swissmedic

Date: 25 November 2026
Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Exdensur

International non-proprietary name:	depemokimab
Pharmaceutical form:	solution for injection in pre-filled pen
Dosage strength(s):	100 mg / mL
Route(s) of administration:	subcutaneous use
Marketing authorisation holder:	GlaxoSmithKline AG
Marketing authorisation no.:	70280
Decision and decision date:	approved on 9 October 2026

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

Table of contents

1 Terms, definitions, abbreviations 3
2 Background information on the procedure 5
2.1 Applicant's request(s) and information regarding procedure 5
2.2 Indication and dosage 5
2.2.1 Requested indication 5
2.2.2 Approved indication 5
2.2.3 Requested dosage 5
2.2.4 Approved dosage 6
2.3 Regulatory history (milestones) 6
3 Medical context 7
4 Quality aspects 7
4.1 Drug substance 7
4.2 Drug product 8
4.3 Quality conclusions 9
5 Nonclinical aspects 10
5.1 Pharmacology 10
5.2 Pharmacokinetics 10
5.3 Toxicology 10
5.4 Nonclinical conclusions 11
6 Clinical aspects 12
6.1 Clinical pharmacology 12
6.2 Dose finding and dose recommendation 12
6.3 Efficacy 12
6.4 Safety 14
6.5 Final clinical benefit risk assessment 15
7 Risk management plan summary 16
8 Appendix 17

1 Terms, definitions, abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
ADR	Adverse drug reaction
AE	Adverse event
ALT	Alanine aminotransferase
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
AU	Absorbance unit
AUC	Area under the plasma concentration-time curve
$AUC_{0\text{-}24h}$	Area under the plasma concentration-time curve for the 24-hour dosing interval
C3	Complement component 3
CHO	Chinese hamster ovary
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
COX-1	Cyclooxygenase-1
CRS	Chronic rhinosinusitis
CRSsNP	Chronic rhinosinusitis without nasal polyps
CRSwNP	Chronic rhinosinusitis with nasal polyps
CYP	Cytochrome P450
DDI	Drug-drug interaction
EMA	European Medicines Agency
ERA	Environmental risk assessment
FcRn	Neonatal fragment crystallisable receptor
FDA	Food and Drug Administration (USA)
FeNO	Fractional exhaled nitric oxide
FTIH	First time in human study
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
ICS	Inhaled corticosteroids
Ig	Immunoglobulin
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IL-4	Interleukin-4
IL-5	Interleukin-5
IL-13	Interleukin-13
INCS	Intranasal corticosteroids
INN	International non-proprietary name
ITT	Intention-to-treat
IV	Intravenous
kDA	Kilodalton
LABA	Long-Acting $Beta_2$-Agonist
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable

NO(A)EL	No observed (adverse) effect level
NP	Nasal polyp
NSAID	Non-steroidal anti-inflammatory drug
OLE	Open-label extension
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
PT	Preferred term
Q4W	Every 4 weeks
Q26W	Every 26 weeks
QTc	Corrected QT interval
RMP	Risk management plan
SAE	Serious adverse event
SC	Subcutaneous
SCS	Systemic corticosteroids
SGRQ	St. George's Respiratory Questionnaire
SOC	System organ class
SwissPAR	Swiss Public Assessment Report
$T_{1/2}$	Half-life
T2	Type 2
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
VRS	Verbal response scale
WCB	Working cell bank

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for depemokimab in the above-mentioned medicinal product.

2.2 Indication and dosage

2.2.1 Requested indication

Asthma
Exdensur is indicated as an add-on maintenance treatment for asthma in adult and adolescent patients aged 12 years and older with type 2 inflammation characterised by an eosinophilic phenotype who are inadequately controlled on medium- to high-dose inhaled corticosteroids (ICS) plus another asthma controller.

Chronic rhinosinusitis with nasal polyps (CRSwNP)
Exdensur is indicated as an add-on treatment for adult patients with inadequately controlled CRSwNP.

2.2.2 Approved indication

Asthma
Exdensur is indicated as add-on maintenance therapy in adults and adolescents from 12 years of age with severe asthma with type 2 inflammation characterised by the following criteria:

- At least two exacerbations in the last 12 months despite treatment with moderate- to high-dose inhaled corticosteroids plus an additional asthma controller and/or the need for treatment with systemic corticosteroids.
- Blood eosinophil count ≥ 0.15 G/L (equivalent to ≥ 150 cells/µL) at initiation of therapy or ≥ 0.3 G/L (equivalent to ≥ 300 cells/µL) within the past 12 months.

Chronic rhinosinusitis with nasal polyps (CRSwNP)
Exdensur is indicated as add-on therapy with intranasal corticosteroids in adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) that cannot be adequately controlled with systemic corticosteroids and/or surgical intervention.

For more detailed information on the patient populations, see *Properties/Effects, Clinical efficacy.*

2.2.3 Requested dosage

Summary of the requested standard dosage:
Asthma
Adults and adolescents aged 12 years and over
The recommended dose of Exdensur is 100 mg administered subcutaneously once every 6 months.
Children aged less than 12 years
The safety and efficacy of depemokimab in children aged less than 12 years have not yet been established. No data are available.

CRSwNP
Adults
The recommended dose of Exdensur is 100 mg administered subcutaneously once every 6 months.
Children and adolescents below the age of 18 years
The safety and efficacy of depemokimab in children with CRSwNP below the age of 18 years have not been established. No data are available.

Special populations
Elderly, renal or hepatic impairment
No dose adjustment is recommended.

2.2.4 Approved dosage

(See appendix)

2.3 Regulatory history (milestones)

Application	29 July 2025
Formal objection	20 August 2025
Response to formal objection	22 August 2025
Formal control completed	28 August 2025
List of Questions (LoQ)	19 December 2025
Response to LoQ	19 March 2026
Preliminary decision	18 June 2026
Response to preliminary decision	31 July 2026
Final decision	9 October 2026
Decision	approval

3 Medical context

Asthma is a chronic respiratory disease characterised by variable respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough, along with variable expiratory airflow limitation. These symptoms fluctuate in intensity and frequency and are often triggered by factors like exercise, allergens, viral infections, or cold air. Asthma is driven by complex interactions between genetic predisposition and environmental exposures.
Severe asthma is defined as asthma that remains uncontrolled despite adherence to an optimised high-dose combination of inhaled corticosteroids and long-acting beta$_2$-agonists (ICS-LABA) and management of contributing factors, or asthma that worsens when high-dose treatment is reduced. Severe asthma is not diagnosed if symptoms improve after addressing modifiable factors. Severe asthma is categorised into phenotypes based on the presence or absence of type 2 (T2) airway inflammation.
T2 inflammation involves cytokines such as interleukin-4 (IL-4), interleukin-5 (IL-5), and interleukin-13 (IL-13). This phenotype can be treated with biologics. Generally, criteria associated with response to approved biologics include elevated blood eosinophils (≥150/µL), increased fractional exhaled nitric oxide (FeNO ≥20 ppb), sputum eosinophils (≥2%), and allergen-driven asthma.
Chronic rhinosinusitis (CRS) is defined as a complex inflammatory condition involving the paranasal sinuses and linings of the nasal passages that lasts 12 weeks or longer. CRS is divided into CRS with nasal polyps (CRSwNP) and CRS without NP (CRSsNP), the distinction being made by the presence or absence of nasal polyps (NPs). CRSwNP represents 20 to 33% of all CRS cases. In a subset of patients, nasal CRS with NP is associated with asthma and adverse reactions to aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) that inhibit cyclooxygenase-1 (COX-1). [UpToDate. *Chronic rhinosinusitis: Clinical manifestations, pathophysiology, and diagnosis.* Last updated: 01.07.2026. Accessed: 23.11.2026].
CRSwNP is characterised by the presence of bilateral NPs in the middle meatus. The characteristic presentation of CRSwNP is gradually worsening nasal congestion/obstruction or blockage, sinus fullness and facial pressure, fatigue, anterior or posterior nasal drainage, and loss of the sense of smell (hyposmia or anosmia). In contrast, fever and severe facial pain are uncommon. CRS with NP and asthma share eosinophilic histopathologic features. [UpToDate. *Chronic rhinosinusitis: Clinical manifestations, pathophysiology, and diagnosis.* Last updated: 01.07.2026. Accessed: 23.11.2026].
Generally, criteria associated with response to approved biologics include recurrent polyps following sinus surgery or not suitable for surgery, confirmed T2 inflammation, at least 2 ineffective treatments with systemic corticosteroids (SCS) in the last year, comorbid bronchial asthma, significant loss of sense of smell and/or significant impairment of quality of life [European position paper 2020/2023].

