needle guard flat against your skin.
- Make sure you can see the inspection window.

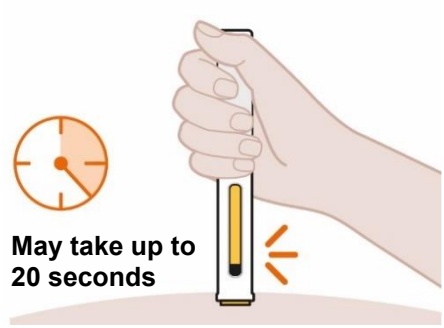
B3



Press Firmly to Start the Injection

- The yellow needle guard will slide up into the pen.
- You may hear a “click” that tells you the injection has started.
- Keep the pen held down against the skin. **Do not** lift or move the pen during the injection.
- The yellow indicator will move down through the inspection window during the injection.
- **Do not** use the pen if the yellow needle guard does not slide up into the pen. Throw away the pen and clear cap according to local health and safety laws.

B4



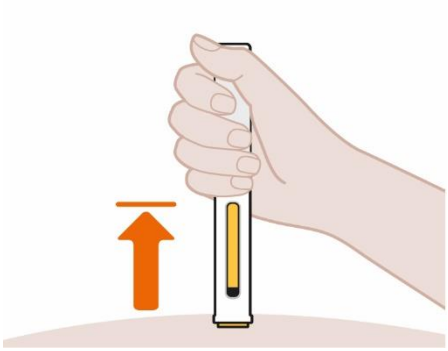
Continue to Hold Down

Your injection is done when you hear the second click. Injection may take up to 20 seconds.

If you do not hear the second click, check that:

- The inspection window is filled with the yellow indicator.
- The black stopper has stopped moving.

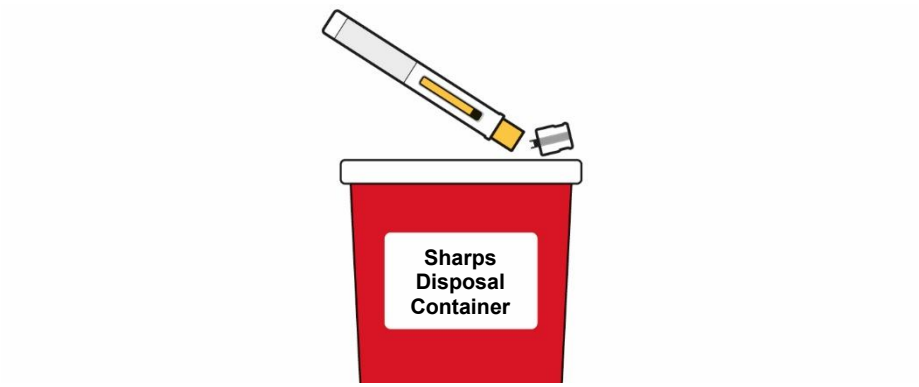
B5



Lift Pen After Injection Completes

- **Do not** rub the injection site.
- **Do not** put the clear cap back onto the EXDENSUR pen.
- There may be a small drop of blood at the injection site. This is normal. Press a cotton ball or gauze on the area and apply an adhesive bandage if you need it.

C. Throw Away



Dispose of the used pen and needle cap according to local requirements. Ask your doctor or pharmacist for advice if necessary.

Keep your used pens and needle caps out of the sight and reach of children

Instructions For Use – Pre-Filled Syringe

INSTRUCTIONS FOR USE

EXDENSUR [ex-DEN-shur]

(depemokimab)

injection, for subcutaneous use

100 mg/mL

This Instructions for Use contains information on how to inject EXDENSUR.

Read These Sections First

Before using your EXDENSUR syringe, it is important that your healthcare provider explain your EXDENSUR dosing instructions, and show you (or your caregiver) how to use the syringe the right way.

Important Information

Read all of these instructions before using your syringe. If you do not follow these instructions, you may not get all your medicine.

