swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report
Extension of therapeutic indication

PALFORZIA

International non-proprietary name:	allergens of peanut (*Arachis hypogaea*)
Pharmaceutical form:	oral powder
Dosage strength(s):	1 mg, 20 mg, 100 mg, 300 mg 0.5 mg and 1 mg, 1 mg and 10 mg, 20 mg and 100 mg
Route(s) of administration:	oral
Marketing authorisation holder:	Stallergenes AG
Marketing authorisation no.:	67733
Decision and decision date:	approved on 25 February 2025

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.

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1 Terms, Definitions, Abbreviations

ADA	Anti-drug antibody
ADME	Absorption, distribution, metabolism, elimination
AE	Adverse event
AIT	Allergen immunotherapy
ALT	Alanine aminotransferase
ANCOVA	Analysis of covariance
API	Active pharmaceutical ingredient
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical Classification System
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
CI	Confidence interval
C_{max}	Maximum observed plasma/serum concentration of drug
COVID-19	Coronavirus Disease 2019
CYP	Cytochrome P450
DBPCFC	Double-blind, placebo-controlled food challenge
DDI	Drug-drug interaction
EMA	European Medicines Agency
EoE	Eosinophilic oesophagitis
ERA	Environmental risk assessment
FDA	Food and Drug Administration (USA)
FPIES	Food protein-induced enterocolitis syndrome
GCP	Good Clinical Practice
GERD	Gastroesophageal reflux disease
GI	Gastrointestinal
GLP	Good Laboratory Practice
HPLC	High-performance liquid chromatography
IC/EC_{50}	Half-maximal inhibitory/effective concentration
ICH	International Council for Harmonisation
Ig	Immunoglobulin
INN	International non-proprietary name
ITT	Intention-to-treat
LoQ	List of Questions
MAH	Marketing authorisation holder
Max	Maximum
Min	Minimum
MRHD	Maximum recommended human dose
N/A	Not applicable
NHLBI	National Heart, Lung, and Blood Institute
NO(A)EL	No observed (adverse) effect level
OIT	Oral immunotherapy
PBPK	Physiology-based pharmacokinetics
PD	Pharmacodynamics
PEESS v2.0	Pediatric Eosinophilic Esophagitis Symptom Scores version 2.0
PIP	Paediatric investigation plan (EMA)
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PSP	Pediatric study plan (US FDA)
RMP	Risk management plan
SAE	Serious adverse event
SPT	Skin prick test

SwissPAR	Swiss Public Assessment Report
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)
YOA	Years of age

2 Background information on the procedure

2.1 Applicant's request(s)

Extension(s) of the therapeutic indication(s)
The applicant requested the addition of a new therapeutic indication or modification of an approved one in accordance with Article 23 TPO.

2.2 Indication and dosage

2.2.1 Requested indication

Treatment of patients aged **1-3 years** to be newly included:

Palforzia can be used to increase the peanut threshold dose tolerated without allergic reactions in patients aged **1** to 17 years with a confirmed* diagnosis of clinically significant peanut allergy.
* The following cumulative conditions must be met for a confirmed diagnosis:
- History of allergic reactions to peanut
- Confirmation of specific sensitisation (IgE and/or skin prick testing)
- Reaction in an oral challenge at a threshold dose of ≤ 300 mg peanut protein or confirmation of strong evidence of sensitisation (see RAMSES study in "Clinical efficacy" section).

Palforzia should only be used as an adjuvant measure in addition to a peanut-avoidant diet.
Palforzia may be continued in patients aged 18 years and older.
During the course of treatment, Palforzia raises the peanut threshold dose that can trigger a reaction.
Fewer allergic reactions due to accidental exposure to peanut were seen with Palforzia compared with placebo during clinical development.
However, allergic reactions to Palforzia treatment (mostly to the preparation) were, overall, more frequent compared to placebo (mostly to food).
Palforzia is not intended for, and does not provide, immediate relief of allergic symptoms.
A sustained effect after stopping the treatment has not been shown.

2.2.2 Approved indication

Treatment of patients aged **1-3 years**.

2.2.3 Requested dosage

Initial Dose Escalation is adapted for patients aged 1-3 years:
Initial Dose Escalation consists of **4 dose levels (0.5-3 mg; Table 1) for patients 1-3 years old** and of 5 dose levels (0.5-6 mg; Table 1) for patients 4-17 years old administered over a duration of approximately 4-5 hours in a single day.

No changes to the other dosage recommendations were requested with the application for extension of indication.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	22 November 2023
Formal objection	13 December 2023
Response to formal objection	23 January 2024
Formal control completed	2 February 2024
List of Questions (LoQ)	27 May 2024
Response to LoQ	28 July 2024
Preliminary decision	27 September 2024
Response to preliminary decision	16 December 2024
Final decision	25 February 2025
Decision	approval

3 Medical context

Peanut allergy can be directed against various peanut components. Its prevalence varies worldwide according to region, eating habits, and cultural environment. Peanut allergies usually appear in early childhood, and although tolerance can develop spontaneously, this tends to be the exception. Treatment to date primarily involves the avoidance of triggering allergens. This can be difficult in severe forms of allergy. Since even small quantities of allergens can trigger reactions, accidental allergen exposures are possible even with a strict diet and good instruction/discipline, for example as a result of a contamination.
As for pollen and mite allergies, allergen immunotherapy with peanut allergens is also attempted for peanut allergies. Allergen immunotherapy (AIT, also known as specific immunotherapy, SIT) entails a controlled uptitration of specific allergens, to which the patients to be treated may respond with allergic reactions if the threshold dose is exceeded. As a result, the threshold dose may be increased and allergic reactions mitigated. As well as relieving allergic symptoms, allergology specialists postulate that AIT produces an improvement in the allergy that persists beyond the treatment period (known as desensitisation or hyposensitisation). The extent and mechanism of positive clinical effects of AIT have not yet been definitively clarified. To date, there are no long-term data that convincingly demonstrate a sustained effect, even after the discontinuation of treatment, that could not also be explained by selection bias as a result of increased study discontinuations during treatment compared to placebo. Allergen immunotherapy can be subdivided into various types based on the administration route. The most common routes are subcutaneous and sublingual administration. Oral administration into the gastrointestinal tract, as for Palforzia, is unusual. Unlike most sublingual immunotherapies, Palforzia contains predominantly digestion-resistant allergens.

Palforzia is currently the only medicinal product approved for oral immunotherapy in patients aged 4 to 17 years with peanut allergy in Switzerland.

4 Nonclinical aspects

The nonclinical documentation submitted with the initial marketing authorisation application supports the approval to add the treatment of patients 1 to 3 years old for Palforzia.

The applicant did not submit new nonclinical studies to support the requested extension of the indication. This was considered acceptable since there are no changes with regard to dosage or method of administration.

No environmental risk is expected by the extension of the indication.

From the nonclinical point of view, there are no objections to approval of the proposed extension of indication.

5 Clinical aspects

5.1 Clinical pharmacology

No new data.

5.2 Dose finding and dose recommendation

A separate dose-finding study was not done in 1 – 3 YOA (years of age) subjects.
The Phase 3 study ARC005 (POSEIDON) in 1 – 3 YOA had a design similar to that of previous studies in 4 – <18 YOA. In contrast to the earlier studies in older children, the initial dose escalation under medical supervision on Day 1 with a stepwise dose escalation of Palforzia (up to 4 single doses of 0.5, 1, 1.5, and 3 mg) was limited to a maximum of 3 mg (compared to 6 mg in studies in 4 – <18 YOA previously).
The doses of Palforzia used in this study during initial dose escalation, up-dosing, and maintenance were selected based on results from the Phase 2 studies (ARC001, ARC002), Phase 3 studies (ARC003, ARC004, ARC007, ARC010), and from published clinical studies.
Since the submitted data showed that the start of treatment with the lowest dose was well tolerated by most patients, it can be considered as sufficiently well documented from a safety perspective and was accepted.

5.3 Efficacy

The purpose of study ARC005 (study 05 of the PIP EMEA-001734-PIP01-14-M06) was to determine the efficacy and safety of Palforzia (AR101) compared with placebo in peanut-allergic children aged 1 to < 4 YOA. Subjects were evaluated for peanut tolerance up to 2000 mg peanut protein in a single dose (4043 mg cumulative) in a double-blind, placebo-controlled food challenge (DBPCFC) after approximately 12 months of treatment.