4 Quality aspects

4.1 Drug substance

INN: depemokimab
Molecular mass: approximately 149 kDa
Extinction coefficient (280 nm): 1.39 AU x cm^2 x mg^{-1}
Molecular structure:
Depemokimab is a recombinant monoclonal antibody based on a human immunoglobulin G1 (IgG1κ) framework, which is directed against IL-5. Depemokimab is a glycoprotein with a molecular weight of approximately 149 kDa and is composed of 2 IgG1 heavy chains of 449 amino acids each and 2 kappa light chains of 220 amino acids each, with the heavy chains connected by disulfide bonds. Amino acid substitutions were introduced into the constant region of the heavy chains to increase the

affinity for the neonatal Fc receptor, resulting in an extended half-life of the antibody in the blood circulation.

Manufacture:
Depemokimab is produced in Chinese hamster ovary (CHO) cells. A two-tiered cell banking system of master cell bank and working cell bank (WCB) is in place. After the WCB vial has been thawed, the cells are grown in suspension culture in a series of seed train bioreactors to generate sufficient cell mass to seed the production bioreactor. The cell culture fluid is harvested, and purification is performed with a series of chromatography, ultra-/diafiltration, viral inactivation, and viral filtration steps.
The cell culture and purification processes for depemokimab drug substance are both validated with several consecutive batches, and the data demonstrated consistent production and efficient removal of impurities.
Several changes were implemented during development of the manufacturing process for depemokimab drug substance, including changes to manufacturing site and production scale. However, comparability studies, which included batch release data, extended characterisation data, and stress stability data, demonstrated comparability between the different processes.
The characterisation of the physicochemical and biological properties of depemokimab and its impurities was performed using state-of-the-art methods.

Specification:
The specifications for release and stability of the drug substance include relevant tests and acceptance criteria, e.g. for identity, purity and impurities, quantity, and potency. Specifications are based on clinical experience, batch analysis data, and stability data, and conform to current compendial or regulatory requirements. Analytical procedures are validated or verified in accordance with current regulatory or compendial requirements. Batch analysis data for development, clinical, and process validation batches of the drug substance were provided.

Stability:
The drug substance is stored frozen. During storage, no significant changes were observed under the proposed storage conditions.

4.2 Drug product

Description and composition:
Depemokimab injection, 100 mg/mL is an aqueous solution containing the excipients L- histidine/ L-histidine HCl monohydrate, L-arginine HCl, trehalose dihydrate, disodium edetate dihydrate (EDTA), and polysorbate 80 at pH 6.0. The drug product is contained in a glass syringe with laminated elastomeric plunger. The finished product is a combination product that consists of a single-dose sterile liquid drug product housed in either a pre-filled pen or a pre-filled syringe with safety syringe device that delivers 100 mg of depemokimab for subcutaneous (SC) administration.

Pharmaceutical development:
Several drug product dosage strengths, formulations, presentations, and filling facilities were used during clinical development. However, comparability studies, which included batch release data and stability data, demonstrated comparability of the relevant quality attributes between the different processes.
Satisfactory information and data were provided regarding the suitability of the device parts of the two combination products, in accordance with current requirements.

Manufacture:
The drug product manufacturing process consists of thawing of the drug substance, dilution and mixing, bioburden-reducing filtration, sterile filtration and aseptic filling, visual inspection, device

assembly and labelling, and secondary packaging. The drug product manufacturing process is validated with several consecutive batches. The data demonstrated consistent production.

Specification:
The specifications for release and stability of the drug product include relevant tests and acceptance criteria, e.g. for identity, purity and impurities, quantity, potency, appearance, pH, osmolality, visible and subvisible particles, bacterial endotoxins, and sterility. The drug product specifications conform to current compendial or regulatory requirements. Analytical procedures are validated or verified in accordance with current regulatory or compendial requirements. Batch analysis data were provided for several batches of finished product, including development batches, clinical batches, and process validation batches.

Container closure system:
The materials of the Type I glass syringe barrel and laminated elastomeric plunger meet compendial requirements.

Stability:
The finished product (pre-filled pen or pre-filled syringe) should be stored at 2°C to 8°C, protected from light. The stability data support a shelf life of 30 months.

4.3 Quality conclusions

Satisfactory and consistent quality of the drug substance and drug product has been demonstrated. Safety of the product regarding viral and non-viral contaminants is adequately addressed. The risk for adventitious agents is minimised.

5 Nonclinical aspects

5.1 Pharmacology

The applicant compared depemokimab with mepolizumab, focusing on their pharmacological and pharmacokinetics properties. Depemokimab demonstrated a higher binding affinity for human IL-5 than mepolizumab and a higher affinity for human neonatal fragment crystallisable receptor (FcRn) at pH 6.0. Both characteristics contribute to its prolonged pharmacological activity and allow for less frequent dosing compared with mepolizumab. At 37°C, depemokimab showed binding affinities of 39.1 pM and 23.9 pM to human and cynomolgus monkey IL-5, with no detectable binding to mouse, rat, rabbit, or dog IL-5. Depemokimab potently inhibited IL-5-mediated TF-1 cell proliferation (IC_{50} approximately 4 pM vs. 105-123 pM for mepolizumab) and eosinophil shape change. Depemokimab was more stable in human and monkey serum after 6 weeks at 37°C compared with mepolizumab (73.1% and 77.1% vs. 51.0% and 64.2%, respectively).
In vivo, a single intravenous (IV) dose of depemokimab (1 mg/kg) reduced eosinophil counts for up to 24 weeks, compared with 7 weeks for mepolizumab. Depemokimab also showed a longer serum half-life ($t_{1/2}$; 24 days vs. 11.5 days) and reduced clearance. Following a single-dose or repeated-dose SC administration (10 and 100 mg/kg), a dose-independent trend towards reduction in eosinophil counts was observed. Total serum IL-5 levels showed variable, not dose-proportional, increases that persisted during the recovery period, indicating target engagement. These findings indicate that depemokimab shows improved pharmacokinetics and efficacy compared to mepolizumab.
Secondary pharmacodynamics studies were not conducted, which is acceptable given the high specificity of depemokimab for human IL-5. Due to the introduced mutations in the Fc part of the antibody and the established experience with mepolizumab, no antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity is expected.
Standalone safety pharmacology studies were not performed. Cardiovascular safety was assessed in the 26-week repeat-dose toxicology study. Corrected QT interval (QTc) interval prolongation was observed in 4 of 6 animals at 100 mg/kg/dose (C_{max} 106-fold, AUC 46-fold human exposure at the therapeutic dose). There were no clinical observations noted that indicated effects on respiratory or central nervous system function in the repeat-dose study.

5.2 Pharmacokinetics

A pharmacokinetic/pharmacodynamic study in cynomolgus monkeys investigated depemokimab following IV (0.05 and 1 mg/kg) and SC (1 mg/kg) administration. After IV dosing, systemic exposure (AUC and C_{max}) increased dose-proportionally and was characterised by prolonged $t_{1/2}$ and slow clearance. Following SC administration at 1 mg/kg, systemic exposure was comparable to that observed after IV dosing, resulting in an estimated absolute bioavailability of 111%. Terminal half-life and clearance rates were similar between SC and IV dosing and slightly shorter than the $t_{1/2}$ observed in humans. There were no sex-related differences in pharmacokinetics.
Standard distribution, metabolism, and excretion studies were not conducted, which is in accordance with ICH S6 (R1) guideline.
An *in silico* placental transfer model was used to compare predicted fetal exposure of depemokimab and mepolizumab in monkeys and humans, taking into account the enhanced FcRn binding affinity of depemokimab. The model predicted fetal exposure to mepolizumab and indicated only minor (2- to 3-fold) increases in fetal pharmacokinetic parameters with depemokimab.