Do not use EXDENSUR syringe if:

- It has been frozen
- It has been dropped or damaged
- The security seal on the carton has been broken
- The expiration date (EXP) has passed

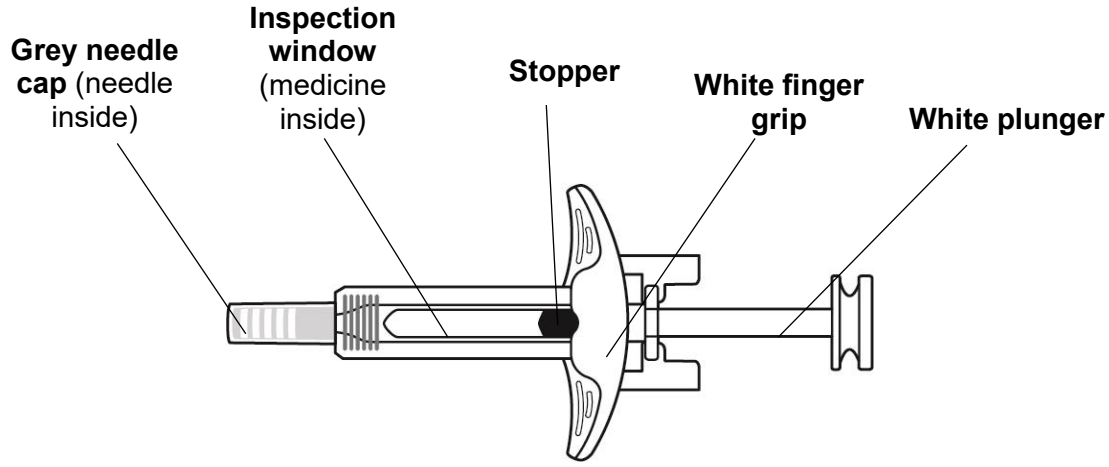
Do not:

- Shake EXDENSUR syringe
- Share or reuse your syringe
- Expose your syringe to heat

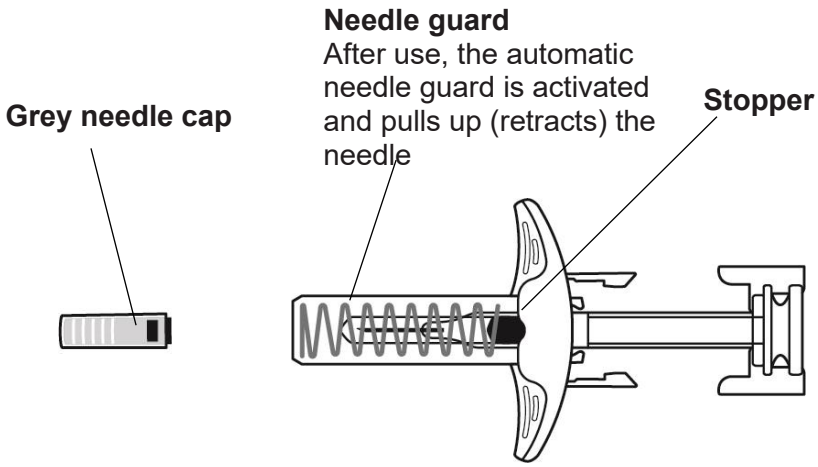
If any of these happen, dispose of the EXDENSUR syringe according to local health and safety laws and use a new EXDENSUR syringe. **Keep out of reach of children. Contains small parts.**

Get to Know Your EXDENSUR Syringe

Before Use



After Use



Storage

Syringe Stored in Carton

Store EXDENSUR in a refrigerator between 2°C to 8°C in the original carton until you are ready to use it. **Do not** freeze.

An unopened carton of EXDENSUR may be kept at room temperature up to 30°C for a maximum of 7 days. After being brought to room temperature, EXDENSUR must be used within 7 days or dispose of the syringe according to local health and safety laws.

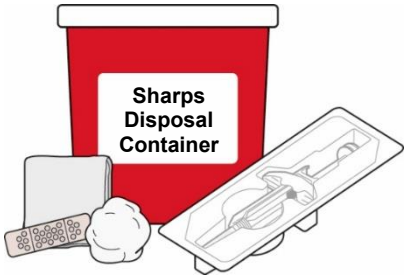
Syringe Removed From Carton

After the EXDENSUR syringe is out of the carton, it must be used within 8 hours or dispose of according to local health and safety laws. **Do not** place back in the refrigerator.

Keep out of reach of children. Contains small parts.

A. Prepare

A1



Gather Supplies

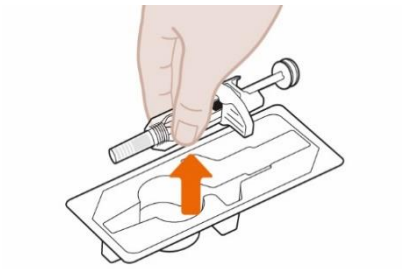
Supplied

- EXDENSUR syringe

Not Supplied

- Alcohol swab
- Cotton ball or gauze
- Adhesive bandage
- Sharps disposal container (See Section C for disposal instructions).