This Phase 3, 2:1 randomised, double-blind, placebo-controlled study was conducted at 14 study sites in North America and 9 sites in Europe. Eligible subjects who developed age-appropriate dose-limiting allergy symptoms after consuming single doses of peanut protein > 3 mg to ≤ 300 mg in a screening DBPCFC were randomly assigned 2:1 to blinded treatment with AR101 or placebo. Randomisation was stratified by geographic region (North America, Europe).
The escalation dose used in the study is the proposed dose for starting the treatment. Subjects began initial dose escalation under medical supervision at the study site on Day 1, with a stepwise dose escalation of the study product (up to 4 single doses of 0.5, 1, 1.5, and 3 mg) administered at 20- to 30-minute intervals as tolerated. Subjects who tolerated the 3 mg dose on Day 1 returned on Day 2 for a single 1 mg dose. Subjects who tolerated the 1 mg dose with no more than mild allergy symptoms that were not dose-limiting began the up-dosing period. Subjects who did not tolerate any dose on Day 1 or Day 2 discontinued early from the study.
The up-dosing period was approximately 6 months (maximum 40 weeks), with dose escalation approximately every 2 weeks. Daily doses of the study product during up-dosing were 1, 3, 6, 12, 20, 40, 80, 120, 160, 200, 240, and 300 mg/day. The first dose of the study product at each new dose level was administered under medical supervision at the study site; the remaining doses at each dose level were administered daily at home as tolerated. Dose adjustments could be allowed. Subjects who tolerated the 300 mg/day dose for 2 weeks within 40 weeks began the maintenance period. Subjects who were unable to tolerate the 300 mg/day dose for 2 weeks within 40 weeks of up-dosing discontinued early from the study.
Subjects who began maintenance treatment continued daily dosing with the study product at 300 mg/day for an overall total of approximately 12 months of treatment, with study site visits every 4 weeks. The duration of maintenance treatment varied from a minimum of 12 weeks to a maximum of 24 weeks depending on the up-dosing interval (24–40 weeks). Dose adjustments were allowed.

After the end of maintenance, subjects had an exit DBPCFC (up to a single highest challenge dose of 2000 mg peanut protein (4043 mg cumulative)). The 300 mg daily dose of the study product had to be tolerated for at least 2 consecutive weeks before having the DBPCFC. Subjects who completed both days of the exit DBPCFC completed the study. Study treatment assignment was unblinded for the subject after all major data queries for the subject were resolved. Eligible subjects had the option to enrol in an open-label, follow-on study ARC008 to receive AR101 treatment. If the follow-on study was not yet available at the study site, blinded study treatment could continue, and the visit schedule was every 4 weeks until the follow-on study was available.

Major exclusion criteria for study ARC005 were more extensive compared to the studies in older children 4 – 17 YOA. Especially, the following exclusion criteria were new included or more extensively described in detail. These exclusion criteria led to modifications of the Information for healthcare professionals in the chapter contraindication, warnings and precautions, and properties and efficiencies compared to the data in children 4 – 17 YOA.
1. History of food protein-induced enterocolitis syndrome (FPIES) within 12 months before screening.
2. History of failure to thrive or any other form of abnormal growth, or developmental or speech delay that precludes age-appropriate communication.
3. History of biopsy-confirmed diagnosis of eosinophilic oesophagitis (EoE); other eosinophilic GI disease; chronic, recurrent, or severe gastroesophageal reflux disease (GERD); or symptoms of dysphagia (e.g. difficulty swallowing, food “getting stuck”).
4. Recurrent GI symptoms considered clinically significant in the opinion of the investigator.
5. Moderate or severe persistent asthma (criteria steps 3-6; National Heart, Lung, and Blood Institute (NHLBI), 2007).
6. Mild asthma (criteria steps 1-2; NHLBI, 2007) that is uncontrolled or difficult to control based on NHLBI 2007 criteria.

The ITT population (including 98 AR101-treated subjects, 100% and 48 placebo-treated subjects, 100%) was used as the primary analysis population for all primary and secondary efficacy endpoints. All subjects received the correct study treatment at randomisation. The ITT and safety populations were the same.
Supportive and sensitivity analyses of the primary efficacy endpoint and key secondary endpoints were performed for subjects in the ITT or the completer population (83 AR101-treated subjects, 84.7% and 45 placebo-treated subjects, 93.8%).

The primary and all key secondary efficacy endpoints were met for this study.

The estimands were calculated according to 2 definitions: the North American estimands and the European estimands.
North America: Treatment with AR101 resulted in a statistically significant treatment effect over placebo in the proportion of subjects who tolerated a single highest dose of at least 600 mg peanut protein (1043 mg cumulative) with no more than mild symptoms at the exit DBPCFC, which is consistent with meaningful clinical benefit. The desensitisation response rate was 73.5% (95% CI: 63.6, 81.9) in subjects of the ITT population who received AR101, compared with 6.3% (95% CI: 1.3, 17.2) in subjects who received placebo. The treatment difference (AR101-placebo) was 67.2% (95% CI: 50.0, 84.5); $p < 0.0001$. The desensitisation response rate exceeded the prespecified margin of 15%.
Europe: Treatment with AR101 resulted in a statistically significant treatment effect over placebo in the proportion of subjects who tolerated a single highest dose of at least 1000 mg peanut protein (2043 mg cumulative) with no more than mild symptoms at the exit DBPCFC, which is consistent with meaningful clinical benefit. Of 98 subjects in the ITT population who received AR101, the desensitisation response rate was 68.4% (95% CI: 58.2, 77.4) compared with 4.2% (95% CI: 0.5, 14.3) for 48 subjects who received placebo. The treatment difference (AR101-placebo) was 64.2% (95% CI: 47.0, 81.4); $p < 0.0001$.

The key secondary efficacy endpoints were evaluated in hierarchical order by major health authority region and were successful for all key secondary endpoints for the North American and European study populations.

There was a decreasing trend in peanut-specific IgE levels in the AR101 group from screening to exit, while in the placebo group an increasing trend from screening to exit was seen. In the ITT population, the geometric mean (SD) peanut-specific IgE of the AR101 group was 7.04 (6.712) kUA/L at screening for 87 subjects and 3.33 (7.813) kUA/L at exit for 76 subjects. For the placebo group, the geometric mean (SD) peanut-specific IgE was 12.26 (8.429) kUA/L at screening for 45 subjects and 22.52 (6.796) kUA/L at exit for 38 subjects.

5.4 Safety

Overall, oral immunotherapy with AR101 in ARC005 appeared to have an acceptable safety profile in patients with peanut allergy. The safety profile was no worse, or was even better, than the one in older paediatric subjects (see Information for healthcare professionals). This is especially true for systemic allergic reactions.
Median exposure to the study product was 12.24 months (range: 0–19 months) for the AR101 group and 12.71 months (range: 4.2–17.3 months) for the placebo group.
The maximum dose of 300 mg/day was reached during up-dosing by 88 (89.8%) AR101-treated subjects and 45 (93.8%) placebo-treated subjects, and was continued by 86 AR101-treated subjects (98.9%) and 45 placebo-treated subjects (100%) during maintenance. The median time to the 80 mg daily dose was 99.5 days for the AR101 group and 100 days for the placebo group, and the median time to the 300 mg daily dose was 188.0 days for the AR101 group and 189.0 days for the placebo group.
Most subjects had 1 or more adverse events of any severity or relationship to the study product (98.0% AR101, 97.9% placebo). The highest incidence of any adverse event was during up-dosing (98.0% AR101, 97.9% placebo), followed by maintenance (90.8% AR101, 91.1% placebo), and initial dose escalation (21.4% AR101, 20.8% placebo).

Overall, the most common system organ classes of treatment-emergent adverse events (≥ 20% of subjects in either treatment group overall with ≥ 5% higher incidence in the AR101 group) in descending order were GI disorders (83.7% AR101, 64.6% placebo); respiratory, thoracic, and mediastinal disorders (78.6% AR101, 68.8% placebo); and general disorders and administration site conditions (62.2% AR101, 52.1% placebo).

No subject had an adverse event that was life threatening or that resulted in death. Six subjects overall (all in the AR101 group, 6.1%) discontinued the study product due to 1 or more adverse events; 5 (5.1%) during up-dosing and 2 (2.3%) during maintenance; 1 subject had an event during both up-dosing and maintenance. The higher adverse events rates with Palforzia leading to discontinuation are to be expected, as the peanut protein can cause allergic and associated reactions. However, the rate with Palforzia was low (6 subjects, 6.1%).

Epinephrine use was summarised by episode, defined as administration of 1 or more epinephrine doses within 2 hours. In the safety population overall, 11 subjects (11.2%) in the AR101 group and 2 subjects (4.2%) in the placebo group had at least 1 episode of epinephrine use. No subject had more than 3 episodes of epinephrine use. In the AR101 group, 11 subjects (11.2%) had a total of 13 episodes of epinephrine use; 12 episodes required 1 dose of epinephrine and 1 episode required 2 doses; 3 events (in 2 subjects, 2.1%) were considered related to the study product. In the placebo group, 2 subjects had 4 episodes of epinephrine use (1 subject had 1 episode; 1 subject had 3 episodes); 3 episodes required 1 dose of epinephrine and 1 episode required 2 doses. Most episodes of epinephrine use were associated with mild or moderate adverse events; 2 events in the AR101 group and 1 event in the placebo group were severe. None of the severe reactions treated with epinephrine were related to study therapy.

EoE was not diagnosed in any subject in either treatment group.

The adverse events were descriptively lower compared with older children and adolescents (see Information for healthcare professionals). This is especially true for severe systemic reactions like anaphylactic shock. This supports the suggestion that early treatment may be beneficial.