5.3 Toxicology

The cynomolgus monkey was selected as the relevant nonclinical species for depemokimab. Toxicology studies comprised a single-dose study and a 26-week repeat-dose study with a 30-week recovery period, using SC administration, the intended clinical administration route. Antibody cross-

reactivity with monkey and human tissues was also assessed. Adequate systemic exposure was achieved throughout the dosing period. Anti-drug antibodies (ADAs) were detected in some animals in the repeat-dose toxicity study; however, reduced exposure was seen in only one animal.
In the single-dose study, monkeys received a SC injection of depemokimab (10 and 100 mg/kg) and were observed for 4 weeks. Adverse vascular inflammation with a morphology similar to spontaneous arteritis was observed in one female at 10 mg/kg and one female at 100 mg/kg, with immune complex granular deposits (monkey immunoglobulin M [IgM], IgG, and/or complement component 3 [C3]) in multiple tissues. An indirect relationship to depemokimab through exacerbation of spontaneous immune complex disease cannot be excluded. The applicant noted that similar findings of granular deposits containing IgG and/or complement, but not the drug as the primary antigen, have been reported with other biologics. Eosinophil counts were decreased, consistent with the expected pharmacology, but showed variability and were not dose dependent. Increased serum IL-5 concentrations indicated target engagement without dose-proportionality. A NOAEL could not be established. Systemic exposure at 10 mg/kg exceeded human therapeutic exposure by 2.4-fold based on AUC.
In the 6-month study, animals received two SC doses (10 or 100 mg/kg on day 1 and week 14). The observed decrease in eosinophil counts, increases in total IL-5 levels, and treatment-unrelated prolongation of QTc interval were observed as described in the pharmacology section above. IL-5 levels remained elevated in 2 of 3 animals in the 10 mg/kg group during the off-dose period. No effects on PR or QRS intervals or electrocardiographic abnormalities were noted. One animal was euthanised during the pretreatment period due to Shigella infection, and one female in the 10 mg/kg group was euthanised for the same reason during the dosing period.
The NOAEL of the repeat-dose study was 100 mg/kg, corresponding to exposure margins of 46-fold (AUC) and 107-fold (Cmax) relative to human therapeutic exposure.
No genotoxicity studies were conducted for depemokimab, in accordance with ICH S6(R1) guideline. Carcinogenicity studies in rodents were not conducted. Based on a weight-of-evidence assessment, including literature data and clinical experience with other anti-IL-5 monoclonal antibodies, the risk of carcinogenicity is considered low. No effects on spermatogenesis were observed in young monkeys. No reproductive and developmental toxicology studies have been conducted with depemokimab.
Juvenile toxicity studies were not conducted with depemokimab, in accordance with the PIP, but data from adolescent monkeys in the toxicity studies showed no adverse effects, including effects on late-developing systems like bone and reproductive organs.
No concerns were identified with respect to impurities or excipients.
The summary of the key nonclinical findings presented in the risk management plan (RMP) is acceptable. Overall, no nonclinical safety concerns were identified that would preclude approval.
As depemokimab is a monoclonal antibody, no environmental risk is anticipated.

5.4 Nonclinical conclusions

The submitted documentation is considered appropriate to conduct a risk assessment for Exdensur with the new active substance depemokimab. The submitted nonclinical data is in line with ICH S6(R1) guideline and supports the approval of depemokimab in the proposed indication.

6 Clinical aspects

6.1 Clinical pharmacology

Depemokimab exhibited approximately dose-proportional pharmacokinetics following SC administration and is characterised by a prolonged terminal half-life of approximately 40-50 days, supporting the recommended dosing interval of 6 months. No clinically relevant accumulation was observed at steady state. Depemokimab is not expected to undergo hepatic metabolism or renal elimination. PopPK analyses demonstrated comparable PK in patients with CRSwNP and in patients with asthma. Age, body weight, renal function, hepatic function and ethnicity had no meaningful effect on depemokimab exposure, and, therefore, no dose adjustment is required based on these intrinsic factors. In addition, PK exposure in adolescent (12–17 years) asthma patients was comparable to that observed in adults, supporting the proposed flat-dose regimen in this population. No dedicated drug-drug interaction studies were performed, and PK interactions are not expected due to the molecular nature of the compound (i.e. antibody).
In patients with CRSwNP, depemokimab produced sustained reductions in blood eosinophil counts, which were associated with improvements in endoscopic NP score and nasal obstruction symptoms.
In patients with asthma, depemokimab produced sustained reductions in blood eosinophil counts, which were associated with reductions in annualised asthma exacerbation rates. Exposure-response analyses further supported the selected dosing regimen.
Immunogenicity was low (<10%), with no apparent impact on PK, PD or safety.
Clinical pharmacology findings supported the proposed dosing regimen and the wording of the Information for healthcare professionals.

6.2 Dose finding and dose recommendation

Asthma and CRSwNP

No specific dose-finding studies were conducted for depemokimab in patients with bronchial asthma or CRSwNP. The dose selection for the phase 3 studies of depemokimab in asthma patients or CRSwNP patients was based on mepolizumab (Nucala), another IL-5 inhibitor, which is approved for both asthma and CRSwNP, with a dose regimen of 100mg SC every 4 weeks (Q4W). Since depemokimab targets the same IL-5 epitope as mepolizumab, it was expected that establishing the same IL-5 neutralisation would lead to the same reduction in blood eosinophils and thus to similar clinical efficacy in both indications. The first time in human study (FTIH) of depemokimab, also an IL-5 inhibitor, in adult patients with mild to moderate asthma and baseline eosinophil counts $\geq$200 cells/µL, a PopPK analysis, PopPKPD analyses, and exposure-response analyses supported the direct transition to the confirmatory phase 3 studies in participants with asthma or CRSwNP. A dose regimen of depemokimab 100 mg SC every 26 weeks (Q26W) was identified to match the mepolizumab-like reduction in blood eosinophils, and was therefore expected to generate similar clinical efficacy and safety in patients with bronchial asthma or CRSwNP.

6.3 Efficacy

Asthma
Two replicate pivotal phase 3 studies, SWIFT-1 and -2, were submitted. These were global, randomised, double-blinded, placebo-controlled, parallel-group, phase 3 studies to investigate the efficacy and safety of depemokimab 100 mg SC Q26W over a 52-week treatment period in adult and adolescent patients with asthma for ≥2 years, a confirmed history of ≥2 exacerbations requiring SCS despite the use of medium-to-high dose inhalative corticosteroids (ICS), elevated blood eosinophil counts of ≥150 cells/µL at screening or ≥300 cells/µL in the past 12 months.

The primary endpoint of both studies was the annualised rate of clinically significant exacerbations over 52 weeks. Secondary endpoints were symptom-related – lung function measurement and the annualised rate of clinically significant exacerbations requiring hospitalisation and/or emergency department visit over 52 weeks.
The primary endpoint was met in both studies. The reduction in the annualised rate of clinically significant exacerbations was 58% in SWIFT 1 and 48% in SWIFT 2 in the depemokimab group compared to the placebo group. This endpoint and its treatment effect was considered clinically relevant.
In both SWIFT studies, the 1st secondary endpoint – defined as “Change from baseline in St. George's Respiratory Questionnaire (SGRQ) total score at week 52” – was not met. Accordingly, no confirmatory statistical inferences could be made for the remaining secondary endpoints in the testing hierarchy either, as the results would not be controlled for multiplicity (type 1 error). Nevertheless, depemokimab consistently achieved numerically better results in all secondary endpoints of the testing hierarchy than placebo.
30 adolescents were included in both SWIFT studies (15 in the depemokimab group, 15 in the placebo group). No separate data were provided for the adolescents, but subgroup analyses from the SWIFT studies showed similar results for both adolescents and adults. Extrapolation of efficacy from adults to adolescents is considered justified, given that pharmacokinetic exposure was comparable between the two populations and the extrapolation approach based on the ICH Guideline E11 is accepted for adolescents with asthma.
The details of the pivotal study designs, the baseline characteristics, and efficacy results can be found in the approved Information for healthcare professionals (Appendix 8).