A2

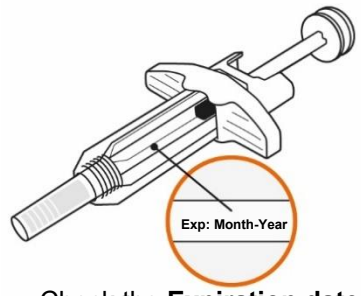


Take the **syringe out** of the tray

Take the Carton Containing Your Syringe Out of the Refrigerator

- Holding the **middle** of the syringe (near the inspection window), carefully take the syringe out of the tray.
- **Do not** remove the grey needle cap at this step.

A3

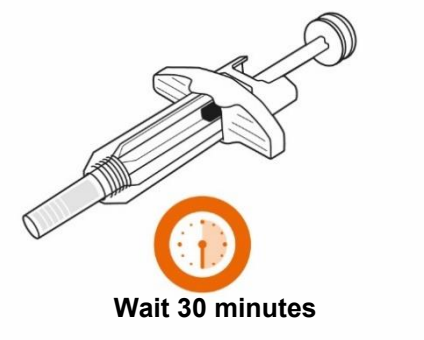


Check the **Expiration date** and the **medicine**

Check Your Syringe

- Check the expiration date. **Do not** use if the expiration date has passed.
- Look at the medicine in the EXDENSUR syringe through the inspection window. The medicine should be clear and colourless to slightly yellow.
- **Do not** inject if EXDENSUR is cloudy or has particles.
- It is normal to see air bubbles. You **do not** need to do anything about it.
- **Do not** shake the syringe.

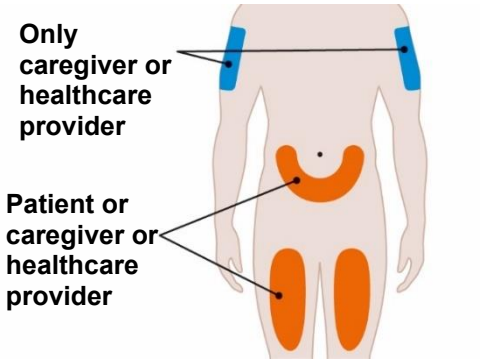
A4



Wait 30 Minutes

- **Do not** remove the grey needle cap.
- Place the syringe on a clean, flat surface away from direct sunlight and out of the reach of children.
- **Wait 30 minutes** to bring to room temperature before you inject. Cold medicine is more painful to inject.
- **Do not** warm your EXDENSUR syringe in a microwave, hot water, or direct sunlight.
- **Do not** use the EXDENSUR syringe if it has been left out of the carton for more than 8 hours.

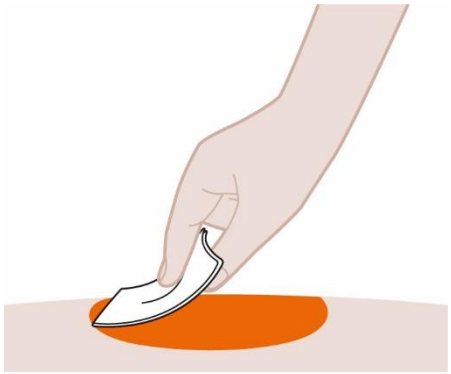
A5



Choose Your Injection Site

- If you are giving yourself the injection, you can inject into your thighs or stomach (abdomen).
- A caregiver can inject into the upper arm, thigh, or abdomen.
- **Do not** inject yourself in the upper arm, as it is more difficult to avoid syringe movement during the injection.
- **Do not** inject where the skin is bruised, tender, red, or hard.
- **Do not** inject within 2 inches (5 cm) of your belly button.

A6

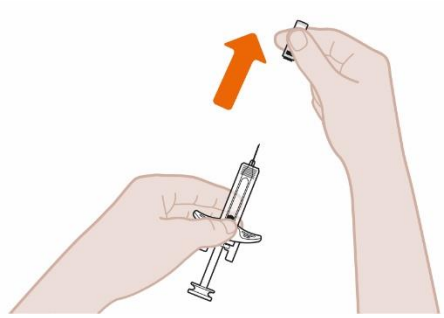


Clean the Injection Site

- Wash your hands with soap and water.
- Clean the injection site with an alcohol swab. Allow skin to air dry.
- **Do not** fan or blow on the cleaned injection site.
- **Do not** touch the cleaned injection site again until you have finished your injection.