5.5 Final clinical benefit-risk assessment

Peanut allergy can be directed against various peanut components. The extension of the indication to children 1 – <4 YOA can provide a benefit due to the earlier treatment initiation. There are currently no other products approved in Switzerland for this indication in this age group.

Benefits:
Phase 3 study ARC005 was successful in demonstrating the clinical efficacy of Palforzia in children 1 – 3 YOA. All primary and all key secondary efficacy endpoints were met. The clinical benefit was further supported at the exit DBPCFC, as the use of any rescue medications was lower for the AR101 group (22.9%) compared with the placebo group (88.9%).

Risks:
Palforzia showed more treatment-emergent adverse events compared to placebo. In descending order these were GI disorders (83.7% AR101, 64.6% placebo); respiratory, thoracic, and mediastinal disorders (78.6% AR101, 68.8% placebo); and general disorders and administration site conditions (62.2% AR101, 52.1% placebo). Vomiting was reported with a higher rate in the Palforzia group (overall 53.1% versus placebo 31.3%). However, these treatment-emergent adverse events were mostly mild or moderate, and discontinuation due to vomiting occurred only in 1 Palforzia subject. Higher graded treatment-emergent adverse events (severe, serious) were reported for few cases and considered acceptable. Discontinuation from the study was low. Systemic hypersensitivity reactions did not occur substantially more often than in the placebo group, and the baseline allergic disease has to be taken into account. In the safety population overall, 11 subjects (11.2%) in the AR101 group and 2 subjects (4.2%) in the placebo group had at least 1 episode of epinephrine use. Most episodes of epinephrine use were associated with mild or moderate adverse events. Serious adverse events were not related. There were no deaths in the study.

The benefit-risk balance for the proposed age group is positive, as Palforzia showed a robust efficacy in children aged 1 to <4 YOA and, although it showed more treatment-emergent adverse events compared to the placebo group, this was acceptable, especially as severe adverse events were rare. The adverse events were descriptively lower compared with older children and adolescents (see Information for healthcare professionals), which applies particularly to severe systemic reactions such as anaphylactic shock.

6 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.

7 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Palforzia 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.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.

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

PALFORZIA, oral powder

Composition

Active substances

Allergens of peanut (*Arachis hypogaea*)

Excipients

PALFORZIA 0.5 mg, 1 mg, 10 mg, 20 mg:
Microcrystalline cellulose, pre-gelatinised starch, colloidal anhydrous silica, magnesium stearate.
PALFORZIA 100 mg and 300 mg:
Microcrystalline cellulose, colloidal anhydrous silica, magnesium stearate.

Pharmaceutical form and active substance quantity per unit

Oral powder
PALFORZIA 0.5 mg
Each 0.5 mg capsule contains allergens of peanut (*Arachis hypogaea*) corresponding to 0.5 mg peanut protein.
PALFORZIA 1 mg
Each 1 mg capsule contains allergens of peanut (*Arachis hypogaea*) corresponding to 1 mg peanut protein.
PALFORZIA 10 mg
Each 10 mg capsule contains allergens of peanut (*Arachis hypogaea*) corresponding to 10 mg peanut protein.
PALFORZIA 20 mg
Each 20 mg capsule contains allergens of peanut (*Arachis hypogaea*) corresponding to 20 mg peanut protein.

PALFORZIA 100 mg
Each 100 mg capsule contains allergens of peanut (*Arachis hypogaea*) corresponding to 100 mg peanut protein.
PALFORZIA 300 mg

Each 300 mg sachet contains allergens of peanut (*Arachis hypogaea*) corresponding to 300 mg peanut protein.

Indications/Uses

PALFORZIA can be used to increase the peanut threshold dose tolerated without allergic reactions in patients aged 1 to 17 years with confirmed* diagnosis of clinically significant peanut allergy.

* The following cumulative conditions must be met for a confirmed diagnosis:

- History of allergic reactions to peanut
- Confirmation of specific sensitisation (IgE and/or skin prick testing)
- Reaction in an oral challenge at a threshold dose of ≤ 300 mg peanut protein or confirmation of strong evidence of sensitisation (see RAMSES study in section “Clinical efficacy”).

PALFORZIA should only be used as an adjuvant measure in addition to a peanut-avoidant diet.

PALFORZIA may be continued in patients 18 years of age and older.

During the course of treatment, PALFORZIA raises the peanut threshold dose that can trigger a reaction. Fewer allergic reactions due to accidental exposure to peanut were seen with PALFORZIA compared with placebo during clinical development. However, allergic reactions to PALFORZIA treatment (mostly to the preparation) were overall more frequent than to placebo (mostly to food). PALFORZIA is not intended for, and does not provide, immediate relief of allergic symptoms. A sustained effect after stopping the treatment has not been shown.

Dosage/Administration

Initial dose escalation and the first dose of each new up-dosing level are to be administered under the supervision of a health care professional qualified in the diagnosis and treatment of allergic diseases and in a health care setting prepared to manage potential severe allergic reactions.
Treatment with PALFORZIA is administered in 3 sequential phases: Initial dose escalation, up-dosing, and maintenance. Initial dose escalation is administered on a single day. Daily dosing of PALFORZIA is required during the up-dosing and maintenance phases.

Self-injectable adrenaline (epinephrine) must be prescribed to all patients.

Initiation of therapy (initial dose escalation phase)

Initial dose escalation consists of 4 dose levels for patients aged 1 to 3 years (0.5-3 mg; **Table 1**) and of 5 dose levels for patients aged 4 to 17 years (0.5-6 mg; **Table 1**) administered over a duration of approximately 4-5 hours on a single day.

Patients should not have active wheezing, a flare of atopic disease (e.g. atopic dermatitis) or suspected intercurrent illness prior to initiation of therapy.

Patients should receive sequential dose escalation of PALFORZIA beginning at 0.5 mg. Each dose should be separated by an observation period of at least 20 to 30 minutes. Patient should be observed after the last dose for at least 60 minutes, or until suitable for discharge in the opinion of the treating physician.
No dose level should be omitted.

Table 1: Dose and capsule presentation for initial dose escalation

Dose	Capsule presentation per dose	Patient age (years)
0.5 mg	1 × 0.5 mg capsule	1 to 17
1 mg	1 × 1 mg capsule	1 to 17
1.5 mg	1 × 0.5 mg capsule; 1 × 1 mg capsule	1 to 17
3 mg	3 × 1 mg capsules	1 to 17
6 mg	6 × 1 mg capsules	4 to 17

The same initial dose escalation pack is used for patients aged 1 to 3 years old and for patients 4 to 17 years old.

A dose can be considered tolerated if no more than transient mild symptoms are observed with no medical intervention/therapy required.

The administration of PALFORZIA must be discontinued if severe symptoms occur, especially if use of adrenaline is required, with any dose during initial dose escalation.
Initial dose escalation can be re-initiated in these patients at the discretion of the treating physician.

Patients who tolerate at least the 1 mg single dose (ages 1 to 3 years) or at least the 3 mg single dose (ages 4 to 17 years) of PALFORZIA during initial dose escalation must return to the health care setting, preferably the next day, for initiation of up-dosing.

Patients aged 1 to 3 years who cannot tolerate doses up to and including the 1 mg single dose of PALFORZIA may not be suitable for treatment with PALFORZIA.

Patients aged 4 to 17 years who cannot tolerate doses up to and including the 3 mg single dose of PALFORZIA may not be suitable for treatment with PALFORZIA.
If the patient is unable to begin up-dosing within 4 days of the initial dose escalation, initial dose escalation should be repeated in a health care setting.

Up-dosing phase

Initial dose escalation must be completed before starting up-dosing.

Patients should not have active wheezing, a flare of atopic disease (e.g. atopic dermatitis) or suspected intercurrent illness prior to the administration of each new up-dosing level.

During up-dosing, no more than one dose should be consumed per day. Patients should be instructed not to consume a dose at home on the same day as a dose is consumed in the clinic.

The dose configurations for up-dosing are shown in **Table 2.**

Table 2: Daily dosing configuration for up-dosing

Dose level	Total daily dose	Presentation of dose	Patient age (years)
0	1 mg	1 × 1 mg capsule	1 to 3
1	3 mg	3 × 1 mg capsules	1 to 17
2	6 mg	6 × 1 mg capsules	1 to 17
3	12 mg	2 × 1 mg capsules; 1 × 10 mg capsule	1 to 17
4	20 mg	1 × 20 mg capsule	1 to 17
5	40 mg	2 × 20 mg capsules	1 to 17
6	80 mg	4 × 20 mg capsules	1 to 17
7	120 mg	1 × 20 mg capsule; 1 × 100 mg capsule	1 to 17
8	160 mg	3 × 20 mg capsules; 1 × 100 mg capsule	1 to 17
9	200 mg	2 × 100 mg capsules	1 to 17
10	240 mg	2 × 20 mg capsules; 2 × 100 mg capsules	1 to 17
11	300 mg	1 × 300 mg sachet	1 to 17

For patients aged 1 to 3 years up-dosing is initiated at a 1 mg dose (Level 0).
For patients aged 4 to 17 years up-dosing is initiated at a 3 mg dose (Level 1).