Patients who had received 2 doses of study medication and who completed one of the SWIFT studies (in either the depemokimab or placebo arm) were eligible to participate in AGILE, a multi-centre, single-arm, open-label, 12-month extension study, the primary objective of which was to evaluate the long-term safety of depemokimab 100 mg administered SC in addition to standard of care in participants with severe asthma with an eosinophilic phenotype. Efficacy was a secondary objective.
The annualised rate of clinically significant exacerbations was 0.56 (95% CI: 0.49, 0.65) in the overall population, 0.58 (95% CI: 0.45, 0.73) in previous placebo and 0.55 (95% CI: 0.47, 0.66) in previous depemokimab groups. These rates are similar to the rate of 0.51 reported in the depemokimab treatment group in the pooled parent studies. Accordingly, the benefit from the parent studies was maintained over the 12 months of this extension study.

NIMBLE, an active-controlled study was also submitted. This was a multi-centre, randomised, double-blind, double-dummy, parallel group non-inferiority phase 3 study of depemokimab 100 mg SC compared with continuation of mepolizumab or benralizumab treatment in participants with severe asthma with an eosinophilic phenotype. The primary endpoint was the annualised rate of clinically significant exacerbations over 52 weeks. Non-inferiority was not met, as the upper bound of the CI was higher than the pre-specified non-inferiority margin of 1.28. Although a 16% relative difference favoured the comparator, the absolute difference was small (0.08 exacerbations/year) and unlikely to be clinically meaningful, a conclusion supported by minimal changes in other secondary endpoints, such as asthma control and lung function measures.

CRSwNP

Two replicate pivotal phase 3 studies, ANCHOR-1 and -2, were submitted. These were global, randomised, double blinded, placebo-controlled, parallel-group phase 3 studies to investigate the efficacy and safety of depemokimab 100 mg SC Q26W over a 52-week treatment period in adult patients with inadequately controlled CRSwNP, despite daily intranasal corticosteroids (INCS) and a history of SCS over $\geq$ 3days and/or NP surgery within the past 2 years.
The studies had 2 co-primary endpoints to capture both the objective assessment of NP size and the patient`s subjective experience of nasal obstruction symptoms.
The 1st co-primary endpoint was defined as “Change from baseline in total endoscopic NP score at week 52”. Both ANCHOR studies met the 1st co-primary endpoint. Depemokimab reduced NP size until week 52, whereas it increased under placebo.

The 2nd co-primary endpoint was defined as “Change from baseline in mean nasal obstruction verbal response scale (VRS) score over weeks 49 to 52”. Again, both ANCHOR studies met the 2nd co-primary endpoint. Depemokimab reduced the nasal obstruction symptoms with greater statistical significance than placebo until week 52.
Neither ANCHOR study met the 1st secondary endpoint, “Change from baseline in rhinorrhoea VRS mean score over week 49 to week 52”. Accordingly, no confirmatory statistical inferences could be made for the remaining secondary endpoints in the testing hierarchy, either as the results would not be controlled for multiplicity (type 1 error). Nevertheless, depemokimab consistently achieved numerically greater improvements in all secondary endpoints of the testing hierarchy compared to placebo.
The details of the pivotal study designs, the baseline characteristics, and efficacy results can be found in the approved Information for healthcare professionals (Appendix 8).

6.4 Safety

Asthma
The safety pool of the pivotal studies – the “SWIFT 1+2 pool” – comprised 501 patients with asthma who had received at least 1 dose of depemokimab 100 mg SC. In the “all study pool”, a total of 1,678 healthy participants, participants with bronchial asthma, and participants with CRSwNP had received at least 1 dose of depemokimab 100 mg SC.
Patients with asthma had received a maximum of 2 doses of depemokimab and the mean duration of exposure to depemokimab was 11.7 months in the SWIFT 1+2 pool. The mean treatment exposure during the AGILE open-label extension (OLE) study , was another 11.0 months for the previous depemokimab group. Thus, patients with asthma had received a maximum of 4 doses of depemokimab over a 104-week (2-year) study period (SWIFT 1+2 pool, then AGILE).

There were no deaths in patients with asthma (or CRSwNP) treated with depemokimab.
Serious adverse events (SAEs) occurred in a slightly lower proportion of participants in the depemokimab 100 mg SC group than in the placebo group (SWIFT 1+2 pool: 7% versus 13%). The SAEs that affected ≥2% participants were asthma (SWIFT 1+2 pool: 2% versus 4%) and pneumonia (<1% versus 2%). In the AGILE OLE study, the percentage of participants with SAEs was similar in the previous depemokimab and previous placebo group (7% versus 8%), and similar to the parent SWIFT studies (7%); the most common SAE was asthma (<1% versus 1%).
The percentage of participants with any treatment-emergent adverse event (TEAE) was similar (slightly lower) in the depemokimab group compared with the placebo group in both the SWIFT 1+2 pool and the pooled pivotal CRSwNP plus asthma studies (72% vs 76%, and 73% vs 78%). In the AGILE OLE study, the percentage of participants with any TEAE was similar in the previous depemokimab and previous placebo groups (61% versus 63%%), and similar or even lower compared to the parent SWIFT studies (61% versus 72%).
Related TEAEs – as assessed by the investigator – were experienced by a slightly higher percentage of patients in the depemokimab group than in the placebo group (SWIFT 1+2 pool: 4% vs 2%). The only related TEAE reported more than once was injection site reaction (4 versus 0 participants in the depemokimab versus placebo group).

There were no major differences in safety data between adolescents and adults.

Those TEAE which were identified as adverse drug reactions (ADRs) are listed and described in the approved Information for healthcare professionals (Appendix 8).
CRSwNP
The safety pool of the pivotal studies, the “ANCHOR 1+2 pool”, comprised 272 patients with CRSwNP who had received at least 1 dose of depemokimab 100 mg SC. In the “all study pool”, a total of 1,678 healthy participants, participants with bronchial asthma, and participants with CRSwNP had received at least 1 dose of depemokimab 100 mg SC.

Patients with CRSwNP had received a maximum of 2 doses of depemokimab and the mean duration of exposure to depemokimab was 11.6 months (ANCHOR 1+2 pool).
Accordingly, experience with depemokimab is limited. No long-term safety data from patients with CRSwNP treated with depemokimab beyond 1 year or 2 doses are available. No further clinical trials in patients with CRSwNP are ongoing or planned. The limited experience is reflected in the Information for healthcare professionals (Appendix 8)/Posology together with a rule for assessing the individual benefit/risk ratio at the latest after 2 administrations prior to considering continuation of depemokimab therapy.
There were no deaths in patients with CRSwNP (or asthma) treated with depemokimab.
SAEs occurred in a slightly lower percentage of participants in the depemokimab 100 mg SC group than in the placebo group (ANCHOR 1+2 pool: 3% versus 6%, all study pool: 8% versus 10%). No individual SAE (PT [preferred term]) was reported for 1% of the participants.
Also, severe AEs occurred less frequently in the depemokimab versus the placebo group in the ANCHOR 1+2 pool (4% versus 9%).
The percentage of participants with any TEAE was similar (slightly lower) in the depemokimab group compared with the placebo group in both the ANCHOR 1+2 Pool and the pooled pivotal CRSwNP plus asthma studies (75% vs 79%, and 73% vs 78%).
Related TEAEs – as assessed by the investigator – were experienced by a slightly higher percentage of patients in the depemokimab group than the placebo group (6% vs 4%, and 5% vs 3%), but no individual TEAE (PT) was reported for ≥1% participants, and there was no apparent pattern based on system organ class (SOC).
Those TEAEs which were identified as ADRs are listed and described in the approved Information for healthcare professionals (Appendix 8).

6.5 Final clinical benefit risk assessment

Asthma
A statistically significant, clinically relevant and consistent treatment effect in adults with severe asthma was demonstrated. Subgroup analyses indicated similar results for adolescents and adults, though data on adolescents remain limited. No prohibitive safety concerns were observed, and there were no major differences between adults and adolescents as regards safety data.
Consequently, based on the pivotal study designs, the benefit-risk ratio was considered positive for add-on maintenance therapy for adult and adolescent patients aged > 12 years with severe asthma with type 2 inflammation, characterised by the following criteria:
- At least two exacerbations within the last 12 months despite treatment with medium- to high-dose inhaled corticosteroids plus another asthma controller and/or the need for treatment with SCS.
- Blood eosinophil count ≥ 0.15 G/L (corresponding to ≥ 150 cells/µL) at treatment initiation or ≥ 0.3 G/L (corresponding to ≥ 300 cells/µL) within the last 12 months.