B. Inject

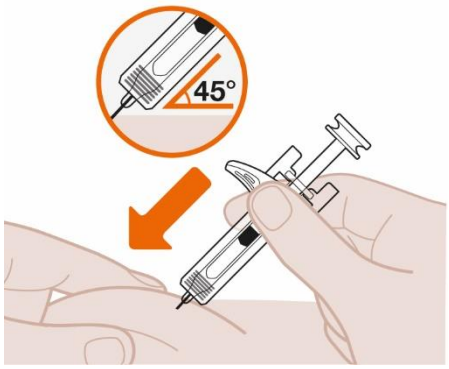
B1



Pull Off the Grey Needle Cap

- Remove the grey needle cap from the syringe by pulling it straight off, away from the needle (as shown). It may take some force to remove the grey needle cap.
- **Do not** handle the syringe by the white plunger while removing the grey needle cap.
- **Do not** let the needle touch any surface.
- **Do not** touch the needle.
- **Do not** try to remove any air bubbles from the syringe.
- **Do not** put the grey needle cap back onto the syringe. This could cause a needle injury.
- Inject within 5 minutes after you remove the grey needle cap.

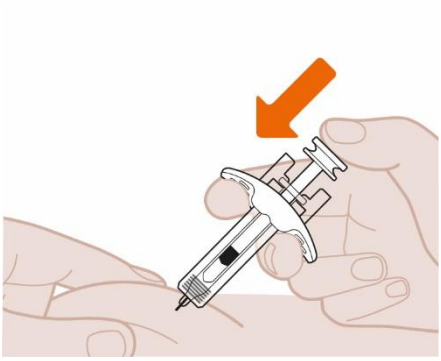
B2



Position the Syringe at the Injection Site

- Use your free hand to gently pinch the skin around the cleaned injection site.
- Keep pinching the skin throughout the injection.
- **Do not** handle the syringe by the white plunger while inserting the needle into the pinched skin.
- Hold the **middle** of the syringe and insert the entire needle into the pinched skin at a 45 degree angle, as shown.

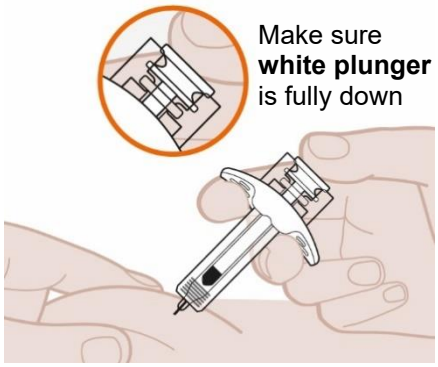
B3



Start the Injection

- Move your thumb to the white plunger and use your fingers to hold onto the middle finger grip, as shown.
- Slowly push down on the white plunger to inject the full dose.

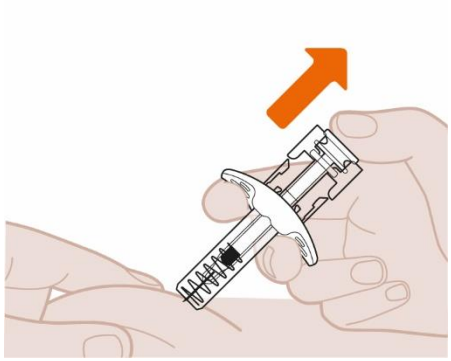
B4



Fully Press the White Plunger

- Make sure the white plunger is pushed all the way down until the stopper reaches the bottom of the syringe and all of the medicine is injected.

B5



Slowly Lift Thumb After Injection Completes

- Slowly lift your thumb up. This will allow the white plunger to come up and the needle to automatically pull up (retract) into the needle guard.
- After removing the syringe from the injection site, release the pinched skin.
- **Do not** rub the injection site.
- **Do not** put the grey needle cap back onto the EXDENSUR syringe.
- There may be a small drop of blood at the injection site. This is normal. Press a cotton ball or gauze on the area and apply an adhesive bandage if you need it.

C. Throw Away

Dispose of the used syringe and needle cap according to local requirements. Ask your doctor or pharmacist for advice if necessary.

Keep your used syringes and needle caps out of the sight and reach of children