Patients are required to return to the health care setting approximately every 2 weeks for each subsequent assessment for a new up-dosing level.

Patients aged 1 to 3 years must complete all levels (Levels 0-11) of up-dosing prior to initiation of maintenance dosing.
Patients aged 4 to 17 years must complete all levels (Levels 1-11) of up-dosing prior to initiation of maintenance dosing.
During up-dosing, subsequent doses of PALFORZIA are increased at 2-week intervals, if tolerated, as shown in Table 2. Patients must not progress through up-dosing more rapidly than the recommended 2-week intervals.

Patients aged 1 to 3 years

Up-dosing requires administration of dose levels 0-11 over a period of not less than 24 weeks, in sequential order: 1 mg, 3 mg, 6 mg, 12 mg, 20 mg, 40 mg, 80 mg, 120 mg, 160 mg, 200 mg, 240 mg, and 300 mg (corresponding to Levels 0-11, respectively).

Patients aged 4 to 17 years
Up-dosing requires administration of dose levels 1-11 over a period of not less than 22 weeks, in sequential order: 3 mg, 6 mg, 12 mg, 20 mg, 40 mg, 80 mg, 120 mg, 160 mg, 200 mg, 240 mg, and 300 mg (corresponding to Levels 1-11, respectively).

The first dose of each up-dosing level (patients aged 1 to 3 years: Levels 0-11 and patients aged 4 to 17 years: Levels 1-11) of PALFORZIA is prepared and administered during a scheduled clinic visit. Patients should be observed for at least 60 minutes after the dose, or until suitable for discharge in the opinion of the treating physician.

A dose level can be considered tolerated if no more than transient mild symptoms are observed with no medical intervention/therapy required.

If the patient tolerates the first dose of the increased dose level, the patient may continue that daily dose level at home for a minimum of 2 weeks.

If the patient does not tolerate the first dose of the increased dose level, the patient should continue the previously tolerated dose level for a further 2 weeks or a dose reduction may be considered. [See *Dose modification instructions*].

Maintenance therapy

All dose levels of up-dosing (patients aged 1 to 3 years: Levels 0-11 and patients aged 4 to 17 years: Levels 1-11) must be completed before starting with the ongoing therapeutic dose (maintenance dose) of 300 mg per day.

No more than one dose should be consumed per day. Patients should be instructed not to consume a dose at home on the same day as a dose is consumed in the clinic.

The maintenance dose is administered as a single 300 mg sachet.
The maintenance dose can be considered tolerated if no more than transient mild symptoms are observed with no or minimal medical intervention/therapy required.

If the patient does not tolerate the first maintenance dose, the level should be reduced (see *Dose adjustment due to adverse effects/interactions*).

Daily maintenance dosing is required to maintain the effect of PALFORZIA.
Efficacy data currently are available for up to 12 months of treatment with PALFORZIA for ages 1 to

3 years. No recommendation can be made about the duration of treatment beyond 12 months. Efficacy data currently are available for up to 24 months of treatment with PALFORZIA for ages 4 to 17 years.

Dose adjustment due to adverse effects/interactions

Dose modification instructions

Dose modifications are not appropriate during initial dose escalation.
Temporary dose modification of PALFORZIA may be required for patients who experience allergic reactions during up-dosing or maintenance.

Patients may be more likely to experience allergic reactions following PALFORZIA dosing in the presence of a medical event such as an intercurrent illness (e.g. viral infection), exacerbation of asthma, or in the presence of other co-factors (e.g. exercise, menstruation, stress, fatigue, sleep deprivation or intake of nonsteroidal anti-inflammatory drugs or alcohol). Temporarily withholding or decreasing PALFORZIA doses may be required in the presence of these medical events or co-factors.

Reactions that are severe, recurrent, bothersome, or last longer than 90 minutes should be clinically evaluated by the treating physician, and the best course of action should be determined. This can include maintaining the dose level for longer than 2 weeks, reducing, or withholding PALFORZIA doses. Prophylactic treatment of intercurrent symptoms may also be considered prior to dosing of PALFORZIA and may include H1- and/or H2-antihistamines or a proton pump inhibitor. Eosinophilic oesophagitis should be taken into consideration in patients with symptoms of oesophagitis (see section “Warnings and precautions”).

During up-dosing, a dose level can be maintained for longer than 2 weeks if a patient is unable to progress to the next level because of allergic reactions or for practical reasons for patient management.

After a dose reduction, up-dosing to the maintenance dose of PALFORZIA should be performed according to **Table 2**. If the patient tolerates the first dose of the increased dose level, the patient may continue that daily dose level at home for a minimum of 2 weeks.

Management of consecutive missed doses

Missed doses of PALFORZIA may pose a significant risk to patients due to potential loss of treatment effects. The guidelines in **Table 3** are to be used at the discretion of the treating physician.

Table 3: Management of consecutive missed doses

Consecutive missed doses	Action

1 to 2 days	Patients may resume PALFORZIA at the same dose level at home.
3 to 4 days	Patients may resume PALFORZIA at the same dose level under medical supervision in a health care setting based on medical judgment.
5 to 14 days	Patients may resume up-dosing with PALFORZIA under medical supervision in a health care setting at a dose of 50% or less of the last tolerated dose.
Greater than 14 days	Patient compliance should be evaluated and it should be considered to re-start up-dosing at 3 mg under supervision in a health care setting.

Following a dose reduction due to missed doses, up-dosing should be resumed as described in **Table 2**.

Patients should be advised that if a daily dose is missed, the next dose should be resumed at the usual time the following day.

If 3 or more consecutive doses are missed, patients should be advised to contact their healthcare provider. The next dose must then be taken under medical supervision in a health care setting based on medical judgment. Taking into consideration the cause of missed doses, it should be assessed whether treatment should be altered or continued.

Elderly

The safety and efficacy of PALFORZIA in adults aged over 55 years has not been established.

Paediatric population aged less than 1 year

The safety and efficacy of PALFORZIA in paediatric patients below the age of 1 year has not been established.

Method of administration

Capsules are not to be ingested and must be discarded when empty.

PALFORZIA oral powder must be taken orally after mixing with an age-appropriate soft food.

After emptying, the contents of each individual capsule or sachet should be mixed with soft food, such as yoghurt, apple sauce, pudding, or other palatable, age-appropriate food. The food must not be heated (no warmer than room temperature) and must be a food to which the patient is not additionally

allergic. The volume of the vehicle food should be such that the entire dose of PALFORZIA can be consumed in a few spoonfuls. (See section “Other information – Instructions for handling”).

Hands should be washed immediately after handling PALFORZIA capsules or sachets.

Timing of doses
During up-dosing and maintenance therapy, when dosing at home it is recommended that each dose of PALFORZIA should be taken at a consistent time each day as part of a meal, preferably in the evening. PALFORZIA should not be taken on an empty stomach or after fasting.

If the patient has been engaged in strenuous exercise prior to dosing, dosing should be delayed until signs of a hypermetabolic state (e.g. flushing, sweating, rapid breathing, and/or rapid heart rate) have passed.

Patients should avoid exercising, taking hot showers or baths prior to or within approximately 2 to 3 hours after dosing.

Patients should not take PALFORZIA within 2 hours of bedtime. Alcohol should not be taken for 2 hours before or 2 hours after a dose.

Contraindications

PALFORZIA is contraindicated in patients with the following:

- Severe or uncontrolled asthma
- A history of eosinophilic oesophagitis (EoE); other eosinophilic gastrointestinal disease; chronic, recurrent, or severe gastroesophageal reflux disease (GERD); symptoms of dysphagia; or recurrent gastrointestinal symptoms of undiagnosed aetiology
- A history of food protein-induced enterocolitis syndrome (FPIES)
- Failure to thrive (applicable for patients aged 1–3 years)
- A history of severe mast cell disorder
- Severe or life-threatening anaphylaxis within 60 days before initiating treatment with PALFORZIA
- Hypersensitivity to any of the excipients as listed in the composition
- Uncontrolled arterial hypertension or cardiovascular diseases

Warnings and precautions

PALFORZIA is not intended for, and does not provide, immediate relief of allergic symptoms. Therefore, this medicinal product is not to be used for emergency treatment of allergic reactions, including anaphylaxis.

Patients should not have active wheezing, uncontrolled severe atopic disease (e.g. atopic dermatitis or eczema), a flare of atopic disease or suspected intercurrent illness prior to initiation of therapy.

Adrenaline

Self-injectable adrenaline must be prescribed to patients receiving PALFORZIA. Patients and/or caregivers must be instructed to recognise the signs and symptoms of an allergic reaction and in the proper use of self-injectable adrenaline. Patients should be instructed to seek immediate medical care upon its use and to stop treatment with PALFORZIA until they have been evaluated by a physician.