CRSwNP
A relatively small but statistically significant and consistent treatment effect of depemokimab in patients with CRSwNPs was demonstrated, which was more pronounced in objective measurements than subjective symptoms. The safety profile of depemokimab 100 mg SC Q26W in patients with CRSwNPs was assessed as acceptable. Consequently, based on the pivotal study designs, the benefit risk ratio was considered positive for an add-on therapy to INCS for adult patients with CRSwNPs which cannot be adequately controlled with SCS and/or surgery.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Exdensur, solution for injection in pre-filled pen, was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo-pro.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

Placeholder for text approval stamp

▼ This medicinal product is subject to additional monitoring, which will enable quick identification of new safety information. Healthcare professionals are requested to report any suspected new or serious adverse reactions. See the “Undesirable effects” section for information on reporting adverse reactions.

EXDENSUR

Composition

Active substances

Depemokimab (genetically engineered using CHO [Chinese hamster ovary] cells).

Excipients

Histidine, histidine hydrochloride monohydrate, trehalose dihydrate, arginine hydrochloride, disodium edetate, polysorbate 80 0.2 mg/mL, water for injections.
Total sodium content: 0.00235 mg/mL

Pharmaceutical form and active substance quantity per unit

Solution for injection in pre-filled pen/pre-filled syringe for SC use: Each pre-filled pen and pre-filled syringe contains 100 mg depemokimab in 1 mL sterile solution (100 mg/mL).

Indications/Uses

Asthma

Exdensur is indicated as add-on maintenance therapy in adults and adolescents from 12 years of age with severe asthma with type 2 inflammation characterised by the following criteria:

- At least two exacerbations in the last 12 months despite treatment with moderate- to high-dose inhaled corticosteroids plus an additional asthma controller and/or the need for treatment with systemic corticosteroids.
- Blood eosinophil count ≥ 0.15 G/L (equivalent to ≥ 150 cells/µL) at initiation of therapy or ≥ 0.3 G/L (equivalent to ≥ 300 cells/µL) within the past 12 months.

Chronic rhinosinusitis with nasal polyps (CRSwNP)

Exdensur is indicated as add-on therapy with intranasal corticosteroids in adults with severe chronic rhinosinusitis with nasal polyps (CRSwNP) that cannot be adequately controlled with systemic corticosteroids and/or surgical intervention.

For more detailed information on the patient populations, see *Properties/Effects, Clinical efficacy.*

Dosage/Administration

Exdensur should be prescribed by doctors who have experience in the diagnosis and treatment of the above-mentioned indications (see “Indications/Uses”).

Documentation of the trade name and batch number is recommended for each treatment to ensure the traceability of biotechnology-based medicinal products.

Usual dosage

Asthma

Adults and adolescents aged 12 years and older

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

Children under 12 years of age

The safety and efficacy of Exdensur in children under 12 years of age have not been investigated in controlled studies.

Duration of treatment:

The success of treatment should be evaluated after 2 doses of Exdensur at the latest and a decision should be made regarding continuation of treatment. To assess the response to add-on therapy, careful recording of asthma control, the need for systemic corticosteroids and the frequency of pre- and on-treatment exacerbations is required. In the event of a response, Exdensur is intended for long-

term treatment. The benefit and need for continuation of therapy should be reviewed at least annually based on the physician's assessment of disease severity and exacerbation control.

Chronic rhinosinusitis with nasal polyps (CRSwNP)

Adults aged 18 years and older

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

Children and adolescents under 18 years of age

The safety and efficacy of Exdensur in children and adolescents under 18 years of age with CRSwNP have not been investigated.

Duration of treatment:

Experience with depemokimab in patients with CRSwNP is limited as there is no long-term experience beyond one year or two doses.

The success of treatment should be evaluated after 2 doses of Exdensur at the latest and a decision should be made regarding continuation of treatment. In the event of a response, Exdensur is intended for long-term treatment. The benefit and need for continuation of therapy should be reviewed at least annually based on the physician's assessment of disease severity.

Specific patient groups

Elderly patients

No dose adjustment is recommended in patients aged 65 years or older (see "*Pharmacokinetics – Specific patient groups"*).

Patients with renal disorders

No dose adjustment is recommended in patients with renal dysfunction (see "*Pharmacokinetics – Specific patient groups"*).

No dose adjustment is recommended in patients with hepatic dysfunction (see "*Pharmacokinetics – Specific patient groups"*).

Mode of administration

Exdensur pre-filled pen and pre-filled syringe should only be injected subcutaneously (SC) into the upper arm, thigh or abdomen (see "*Instructions for handling*" and separate instructions for use included in the pack).

Exdensur may be self-administered by the patient in the thigh or abdomen or by a caregiver in the upper arm, thigh or abdomen if the physician considers it appropriate and the patient or caregiver has been trained in the relevant injection technique.

Missed doses
A missed dose should be administered as soon as possible. If the missed dose is administered 1 month or more after the scheduled dose, the 6-month (every 26 weeks) injection schedule should be resumed from the date of administration of the missed dose.

Contraindications

Hypersensitivity to depemokimab or any of the excipients.
Depemokimab must not be used to treat acute asthma symptoms or exacerbations, see also "*Warnings and precautions"*.

Warnings and precautions

Hypersensitivity reactions
Immediate and delayed systemic reactions, including hypersensitivity reactions (such as anaphylaxis, angioedema, urticaria and pruritus) may occur following administration of depemokimab (see "*Undesirable effects"*). Such reactions usually occur within hours of administration, but sometimes with a delay (i.e. several days). In the event of a hypersensitivity reaction, appropriate treatment as clinically indicated is recommended. Monitoring for signs of recurrent hypersensitivity reactions is recommended when depemokimab is re-administered. In the event of a severe or recurrent hypersensitivity reaction, permanent discontinuation of depemokimab therapy should be considered.

Asthma-related adverse events or exacerbation
Asthma-related adverse events or exacerbations may occur during treatment with depemokimab. It is recommended that patients be instructed to seek medical help if their asthma remains uncontrolled or worsens after initiating treatment with depemokimab, see also "*Contraindications"*.

Inadequate response to therapy
In case of non-response to depemokimab, the long half-life of depemokimab should be taken into account when choosing the appropriate time to start treatment with another biologic (see "Pharmacokinetics").

Corticosteroid dose reduction
Abrupt discontinuation of on-going medication (including systemic and inhaled corticosteroids) after initiation of depemokimab therapy is not recommended. The dose of any ongoing medication may need to be reduced gradually and under medical supervision.

Parasitic (helminthic) infestation

Eosinophils may be involved in the immunological response to some helminthic infestations. Patients with pre-existing helminthic infestations were excluded from participation in the clinical programme. Patients with pre-existing helminthic infestations should be treated prior to administration of depemokimab. If patients develop a helminthic infestation during treatment with depemokimab and fail to respond to anthelminthic treatment, the next dose of depemokimab should be postponed until the infestation has cleared.

Sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per 100 mg injection (= 1 mL), i.e. it is essentially “sodium-free”.

Polysorbate

This medicinal product contains 0.2 mg of polysorbate 80 per 100 mg injection (= 1 mL). Polysorbates may cause allergic reactions.

Interactions

Depemokimab has low potential for drug-drug interactions due to its metabolism and mechanism of action.

Pregnancy, lactation

Pregnancy

The effects of depemokimab on human pregnancy are unknown. Linear transport of monoclonal antibodies such as depemokimab is expected across the placenta as pregnancy progresses. The higher affinity of depemokimab for the neonatal Fc receptor could lead to increased transmission via the placenta compared to unchanged monoclonal antibodies. The possible clinical effects are unknown. Reproductive toxicity studies have not been performed with depemokimab (see *“Preclinical data”*).

Depemokimab should only be used during pregnancy if treatment is clearly required.