PALFORZIA may not be suitable for patients who are taking medications that can inhibit the effect of adrenaline:

- *Beta-adrenergic blockers:* Patients taking beta-adrenergic blockers may be unresponsive to the usual doses of adrenaline used to treat serious systemic reactions, including anaphylaxis. Specifically, beta-adrenergic blockers antagonise the cardio-stimulating and bronchodilating effects of adrenaline.
- *Alpha-adrenergic blockers, ergot alkaloids:* Patients taking alpha-adrenergic blockers may be unresponsive to the doses of adrenaline used to treat serious systemic reactions, including anaphylaxis. Specifically, alpha-adrenergic blockers antagonise the vasoconstricting and hypertensive effects of adrenaline. Similarly, ergot alkaloids may reverse the pressor effects of adrenaline.

PALFORZIA should be used with caution when taken in conjunction with medicinal products that can potentiate the effect of adrenaline. These medicinal products include the following:

- *Tricyclic antidepressants, monoamine oxidase inhibitors, and certain antihistamines:* The adverse effects of adrenaline may be potentiated in patients taking tricyclic antidepressants, levothyroxine sodium, monoamine oxidase inhibitors, and the antihistamines chlorpheniramine and diphenhydramine.
- *Cardiac glycosides, diuretics:* Patients who receive adrenaline while taking cardiac glycosides or diuretics should be observed carefully for the development of cardiac arrhythmias.

Systemic allergic reactions including anaphylaxis

When treated with PALFORZIA, peanut-allergic patients are exposed to peanut allergens that cause allergic symptoms. Therefore, allergic reactions to PALFORZIA are expected in these patients. These reactions mostly occur during the first 2 hours after ingestion of the dose and are usually mild or moderate; however, more severe reactions may occur up to 4 hours after taking PALFORZIA. Dose modifications should be considered for patients who experience moderate or severe adverse allergic reactions to PALFORZIA (see *Dose adjustment due to adverse effects/interactions – Dose*

modification instructions). Patients aged 12 years or older and/or with high sensitivity to peanut may be at higher risk of experiencing allergic symptoms during treatment.

PALFORZIA can cause systemic allergic reactions including anaphylaxis, which may be life-threatening. Treatment with PALFORZIA must not be initiated in a patient who has had severe or life-threatening anaphylaxis within the previous 60 days.

Severe adverse reactions such as difficulty swallowing, difficulty breathing, changes in voice or feeling of fullness in the throat, dizziness or fainting, severe stomach cramps or pain, vomiting, diarrhoea, or severe flushing or itching of the skin require immediate treatment, including use of adrenaline, and subsequent medical evaluation.

Patients and/or caregivers must be educated to recognise the signs and symptoms of allergic reactions. Patients and/or caregivers should be instructed to contact a health care professional before administering the next dose of PALFORZIA if symptoms of an escalating or persistent allergic reaction occur. Patients should be instructed to promptly treat the reaction and seek immediate medical attention if they develop symptoms of a severe allergic reaction. In case a severe adverse reaction develops, this must be treated promptly (e.g., with self-administration of intramuscular adrenaline) and immediate medical attention should be sought directly afterwards. In the emergency department, treatment should follow the anaphylaxis guidelines.

Patients may be more likely to experience allergy symptoms after dosing of PALFORZIA in the presence of a medical event such as an intercurrent illness (e.g., viral infection), exacerbation of asthma, or in the presence of other co-factors (e.g., exercise, menstruation, stress, fatigue, sleep deprivation, fasting, intake of nonsteroidal anti-inflammatory drugs or alcohol). Patients and/or caregivers should be counselled proactively about the potential for the increased risk of anaphylaxis in the presence of these co-factors, which may be modifiable or non-modifiable. On an individual basis and when needed, the time of dosing should be adjusted to avoid modifiable cofactors. If it is not possible to avoid any of the modifiable cofactors or if affected by non-modifiable co-factors, withholding or decreasing the PALFORZIA dose temporarily should be considered.

Desensitisation response

Strict daily, long-term dosing in conjunction with a peanut-avoidant diet is required to achieve desensitisation and maintain the treatment effect of PALFORZIA. Treatment interruptions, including non-daily dosing, may potentially lead to an increased risk of allergic reactions or even anaphylaxis. As with any immunotherapy treatment, clinically meaningful desensitisation may not occur in all patients.

Increase of the peanut threshold dose

PALFORZIA cannot achieve an increase of the peanut threshold dose in all patients. Daily use of the 300 mg maintenance dose is required to maintain the increase once achieved.

Asthma

In patients with asthma, treatment with PALFORZIA may only be initiated when the asthma status is controlled. PALFORZIA has not been studied in patients on long-term systemic corticosteroid therapy. Immunotherapy with PALFORZIA should be temporarily withheld if the patient is experiencing an acute asthma exacerbation. Following resolution of the exacerbation, resumption of PALFORZIA should be undertaken cautiously. Patients who have recurrent asthma exacerbations should be re-evaluated and discontinuation of PALFORZIA therapy should be considered.

Concomitant illnesses

PALFORZIA may not be suitable for patients with certain medical conditions that may reduce the ability to survive a severe allergic reaction or increase the risk of adverse reactions after adrenaline administration. Examples of these medical conditions include, but are not limited to, markedly compromised lung function (chronic or acute, e.g. severe cystic fibrosis), unstable angina, recent myocardial infarction, significant arrhythmias, cyanotic congenital heart disease, uncontrolled hypertension, and inherited metabolic disorders.

Gastrointestinal adverse reactions including eosinophilic oesophagitis (EoE)

In patients who develop chronic or recurrent gastrointestinal symptoms, dose modification may be considered (see Dosage/Administration). EoE has been reported in association with PALFORZIA (see Undesirable effects). For chronic/recurrent gastrointestinal symptoms, especially upper gastrointestinal symptoms (nausea, vomiting, dysphagia), the potential for a diagnosis of IgE or non-IgE-mediated gastrointestinal food allergies such as EoE should be considered in all age groups or in the event of food refusal and failure to thrive, which occurs particularly in toddlers and younger patients (ages 1 to 3 years). FPIES, a food-associated gastrointestinal disorder that is not mediated by IgE, which can occur in toddlers, should additionally be considered in toddlers who experience significant food-associated gastrointestinal symptoms. In patients who experience severe or persistent gastrointestinal symptoms, including dysphagia, gastroesophageal reflux, chest pain, or abdominal pain, treatment must be discontinued and a diagnosis of EoE should be considered.

Concomitant allergen immunotherapy

PALFORZIA has not been studied in patients receiving concomitant allergen immunotherapy. Caution should be exercised when administering this medicinal product in conjunction with other allergen immunotherapies as the risk for severe allergic reactions may be enhanced.

Interactions

No formal interaction studies have been performed with PALFORZIA.

Pregnancy, lactation

Pregnancy

Treatment with PALFORZIA should not be initiated during pregnancy. There is no clinical experience from PALFORZIA in pregnant women.

Treatment with PALFORZIA is associated with a risk of allergic reactions including anaphylaxis, especially during the first 12 months of therapy. Anaphylaxis can cause a dangerous decrease in blood pressure, which could result in compromised placental perfusion and significant risk to a foetus during pregnancy. In addition, the effect of PALFORZIA on the immune system of the mother and foetus during pregnancy is unknown.

In patients who become pregnant under PALFORZIA, the benefits of continuing treatment with a continued increased threshold dose should be weighed against the risks of anaphylactic reactions while remaining on PALFORZIA.

Lactation

Peanut allergens have been found in human milk after consumption of peanuts. There are no data available to assess the effects of PALFORZIA on the breastfed infant, or the effects on milk production and excretion of the medicinal product into milk in the nursing woman. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for PALFORZIA and any other potential adverse effects on the breastfed child from PALFORZIA or from the underlying maternal condition.

Fertility

There are no specific clinical or nonclinical data on the effects of PALFORZIA on fertility.

Effects on ability to drive and use machines

The effect on the ability to drive or use machines has not been specifically studied. PALFORZIA has a minor influence on the ability to drive and use machines. Caution should be exercised for 2 hours after dosing in case any symptoms of an allergic reaction occur that could impact the ability to drive or use machines.

Undesirable effects

Safety profile for ages 4 to 17 years
The safety profile of PALFORZIA in patients with peanut allergy aged 4-17 years is derived from 5 clinical studies involving 944 unique subjects who received at least 1 dose of PALFORZIA.

The most common adverse events under PALFORZIA were abdominal pain (49.5%), throat irritation (41.4%), pruritus (33.9%), nausea (33.3%), urticaria (28.7%), vomiting (28.5%), oral pruritus (26.0%), upper abdominal pain (22.9%), abdominal discomfort (22.8%), cough (22.0%), sneezing (18.5%), oral paraesthesia (17.4%), anaphylactic reaction (14%), throat tightness (14.0%), rhinorrhoea (13.3%), rash (11.7%), nasal congestion (11.2%), lip pruritus (10.5%) and diarrhoea.
Most adverse events were mild or moderate in severity.
The incidence of adverse events was higher during up-dosing (85.9%) than during initial dose escalation (45.7%) and maintenance (57.9%).
During the period of 0 to 13 weeks until the period of >52 weeks (during maintenance therapy with 300 mg/day), the incidence of adverse reactions usually decreased which may, in part, be due to study discontinuation in a small number of patients with severe adverse reactions and the resulting selection of the study population.
In subjects who discontinued PALFORZIA (11.8%), discontinuation was due to one (1) or more adverse reactions. The majority of patients discontinued during up-dosing (8.8%). During initial dose escalation, 2.1% discontinued therapy, and 1.4% during the 300 mg/day dosing.
The most common adverse reactions leading to discontinuation of treatment were abdominal pain (2.6%), vomiting (2.3%), nausea (1.5%), and anaphylactic reaction (1.1%), including anaphylaxis.
The median time from administration of PALFORZIA in a clinical setting to onset of the first symptom ranged from 4 to 8 minutes. The median time from onset of the first symptom to resolution of the last symptom ranged from 15 to 30 minutes.

Safety profile for ages 1 to 3 years
The safety profile of PALFORZIA in patients with peanut allergy aged 1-3 years is derived from the ARC005 clinical study involving 98 unique subjects who received at least 1 dose of PALFORZIA.
Vomiting was the most common adverse event (Palforzia sum across all dosing phases 53.1% versus placebo 31.3%). However, discontinuation of treatment due to vomiting occurred in only one subject with Palforzia.
The most common adverse reactions (of any severity) are urticaria (30.6%), cough (20.4%), erythema (19.4%), sneezing (16.3%), abdominal pain (15.3%), vomiting (15.3%) and rhinorrhoea (14.3%).
The incidence of adverse reactions was higher during up-dosing (68.4%) than during initial dose escalation (15.3%) and maintenance (34.5%).
6.1% of subjects discontinued the study product due to one or more adverse reactions. In the majority of patients, treatment discontinuation took place during up-dosing (8.7%). The treatment was discontinued in 2.1% during initial dose escalation and in 1.2% during daily 300 mg dosing.
Gastrointestinal disorders were the most common reasons leading to discontinuation of treatment in 5 (5.1%) subjects: 1 (1.0%) subject each with abdominal discomfort, abdominal pain, eructation, regurgitation and vomiting. Respiratory, thoracic and mediastinal disorders were the reasons leading

to discontinuation of treatment in 4 (4.1%) subjects: 2 (2.0%) subjects with cough and 1 (1.0%) subject each with asthma and throat clearing.
Overall, the adverse events profile in subjects aged 1-3 years was similar to the profile observed in subjects aged 4-17 years. However, the intensity of the adverse events in younger study subjects was less severe (51.0% of adverse events in subjects aged 1-3 years were mild, compared to 39.4% of adverse events rated as mild in subjects aged 4-17 years). Furthermore, fewer adverse events were attributed to the treatment with Palforzia (75.5% of adverse events in subjects aged 1-3 years were associated with the treatment, compared to 90.4% in subjects aged 4-17 years). Anaphylactic reactions (systemic allergic reaction) also had a milder course and were less frequently associated with Palforzia treatment. In the ARC005 study in toddlers, no severe anaphylactic reactions occurred (anaphylaxis, severe systemic allergic reaction).

Tabulated list of adverse reactions

Table 4a and Table 4b are based on data from the PALFORZIA clinical trial program. Listed events are divided into groups according to the MedDRA system organ class and frequency: Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), and very rare (<1/10,000).

Table 4a: Adverse reactions for ages 4 to 17 years

System Organ Class	Frequency	Adverse reaction
Infections and infestations	*Common*	Conjunctivitis
Immune system disorders	*Very common*	Anaphylactic reaction (mild or moderate) (14.7%) Systemic adrenaline use for any reason (14.9%)
	Common	Anaphylactic reaction (severe)
Nervous system disorders	*Common*	Headache
	Uncommon	Dysgeusia Drooling
Eye disorders	*Common*	Eye pruritus Ocular hyperaemia Eye swelling
Ear and labyrinth disorders	*Common*	Ear pruritus
	Uncommon	Ear pain
Vascular disorders	*Common*	Flushing
Respiratory, thoracic, and mediastinal disorders	*Very common*	Throat irritation (40.7%) Cough (22.0%) Sneezing (18.5%) Throat tightness (12.7%)

	Common	Wheezing Dyspnoea Pharyngeal paraesthesia Chronic throat clearing Dysphonia
	Uncommon	Pharyngeal oedema Choking
Gastrointestinal disorders	*Very common*	Abdominal pain (49.4%) Nausea (33.2%) Vomiting (28.5%) Oral pruritus (26.0%) Abdominal discomfort (22.8%) Abdominal pain upper (22.8%) Paraesthesia oral (17.4%) Lip pruritus (10.5%)
	Common	Lip swelling Diarrhoea Dysphagia Gastro-oesophageal reflux disease
	Uncommon	Eosinophilic oesophagitis Swollen tongue Enlarged uvula
Skin and subcutaneous tissue disorders	*Very common*	Pruritus (33.7%) Urticaria (28.5%) Rash (11.7%)
	Common	Erythema Swelling of face Angioedema
General disorders and administration site conditions	*Common*	Chest discomfort Chest pain Fatigue Sensation of foreign body
	Uncommon	Face oedema

Table 4b: Tabulated list of adverse reactions for ages 1-3 years

MedDRA system organ class	*Frequency*	Adverse reaction
Respiratory, thoracic and mediastinal disorders	*Very common*	Cough (53.1%) Sneezing (23.5%) Rhinorrhoea (42.9%) Nasal congestion (14.3%) Wheezing (14.3%) Asthma (11.2%)
	Common	Stridor Throat clearing Dysphonia Throat discomfort Allergic rhinitis
Gastrointestinal disorders	*Very common*	Vomiting (53.1%) Diarrhoea (34.7%) Abdominal pain (23.5%) Upper abdominal pain (14.3%) Constipation (11.2%) Oral pruritus (10.2%)
	Common	Oral discomfort Flatulence Nausea Decreased appetite Swollen lips
Skin and subcutaneous tissue disorders	*Very common*	Urticaria (52.0%) Erythema (34.7%) Pruritus (27.6%) Eczema (24.5%) Rash (23.5%) Perioral dermatitis (17.3%)
	Common	Dermatitis diaper Skin irritation Facial swelling
General disorders and administration site conditions	*Very common*	Pyrexia (51.0%)
Nervous system disorders	*Very common*	Headache (10.2%)
Psychiatric disorders	*Common*	Irritability
Eye disorders	*Common*	Eye pruritus Eye swelling Ocular hyperaemia

Description of specific adverse reactions

Anaphylaxis (severe systemic allergic reactions)

For the purpose of reporting the clinical study results, the term systemic allergic reaction is used to describe anaphylactic reaction events of any severity. The term anaphylaxis is used to distinguish anaphylactic reaction events that were severe.

For ages 4 to 17 years

Systemic allergic reactions of any severity were reported in 15.8% of subjects, including 0.6% during initial dose escalation, 8.7% during up-dosing, and 10.5% during maintenance. The majority of subjects who had systemic allergic reactions had reactions of mild or moderate severity. Severe systemic allergic reaction (anaphylaxis) was reported in 10 subjects (1.1% overall), including 4 subjects (0.4%) during up-dosing and 6 (0.8%) during maintenance at 300 mg/day. 1.6% discontinued the treatment due to systemic allergic reaction, including 0.3% with anaphylaxis. Of the total population, 11.0% of subjects reported a single episode of systemic allergic reaction and 4.8% reported two or more systemic allergic reactions. Existing data suggest an increased risk of systemic allergic reaction for adolescents (22.5%) than for children (≤11 years; 12.5%).

In the clinical studies, the most commonly reported symptoms of systemic allergic reactions included skin disorders (urticaria, flushing, pruritus, face swelling, rash), respiratory disorders (dyspnoea, wheezing, cough, throat tightness, rhinorrhoea, throat irritation), and gastrointestinal disorders (abdominal pain, nausea, vomiting). The onset of most (87.0%) episodes of systemic allergic reaction was within 2 hours of the administration of the medication.

In the PALFORZIA safety population, 15.3% of subjects reported at least one episode of adrenaline use for any reason. 1.8% of subjects reported at least one episode during initial dose escalation, 9.1% during up-dosing, and 9.2% during maintenance. Of subjects who reported adrenaline usage, 91.8% subjects required a single dose and 92.7% of adrenaline usage was for events of mild to moderate severity.

For ages 1 to 3 years

In a controlled clinical trial, a similar frequency of systemic allergic reactions of any severity occurred in patients treated with PALFORZIA and placebo (9 events in 98 patients versus 4 events in 48 patients, respectively). There were no allergic reactions associated with accidental peanut exposure. Reactions were mostly non-life threatening and the majority were mild to moderate. Severe systemic reactions occurred in none of the patients.

Relative to all allergic reactions, 80 PALFORZIA-treated subjects (81.6%) and 36 placebo-treated subjects (75.0%) experienced events considered to be allergic in nature (hypersensitivity events).