Lactation

No data are available on the excretion of depemokimab in human or animal milk. However, depemokimab is a humanised monoclonal antibody (immunoglobulin G1 [IgG1] kappa), and immunoglobulin G (IgG) is known to be excreted in breast milk in small amounts.

A decision regarding discontinuation of breast-feeding or treatment with depemokimab should depend on an assessment of the benefit of breast-feeding to the child versus the benefit of treatment to the mother.

Fertility

No fertility data are available for humans. Animal studies have not revealed any adverse effects of anti-IL-5 treatment on fertility (see *"Preclinical data"*).

Effects on ability to drive and use machines

There have been no studies to investigate the effect of Exdensur on the ability to perform tasks that require judgement, motor or cognitive skills. A detrimental effect on these activities is not to be anticipated given the pharmacology of Exdensur. An assessment should be made of whether a patient is capable of mastering tasks requiring judgement, motor or cognitive skills, taking into account the patient's clinical status and the side effect profile of Exdensur.

Undesirable effects

Clinical trial data

Depemokimab was studied in a clinical development programme involving adolescent (12 years and older) and adult patients with asthma (SWIFT-1 and SWIFT-2 studies) and adult patients with CRSwNP (ANCHOR-1 and ANCHOR-2 studies). In these four randomised, 52-week, placebo-controlled, multicentre studies, patients received either subcutaneous (SC) depemokimab or subcutaneous (SC) placebo once every six months. A total of 773 patients received at least one 100 mg dose of depemokimab in these studies.

Summary of the safety profile

The most common adverse reactions reported with depemokimab are local injection site reactions (2%).

Adverse reactions have been listed by MedDRA body system organ class and frequency (see Table 1).

The frequency of adverse reactions is defined using the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000) and not known (frequency cannot be estimated from available data).

Table 1. Undesirable effects

System organ class	Adverse reaction	Frequency
Immune system disorders	Hypersensitivity reactions (systemic allergy)[a, b]	Uncommon
Skin and subcutaneous tissue disorders	Pruritus	Common
General disorders and administration site conditions	Administration-related systemic reactions (non-allergic)[b,c]	Common
	Local injection site reactions[d]	Common

[a] Observed in a phase I study and an open-label extension study.

[b] The majority of events (85%) resolved within ≤7 days, with most events (65%) resolving in ≤2 days after onset.

[c] Symptoms include headache, fatigue and rash.

[d] Symptoms include pain, erythema, swelling and itching. Most events were mild and 79% resolved within ≤7 days, with most events (56%) resolving in ≤2 days of onset.

Description of specific undesirable effects and additional information

Systemic reactions (allergic)

Hypersensitivity reactions such as anaphylaxis and angioedema have been reported with other monoclonal antibodies directed against IL-5 or its receptor. These reactions may occur based on experience with this class of drugs.

Systemic reactions (non-allergic)

Throughout the clinical development programme, non-allergic administration-related reactions (e.g. headache, fatigue, rash) have been reported in 1% of patients treated with depemokimab. In the 52-week placebo-controlled studies in asthma and CRSwNP, systemic non-allergic reactions were reported in < 1% of patients receiving depemokimab.

Systemic reactions (non-allergic) reported with depemokimab were non-serious and of mild or moderate intensity. The majority of events were transient: 88% of events resolved within ≤ 7 days of onset, while 67% of events resolved within ≤ 2 days.

Immunogenicity

Of patients who received at least one 100 mg SC dose of depemokimab 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) tested positive for anti-depemokimab antibodies (ADA) during the 52-week studies.

9% (55/622) of patients were ADA-positive in an ongoing 52-week open-label extension asthma study (AGILE; n = 395 with 104-week data collection) while 4% (34/841) were positive in an ongoing 52-week study of asthma patients previously treated with either mepolizumab or benralizumab (NIMBLE). In the placebo-controlled studies of asthma and CRSwNP indications and in the 52-week open-label extension study in asthma (AGILE), < 1% of patients (n = 7) had neutralising antibodies.
Anti-depemokimab antibodies did not significantly impact depemokimab pharmacokinetics and no correlation was observed between antibody titres and changes in eosinophil count. Patients who were ADA-positive generally had a similar adverse reaction profile to ADA-negative patients. No effect of ADA on the pharmacokinetics or pharmacodynamics or safety of depemokimab has been observed, but data are still limited.

Paediatric population
Fifteen adolescents (aged 12-17 years) received depemokimab in two placebo-controlled asthma studies (SWIFT-1 and SWIFT-2) lasting 52 weeks. The safety profile was generally similar to that seen in adults. No additional undesirable effects were identified.
Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

There is no clinical experience with depemokimab overdose, and no specific treatment is available. Patients who have taken an overdose of the drug should be treated with appropriate supportive measures and monitored as necessary.
Further management should be undertaken as clinically indicated or as recommended by the National Poison Centre, if necessary.

Properties/Effects

ATC code

R03DX12

Mechanism of action

Depemokimab targets human IL-5 with high binding affinity (10.5 pM) and specificity, thereby blocking binding to the IL-5 receptor alpha expressed on the cell surface with picomolar potency (IC_{50} 4 pM) *in vitro*. Depemokimab contains a triple amino acid substitution (YTE) in the fragment crystallisable (Fc)

region, which increases binding to the neonatal Fc receptor and thereby extends the elimination half-life. These modifications allow for dosing at six-monthly intervals.
IL-5 is a key cytokine in type 2 inflammation along with IL-4 and IL-13. IL-5 -mediated type 2 inflammation is an important component of the pathogenesis of asthma and chronic rhinosinusitis with nasal polyps. IL-5 is the most important cytokine responsible for the growth and differentiation of eosinophils in the bone marrow, as well as for recruitment, activation and survival of eosinophils in the tissues. Additional cell types that express IL-5R alpha, including mast cells, plasma cells, epithelial cells and fibroblasts, are also involved in inflammation.

Pharmacodynamics

Placebo-controlled studies involving adult and adolescent asthmatic patients aged 12 years and older revealed that a 100 mg dose of depemokimab administered subcutaneously (SC) every 6 months for 52 weeks reduced the blood eosinophil count to an adjusted geometric mean of 56 cells/µL at Week 52. This corresponds to a geometric mean reduction of 79% (95% CI: 75.8; 81.8) as compared with placebo. This reduction in the number of eosinophils in the blood was observed within the first 2 weeks of treatment (at the first assessment) and persisted for the entire duration of treatment.
Placebo-controlled studies in adult patients with CRSwNP revealed that a 100 mg dose of depemokimab administered subcutaneously (SC) every 6 months for 52 weeks reduced the blood eosinophil count in blood to an adjusted geometric mean of 46 cells/µL at Week 52. This corresponds to a geometric mean reduction of 85% (95% CI: 82.4; 86.7) as compared with placebo. This reduction in the number of eosinophils in the blood was observed within the first 4 weeks of treatment (at the first assessment) and persisted for the entire duration of treatment.
A clinical pharmacology study in patients with mild to moderate asthma, revealed that a single 100 mg SC dose of depemokimab led to rapid reduction in the blood eosinophil count. The blood eosinophil count was reduced by 54% at the first post-dose assessment 24 hours after administration as compared with placebo.

Clinical efficacy

Asthma

The efficacy of depemokimab was evaluated in two 52-week, randomised (depemokimab to placebo ratio 2:1), double-blind, placebo-controlled, parallel-group, multicentre, replication clinical studies (SWIFT-1 and SWIFT-2). Both studies included patients aged 12 years and older with asthma with type 2 inflammation characterised by an eosinophilic phenotype. In these studies, depemokimab 100 mg was administered subcutaneously once every 6 months for a total of 2 doses in addition to standard of care (SoC) (medium- to high-dose inhaled corticosteroids (ICS) plus at least one additional asthma controller). Patients were required to have experienced two or more asthma

exacerbations in the last 12 months requiring treatment with systemic corticosteroids (SCS) while receiving standard of care (SoC) and/or requiring treatment with systemic corticosteroids. Patients were also required to have a blood eosinophil count of ≥ 150 cells/µL at screening or an eosinophil count of ≥ 300 cells/µL documented in the year prior to study entry and impaired lung function at baseline (forced expiratory volume in one second [FEV_1] before bronchodilator administration < 80% of the target value in adults and [FEV_1] < 90% or an FEV_1-FVC ratio [forced vital capacity] < 0.8 in adolescents). Patients were enrolled without requiring a minimum baseline Asthma Control Questionnaire-5 (ACQ-5) score. Depemokimab was administered as add-on to ongoing basic asthma therapy, which was continued throughout the duration of the studies. The full analysis set (FAS) population comprised 762 patients who were randomised and received at least one dose of depemokimab or placebo in both studies (382 in SWIFT-1 and 380 in SWIFT-2).
Patient demographics and baseline characteristics in these two studies have been depicted in Table 2.