Administration of adrenaline to patients aged 1 to 3 years
Adrenaline consumption was summarised by episodes, defined as the administration of 1 or more epinephrine doses within 2 hours. In the overall safety population, 11 subjects (11.2%) in the PALFORZIA group and 2 subjects (4.2%) in the placebo group had at least one episode of adrenaline use. None of the subjects had more than 3 episodes of adrenaline use. In the PALFORZIA group, 11 subjects (11.2%) had a total of 13 episodes of adrenaline use; 12 episodes required 1 adrenaline dose and 1 episode required 2 doses; 3 events (in 2 subjects, 2.1%) were considered to be related to the study product. In the placebo group, 2 subjects had 4 episodes of adrenaline use (1 subject had 1, 1 subject had 3 episodes); 3 episodes required 1 adrenaline dose and 1 episode required 2 doses. Most episodes of adrenaline use were associated with mild or moderate adverse events; 2 events in the PALFORZIA group and 1 event in the placebo group were serious.

Eosinophilic oesophagitis (EoE)
For ages 4 to 17 years
In clinical studies, 12 out of 1,217 subjects were diagnosed with biopsy-confirmed eosinophilic oesophagitis while receiving PALFORZIA, compared with 0 of 443 subjects receiving placebo. After discontinuation of PALFORZIA, symptomatic improvement was reported in 12 of 12 subjects. In 8 subjects with available follow-up biopsy results, eosinophilic oesophagitis was resolved in 6 subjects and improved in 2 subjects. All events were diagnosed in subjects aged 4 to 17 years.

For ages 1 to 3 years
There were no patients diagnosed with eosinophilic oesophagitis. No subject with a chronic or recurrent GI event was diagnosed with EoE. No subjects were seen by a GI specialist or underwent a biopsy.

Safety in patients aged 18 years and over
The safety profile of PALFORZIA in patients who turned 18 years old whilst participating in the phase 3 clinical trial program was similar to the safety profile of the overall 4- to 17-year-old population.

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

Administration of PALFORZIA at greater than recommended doses in peanut-allergic patients increases the risk of side effects, including the risk of systemic allergic reactions or severe single-organ allergic reactions. In the case of severe reactions such as angioedema, difficulty

swallowing, difficulty breathing, changes in voice or a feeling of fullness in the throat, immediate treatment with the relevant symptomatic medicine(s) and follow-up care with a medical evaluation is required.

Properties/Effects

ATC code

V01AA08.

Mechanism of action

PALFORZIA can increase the peanut threshold dose tolerated without an allergic reaction in patients with peanut allergy. The precise mechanism of the treatment is not fully understood.

Pharmacodynamics

An increase in peanut-specific IgG G4 was observed during treatment with PALFORZIA. This laboratory parameter change has not yet been shown to be of clinical relevance.
Based on current evidence, it must be assumed that the therapy-induced increase of the peanut threshold dose will be lost within a few days after interruption or discontinuation of treatment.
Daily maintenance dosing is required until evidence of disease-modifying effects has been shown.

Clinical efficacy

In all PALFORZIA clinical studies, efficacy was measured using a DBPCFC. This food challenge is a model for real-world accidental exposure to food allergens and was performed according to the Practical Allergy (PRACTALL) guidelines for safety, assessment, and scoring with modification to include a 600 mg protein dose (between the 300 mg and 1,000 mg challenge doses).

Phase 2
ARC001, the first-in-human study, was a multicentre, randomised, double-blind, placebo-controlled phase 2 study conducted for up to 9 months to demonstrate the efficacy of PALFORZIA compared with placebo in peanut-allergic subjects aged 4 to 26 years. At entry, patients had dose-limiting symptoms after consuming ≤ 100 mg of peanut protein in a DBPCFC. At the exit DBPCFC, 23 of 29 (79%) PALFORZIA-treated patients versus 5 of 26 (19%) placebo-treated patients tolerated the single highest dose of at least 300 mg peanut protein with no more than mild allergy symptoms after a median 22 weeks of treatment, including 2 weeks at 300 mg/day.

Phase 3
The efficacy of PALFORZIA was demonstrated in 3 randomised, double-blind, placebo-controlled, multicentre, phase 3 pivotal studies, PALISADE (4 to 17 years), ARTEMIS (4 to 17 years) and

POSEIDON (1 to 3 years). These studies recruited patients with a documented history of peanut allergy, and dose-limiting symptoms after consuming increasing doses of peanut protein at a screening DBPCFC. Subjects with a severe or life-threatening anaphylaxis event within 60 days and those with severe or uncontrolled asthma were excluded from the studies. Following blinded treatment over approximately 6 months (PALISADE and POSEIDON) and 3 months (ARTEMIS) of up-dosing and 3 or 6 months of maintenance dosing with PALFORZIA, or placebo, patients completed an exit DBPCFC to assess a therapy-induced increase in the threshold dose tolerated without the occurrence of severe allergic reactions to peanut. For PALISADE and ARTEMIS, after an initial dose escalation ranging from 0.5 mg to 6 mg on day 1 and confirmation of tolerability of the 3 mg dose on day 2, subjects underwent up-dosing for 20 to 40 weeks starting at 3 mg until the 300 mg dose was reached. For POSEIDON, after an initial dose escalation ranging from 0.5 mg to 3 mg on day 1 and confirmation of tolerability of the 1 mg dose on day 2, subjects underwent up-dosing for 20 to 40 weeks starting at 1 mg until the 300 mg dose was reached. For all three studies, the up-dosing period varied for each subject depending on doses tolerated.

For the primary efficacy analysis population, PALISADE (ARC004) recruited 496 subjects aged 4 to 17 years who had received at least one dose of study treatment. In this study, eligible subjects had dose-limiting symptoms after consuming ≤ 100 mg of peanut protein at the screening DBPCFC. Demographic and baseline characteristics were well matched between the treatment groups. Of the subjects treated with PALFORZIA in the primary analysis population, 72% had a medical history of systemic allergic reactions, 66% reported multiple food allergies, 63% had a medical history of atopic dermatitis, and 53% had a present or previous diagnosis of asthma. The patient population for the primary analysis was 78% white and 57% were male. The median age of the patients was 9 years. After approximately 1 year of blinded study treatment (~ 6 months of up-dosing and ~ 6 months of maintenance therapy), subjects completed an exit DBPCFC to assess the increase of the threshold dose to peanut.

ARTEMIS (ARC010) recruited subjects aged 4 to 17 years in Europe. The primary efficacy analysis population consisted of 175 subjects aged 4 to 17 years who had received at least one dose of study treatment. In this study, eligible subjects had dose-limiting symptoms after consuming ≤ 300 mg of peanut protein at the screening DBPCFC. Demographic and baseline characteristics were generally well matched between the treatment groups. Of the subjects in the primary analysis group, subjects had a medical history of food allergies other than peanut (61.4% AR101, 48.8% placebo), atopic dermatitis (59.1%, 51.2%), allergic rhinitis (47.7%, 37.2%), and asthma (42.4%, 32.6%). The median age of the subjects was 8.0 years. More than half of the subjects were male (54.3%) and most subjects were white (81.7%). After approximately 9 months of blinded study treatment (~ 6 months of up-dosing and ~ 3 months of maintenance therapy), subjects completed an exit DBPCFC to assess the increase of the threshold dose to peanut.

RAMSES (Real-World AR101 Market-Supporting Experience Study)
The RAMSES study was a double-blind, placebo-controlled, 2:1 parallel-group comparison of a treatment with up-dosing until the dose of 300 mg/day was reached. The whole study lasted a maximum of 48 weeks. The patients were in total 506 children and adolescents with a history of peanut allergy and distinct sensitization (serologically sensitized to peanut ≥ 14 kUA/L, skin prick test with wheals ≥ 8 mm). The primary goal was to investigate safety. More treatment dropouts and allergic events occurred with PALFORZIA (AR 101) compared to placebo. However, on treatment with PALFORZIA there were fewer adverse events involving accidental allergen exposure with no connection with the study medication.

POSEIDON (ARC005) recruited patients aged 1 to 3 years in Europe and North America, with patients with moderate and severe asthma and with difficult to control mild asthma (based on NHLBI 2007 criteria), patients with a history of food protein-induced enterocolitis syndrome (FPIES), patients with biopsy-confirmed diagnosis of eosinophilic esophagitis (EoE) and children with a failure to thrive being excluded (see Contraindications and Warnings and precautions). The primary efficacy analysis population consisted of 98 subjects aged 1-3 years who had received at least 1 dose of study treatment. In this study, eligible patients experienced dose-limiting symptoms after consuming > 3 mg and ≤ 300 mg of peanut protein at the screening DBPCFC. Of the patients in the primary analysis group, there was a history of food allergies other than peanut (72.4% PALFORZIA, 68.8% placebo), allergic rhinitis (13.3%, 20.8%), atopic dermatitis (63.3%, 60.4%), asthma (8.2%, 8.3%). The median age of subjects was 2.0 years. More than half of the subjects were male (58.3%) and most subjects were white (67.1%). After approximately 12 months of blinded study treatment (~ 6 months of up-dosing and ~ 6 months of maintenance therapy), patients completed an exit DBPCFC to assess the increase of the threshold dose to peanuts.