Table 2. Demographics and baseline characteristics (FAS population)

	SWIFT-1 N=382	**SWIFT-2 N=380**
Age (years) of patients, mean (SD)	54 (14.2)	53 (16.2)
Women, n (%)	223 (58)	241 (63)
European, n (%)	316 (83)	272 (72)
Asthma duration, years, mean (SD)	22 (16.2)	25 (18.5)
Mean FEV_1 in % of the target value prior to bronchodilator administration (SD)	62 (15.2)	62 (15.9)
Mean % reversibility (SD)	17 (15.3)	18 (17.4)
Eosinophil count, cells/µL, median (min, max)	310 (20; 2360)	340 (10; 4440)
Mean number of exacerbations in the previous year (SD)	2.2 (0.69)	2.7 (1.92)
Medium-dose ICS(%)[a]	179 (47)	154 (41)
High-dose ICS (%)[a]	203 (53)	226 (59)
ICS + LABA + LAMA (%)	95 (25)	127 (33)
Mean SGRQ total score (SD), range 0–100	44.3 (20.70)	44.5 (18.69)

	SWIFT-1 N=382	SWIFT-2 N=380
Patients with ACQ ≥1.5 at baseline (%)	280 (75)	279 (75)
OCS use (%)	21 (5)	19 (5)
Total IgE, U/µL, Median (min, max)	185 (1.9; 12,142)	180 (2.2; 16,198)

ACQ-5 = Asthma Control Questionnaire; FEV_1 = forced expiratory volume in one second; IgE = immunoglobulin E; ICS = inhaled corticosteroid; OCS = oral corticosteroid; SGRQ = St. George's Respiratory Questionnaire.
[a] medium ICS dose = 440 µg fluticasone propionate (FP) daily metered dose or equivalent; high ICS dose > 440 µg FP daily metered dose or equivalent.

Exacerbations

The primary efficacy endpoint of SWIFT-1 and SWIFT-2 was the annualised rate of clinically significant exacerbations over the 52-week treatment period. A clinically significant exacerbation was defined as worsening of asthma requiring SCS (IV or oral steroids for at least three days or a single intramuscular [IM] corticosteroid dose) and/or hospitalisation and/or emergency department visit. Patients receiving SCS as maintenance therapy required doubling of the ongoing maintenance dose for at least 3 days. All patients who experienced an exacerbation were treated with SCS and most remained in the study.

The annualised rate of asthma exacerbations in SWIFT-1 and SWIFT-2 was significantly lower in patients receiving depemokimab as compared to those receiving placebo (Table 3). During the 52-week treatment period, fewer patients experienced exacerbations in the depemokimab groups (32% and 32%) as compared with the placebo groups (46% and 50%) in SWIFT-1 and SWIFT-2, respectively.

Table 3. Results of primary exacerbation endpoint (FAS population)

	SWIFT-1		SWIFT-2	
	Depemokimab N=250	**Placebo N=132**	**Depemokimab N=252**	**Placebo N=128**
Annualised asthma exacerbation rate				
Exacerbation rate/year	0.46	1.11	0.56	1.08
Rate ratio (95% CI) Reduction in % (95% CI)	0.42 (0.30; 0.59) 58% (41%; 70%)		0.52 (0.36; 0.73) 48% (27%; 64%)	
P-value	< 0.001		< 0.001	

FAS = full analysis set

The percentage of patients with exacerbations requiring hospitalisation and/or an emergency department visit was lower in patients treated with depemokimab (1% and 4%) as compared with those treated with placebo (8% and 10%) in SWIFT-1 and SWIFT-2, respectively. A pooled analysis of SWIFT-1 and SWIFT-2 revealed that the 3% of patients on depemokimab with exacerbations required hospitalisation and/or an emergency department visit over 52 weeks as compared with 9% of those who received placebo. Depemokimab reduced the rate of exacerbations by 72% as compared with placebo (rate ratio [RR]: 0.28 (95% CI: [0.13; 0.61]).

Open-label extension study on asthma (AGILE)

Patients who completed either the SWIFT-1 or SWIFT-2 studies were eligible to participate in an open-label extension study (AGILE) wherein they all received up to two doses of depemokimab over an additional 52 weeks. The analysis of AGILE (n = 629) showed an annualised exacerbation rate of 0.56 (95% CI: 0.49; 0.65).

Chronic rhinosinusitis with nasal polyps

The efficacy of depemokimab in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) was evaluated in two 52-week, randomised, double-blind, placebo-controlled, parallel-group, multicentre, replication clinical studies (ANCHOR-1 and ANCHOR-2). These studies investigated the efficacy of 100 mg depemokimab administered subcutaneously once every 6 months; a total of 2 doses in addition to standard of care (SoC) (intranasal corticosteroids, saline nasal irrigation, short-term systemic corticosteroids (except during run-in), inhaled corticosteroids with nasal exhalation (ICS/ETN) and/or antibiotics). All patients had either been treated with systemic corticosteroids (SCS) within the past 2 years and/or had a medical contraindication/intolerance to SCS and/or had a documented history of prior surgery for nasal polyps (NP) prior to screening. Randomised patients were required to have an endoscopic bilateral NP score of at least 5 of a maximum score of 8, with a minimum score of 2 in each nasal cavity and a mean nasal obstruction Verbal Response Scale (VRS) score of 2 or greater at baseline. Other than nasal obstruction, there were no other inclusion criteria regarding symptoms or quality of life at randomisation. A total of 528 patients (271 in ANCHOR-1 and 257 in ANCHOR-2) were enrolled in the full analysis set (FAS) population.
The demographics and baseline characteristics of patients participating in these two studies have been depicted in Table 4 below.

Table 4. Demographics and baseline characteristics (FAS population)

	ANCHOR-1 N=271	**ANCHOR-2 N=257**
Age (years) of patients, mean (SD)	54 (13.4)	50 (12.9)

	ANCHOR-1 N=271	ANCHOR-2 N=257
Women, n (%)	83 (31)	80 (31)
European, n (%)	185 (70)	197 (77)
Duration (years) of CRSwNP, mean (SD)	13 (11.2)	11 (8.7)
Patients with ≥1 prior NP surgery, n (%)	171 (63)	162 (63)
SCS 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/µL, median (min, max)	360 (10; 10,550)	360 (30; 1,670)
Total endoscopic NP score[a b c], mean (SD), max. score=8	6.0 (1.35)	5.9 (1.29)
Mean nasal obstruction VRS score[a, d], mean (SD), max. score=3	2.5 (0.48)	2.6 (0.42)
Mean rhinorrhoea VRS score[a, d], mean (SD), max. score=3	2.2 (0.70)	2.3 (0.67)
Mean loss of smell VRS score[a, d], mean (SD), max. score=3	2.7 (0.55)	2.8 (0.41)
LMK CT score[a, b], mean (SD), max. score=24	18.7 (4.08)	18.9 (4.19)
SNOT-22 total score[a, e], mean (SD), max. score=110	57.4 (22.15)	60.1 (19.95)
Patients 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, SCS = systemic 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 of both nostrils (0-8 scale) where each nostril was graded (0=no polyps; 1=small polyps in the middle meatus not extending below inferior border of the middle concha; 2=polyps extending below the lower border of the middle concha; 3=large polyps extending up to the lower border of the inferior concha or polyps medial to the middle concha; 4=large polyps causing near-complete congestion/obstruction of the inferior meatus).

[d] Documented daily by patients on a 0 to 3 scale where 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 relating to symptoms and impact associated with CRSwNP (nasal, non-nasal, ear/face, sleep, fatigue, emotional consequences). Higher scores indicate worse health-related quality of life.

Total endoscopic nasal polyps score and nasal obstruction VRS score

The co-primary efficacy endpoints in each study were change from baseline in total endoscopic NP score (0-8 scale) at Week 52, as graded by central blinded readers, and change of the mean nasal obstruction VRS score from baseline (0-3 scale [0=no symptoms, 1=mild symptoms, 2=moderate symptoms, 3=severe symptoms]) over Weeks 49 to 52, as self-reported by patients using a daily diary. Patients who received depemokimab showed a statistically significant improvement (reduction) in total endoscopic NP score at Week 52 and nasal obstruction VRS score over Weeks 49 to 52 as compared to placebo in both ANCHOR-1 and ANCHOR-2. The results of the co-primary endpoints in each of the ANCHOR studies and the results of a pooled analysis of ANCHOR-1 and ANCHOR-2 have been depicted in Table 5.

Table 5. Results of co-primary endpoints (FAS population)

	ANCHOR-1		**ANCHOR-2**		**Pooled**	
	Depemokimab N=143	**Placebo N=128**	**Depemokimab N=129**	**Placebo N=128**	**Depemokimab N=272**	**Placebo N=256**
Total endoscopic NP score at Week 52[a, b]						
n[c]	128	120	120	115	248	235
LS mean (SE)	5.4 (0.14)	6.2 (0.15)	5.4 (0.14)	6.0 (0.15)	5.4 (0.10)	6.1 (0.10)
LS mean change from baseline (SE)	-0.6 (0.14)	0.2 (0.15)	-0.5 (0.14)	0.1 (0.15)	-0.5 (0.10)	0.1 (0.10)
Adjusted treatment difference[d] (95% CI)	-0.7 (-1.1; -0.3)		-0.6 (-1.0; -0.2)		-0.7 (-0.9; -0.4)	
P-value	< 0.001		0.004		-	
Mean nasal obstruction VRS score over Weeks 49 to 52[a, b]						
n[c]	125	116	119	111	244	227
LS mean (SE)	1.77 (0.079)	2.00 (0.083)	1.83 (0.076)	2.07 (0.078)	1.80 (0.055)	2.04 (0.057)

	ANCHOR-1		ANCHOR-2		Pooled	
	Depemokimab N=143	Placebo N=128	Depemokimab N=129	Placebo N=128	Depemokimab N=272	Placebo N=256
LS mean change from baseline (SE)	-0.76 (0.079)	-0.53 (0.083)	-0.77 (0.076)	-0.53 (0.078)	-0.77 (0.055)	-0.53 (0.057)
Adjusted treatment difference[d] (95% CI)	-0.23 (-0.46; 0.00[e])		-0.25 (-0.46; -0.03)		-0.24 (-0.39; -0.08)	
P-value	0.047		0.025		-	

FAS = full analysis set; LS = least squares; NP = nasal polyps; VRS = verbal response scale.

[a] Patients who had nasal surgery or had taken disease-modulating drugs for CRSwNP prior to the time point of interest were assigned the worst possible value of the relevant score for all assessments following surgery or initiation of disease-modulating drugs.

[b] Based on Mixed Model for Repeated Measures (MMRM) analyses with covariates of treatment, baseline score, log(e) baseline blood eosinophil count, region, previous surgery for nasal polyps, visit and interaction terms for visit baseline and visit treatment. The study was included as an additional covariate for the pooled analysis.

[c] Number of patients with analysable data at the given time point.

[d] Adjusted treatment difference (depemokimab vs. placebo).

[e] The upper limit of the 95% CI represents a rounded value of -0.003.

A pooled analysis of ANCHOR-1 and ANCHOR-2 revealed a treatment difference in favour of depemokimab by Week 12 (first timepoint assessed) for the total endoscopic NP score and by Weeks 1-4 (first timepoint assessed) for the nasal obstruction VRS mean score that was maintained up to Week 52.

In a pooled subgroup analysis of the co-primary endpoints, patients with/without comorbid asthma or blood eosinophil counts above or below 300 cells/µL at baseline revealed evidence of improvement with depemokimab as compared with placebo that were consistent with that of the overall population.

Pharmacokinetics

Depemokimab exhibited approximately dose-proportional pharmacokinetics over a dose range of 10 to 300 mg in patients with asthma following subcutaneous administration. Depemokimab pharmacokinetics were consistent in patients with asthma and CRSwNP with an average steady-state concentration of 5.9 µg/mL and 5.2 µg/mL, respectively, following subcutaneous administration of 100 mg depemokimab every 6 months.

Absorption

The maximum observed plasma concentrations (C_{max}) after a single subcutaneous dose (doses ranging from 2 to 300 mg) were achieved after a median of 8 to 14 days. No accumulation was observed following repeated subcutaneous administration once every 6 months.

Distribution

The mean volume of distribution is 6 to 9 L after a single subcutaneous dose of depemokimab.

Metabolism

Depemokimab is a monoclonal antibody, which is catabolised by ubiquitous proteolytic enzymes not confined to liver tissue alone.

Elimination

The geometric mean terminal elimination half-life ranged from 38 to 53 days after a single subcutaneous dose of depemokimab, with geometric mean apparent clearance values ranging from 0.081 to 0.16 L/day.

Kinetics in specific patient groups

Population pharmacokinetic analyses have not shown clinically relevant effects of age, race, or gender on depemokimab pharmacokinetics.

Children and adolescents

Pharmacokinetic data in the paediatric population are limited. The pharmacokinetics of depemokimab in adolescents aged 12 to 17 years with asthma were similar to those in adults.
Depemokimab pharmacokinetics have not been studied in paediatric patients under 12 years of age.

Renal dysfunction

No formal studies have been conducted to investigate the effect of renal dysfunction on depemokimab pharmacokinetics. Population pharmacokinetic analyses have shown that no dose adjustment is required in patients with an estimated glomerular filtration rate [eGFR] of <60 mL/min/1.73 m^2. Data are limited in patients with an eGFR of <60 mL/min/1.73 m^2.
Kidney dysfunction is not expected to have a significant impact on clearance since depemokimab is not excreted through the kidneys.

Hepatic dysfunction

No formal studies have been conducted to study the effect of hepatic dysfunction on depemokimab pharmacokinetics. Since depemokimab is degraded by widely distributed proteolytic enzymes, not confined to liver tissue alone, changes in hepatic function are unlikely to have an effect on the elimination of depemokimab. Based on the population pharmacokinetic analysis, baseline hepatic

function biomarkers (alanine aminotransferase [ALT], aspartate aminotransferase [AST], and bilirubin) had no clinically relevant effect on apparent depemokimab clearance.

Preclinical data

Carcinogenicity, mutagenicity

No genotoxicity or carcinogenicity studies have been performed.

Reproductive toxicology

No adverse histopathological findings in the reproductive organs were observed in Javanese monkeys receiving depemokimab up to 100 mg/kg SC for 6 months.

Reproductive toxicity studies have not been conducted with depemokimab. No effects on development were observed in animal studies targeting IL-5 signalling pathways.

Other information

Shelf life

The medicinal product must not be used after the “EXP” date on the packaging.

Special precautions for storage

Store in a refrigerator (2°C to 8°C) and protect from light in the original packaging until used. Do not freeze.

Keep out of the reach of children.

If needed, the pre-filled pen and pre-filled syringe may be removed from the refrigerator and stored at room temperature (up to 30°C) for up to 7 days in the original unopened packaging, protected from light. The medicine should be discarded if it has been stored outside the refrigerator for more than 7 days.

The pre-filled pen and pre-filled syringe must be used within 8 hours once the packaging has been opened. The medicinal product should be discarded if not administered within 8 hours.

Instructions for handling

Detailed instructions on using the pre-filled pen and pre-filled syringe are available in the instructions for use included in the packaging.

The pre-filled pen and pre-filled syringe are intended for single use.

Authorisation number

70280, 70512 (Swissmedic)

Packs

Pre-filled pen:

Pack containing one pre-filled pen of 100 mg/mL (B)

Pre-filled syringe:

Pack containing one pre-filled syringe of 100 mg/mL (B)

Marketing authorisation holder

GlaxoSmithKline AG, 6340 Baar

Date of revision of the text

June 2026