Efficacy data
The primary efficacy endpoint in all 3 studies PALISADE (ARC004), ARTEMIS (ARC010) and POSEIDON (ARC005) was the proportion of subjects aged 1 to 17 years who tolerated a single highest dose of at least 1,000 mg peanut protein with no more than mild allergic symptoms at the exit DBPCFC. Key secondary endpoints in this age group included determination of the desensitisation response rates after single doses of 300 mg and 600 mg peanut protein and the maximum severity of symptoms at the exit DBPCFC.

<u>Increase of the tolerated peanut threshold dose</u>
Overall, treatment with PALFORZIA in PALISADE, ARTEMIS, and POSEIDON resulted in statistically significant differences compared to placebo regarding the proportion of subjects who tolerated a single dose of 300, 600, or 1,000 mg peanut protein with no more than mild allergy symptoms at the exit DBPCFC. The summary of the proportion for primary and secondary efficacy endpoints for the intention to treat (ITT) populations in PALISADE, ARTEMIS, and POSEIDON is provided in **Table 6**.

Table 6: POSEIDON, PALISADE and ARTEMIS: Summary of response rates for primary and secondary efficacy endpoints (ITT population, 1-17 years)

Endpoint	POSEIDON (ARC005)		PALISADE (ARC004)		ARTEMIS (ARC010)	
	PALFORZIA N = 98	Placebo N = 48	PALFORZIA N = 372	Placebo N = 124	PALFORZIA N = 132	Placebo N = 43
Primary efficacy endpoint						
Proportion of subjects who tolerated 1 000 mg peanut protein (95% CI) [1]	68.4% (58.2, 77.4)	4.2% (0.5, 14.3)	50.3% (45.2, 55.3)	2.4% (0.8, 6.9)	58.3% (49.4, 66.8)	2.3% (0.1, 12.3)
Treatment difference (PALFORZIA-placebo) [95% CI] [2]	64.2% (47.0, 81.4)		47.8% (38.0, 57.7)		56.0% (44.1, 65.2)	
P-value [2]	< 0.0001		< 0.0001		< 0.0001	
Key secondary efficacy endpoints						
Proportion of subjects who tolerated 600 mg peanut protein (95% CI) [1]	73.5% (63.6, 81.9)	6.3% (1.3, 17.2	67.2% (62.3, 71.8)	4.0% (1.7, 9.1)	68.2% (59.5, 76.0)	9.3% (2.6, 22.1)
Treatment difference (PALFORZIA-placebo) [95% CI] [2]	67.2% (50.0, 84.5)		63.2% (53.0, 73.3)		58.9% (44.2, 69.3)	
P-value [2]	< 0.0001		< 0.0001		< 0.0001	
Response rate: proportion of subjects who tolerated 300 mg peanut protein (95% CI) [1]	79.6% (70.3, 87.1)	22.9% (12.0, 37.3)	76.6% (72.1, 80.6)	8.1% (4.4, 14.2)	73.5% (65.1, 80.8)	16.3% (6.8, 30.7)
Treatment difference (PALFORZIA-placebo) [95% CI] [2]	56.7% (39.8, 73.5)		68.5% (58.6, 78.5)		57.2% (41.2, 69.3)	
P-value [2]	< 0.0001		< 0.0001		< 0.0001	

Subjects without an exit DBPCFC were counted as non-responders.

[1] PALISADE (ARC004): Based on Wilson (score) confidence limits, POSEIDON (ARC005) and ARTEMIS (ARC010): Based on exact Clopper-Pearson intervals.

[2] POSEIDON (ARC005) and PALISADE (ARC004): Based on the Farrington-Manning confidence limits. ARTEMIS: Based on exact unconditional confidence limits using the score statistic; p-values were based on Fisher's exact test.

Maximum severity of symptoms

These data (summarised in **Table 7**) show that at any dose of peanut protein tested, PALFORZIA-treated subjects developed fewer severe symptoms compared with placebo-treated subjects.

Table 7: POSEIDON, PALISADE, and ARTEMIS: Maximum severity of symptoms at exit DBPCFC (ITT population, 1-17 years)

Endpoint	POSEIDON (ARC005)		PALISADE (ARC004)		ARTEMIS (ARC010)	
	PALFORZIA N = 98	Placebo N = 48	PALFORZIA N = 372	Placebo N = 124	PALFORZIA N = 132	Placebo N = 43
Maximum severity of symptoms at any challenge dose [1]						
None	50 (51.0%)	2 (4.2%)	140 (37.6%)	3 (2.4%)	47 (35.6%)	0 (0.0%)
Mild	29 (29.6%)	23 (47.9%)	119 (32.0%)	35 (28.2%)	55 (41.7%)	16 (37.2%)
Moderate	17 (17.3%)	21 (43.8%)	94 (25.3%)	73 (58.9%)	24 (18.2%)	20 (46.5%)
Severe	2 (2.0%)	2 (4.2%)	19 (5.1%)	13 (10.5%)	6 (4.5%)	7 (16.3%)
P-value [2]	< 0.0001		< 0.0001		< 0.0001	

[1] Subjects without an exit DBPCFC were assigned the maximum severity of symptoms during the screening DBPCFC (no change from screening).

[2] Treatment difference was tested using the Cochran-Mantel-Haenszel statistic (with equally spaced scores) stratified by geographic region [Europe, North America (PALISADE, POSEIDON) and country (ARTEMIS)].

Response rates in subjects who turned 18 years during therapy

The response rate of PALFORZIA-treated subjects who turned 18 years whilst participating in a study and tolerated a single highest dose of at least 1,000 mg peanut protein with no more than mild allergic symptoms at the exit DBPCFC (15/27, 55.6%) was consistent with the overall primary efficacy of the subjects aged 1 to 17 years.

Safety and efficacy in paediatric patients and in patients above 18 years

The safety and efficacy of PALFORZIA in children below 1 year and initiated in patients above 18 years has not yet been proven.

Long-term data

Long-term efficacy has been demonstrated in 103 subjects and 26 subjects who completed 12 and 18 months, respectively, of PALFORZIA maintenance treatment with the ongoing therapeutic dose (300 mg daily) through participation in both PALISADE and the open-label, follow-on ARC004 study. A comparison of response rates after longer-term maintenance therapy with PALFORZIA can be made by comparing the response rates for the 12-month and 18-month maintenance cohorts in ARC004 with those who completed PALISADE (Table 9).

Table 9: Percentage of challenge doses tolerated following continued maintenance during exit DBPCFC (PALISADE and ARC004 completer populations, 417 years)

	PALISADE	ARC004	
	6-month maintenance (N = 296)	**12-month maintenance (N = 103)**	**18-month maintenance (N = 26)**
Subjects who tolerated a single dose of peanut protein (response rate) [95% CI]			
2,000 mg	n/a [1]	50 (48.5%) [38.6%, 58.6%]	21 (80.8%) [60.6%, 93.4%]
1,000 mg	187 (63.2%) [57.5%, 68.5%]	83 (80.6%) [71.6%, 87.7%]	25 (96.2%) [80.4%, 99.9%]
600 mg	250 (84.5%) [79.9%, 88.1%]	92 (89.3%) [81.7%, 94.5%]	25 (96.2%) [80.4%, 99.9%]
300 mg	285 (96.3%) [93.5%, 97.9%]	101 (98.1%) [93.2%, 99.8%]	26 (100%) [86.8%, 100.0%]

[1] 1,000 mg was the highest challenge dose of peanut protein in PALISADE.

Pharmacokinetics

No clinical studies investigating the pharmacokinetic profile and metabolism of PALFORZIA have been conducted. PALFORZIA contains naturally occurring allergenic peanut proteins. After oral administration, the proteins are hydrolysed to amino acids and small polypeptides in the lumen of the gastrointestinal tract.

Absorption

No data.

Distribution

No data.

Metabolism

No data.

Elimination

No data.

Preclinical data

No conventional preclinical studies on safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenicity and reproductive toxicity have been performed.

Other information

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

Shelf life

Do not use this medicine after the expiry date marked as "EXP" on the pack.

Special precautions for storage

Do not store above 25°C.
Keep out of the reach of children.

Instructions for handling

To empty the contents of each capsule, the two ends of the capsule should be pulled apart gently, and gently rolled between the finger and thumb.
Sachets should be opened by carefully cutting or tearing along the line indicated.
After opening, gently tap the two halves of the capsule or sachet to ensure that all the powder is emptied.
Hands should be washed immediately after handling PALFORZIA capsules or sachets.
Inhalation of the powder must be avoided, as this may worsen asthma or cause an allergic reaction.
PALFORZIA must not be added to food that has been heated above room temperature before consumption.
Ensure that PALFORZIA is consumed as soon as possible after it has been mixed with the food as much as possible.
The volume of the food should be such that the entire dose can be consumed in a few spoonfuls.
PALFORZIA should be consumed immediately after mixing, but can be mixed if necessary and refrigerated for up to 8 hours.

Authorisation number

67733 (Swissmedic)

Packs

<u>For medical use only – pack for induction therapy (initial dose escalation)</u>
2 capsules of 0.5 mg, 11 capsules of 1 mg (corresponds to 5 doses) [A]

<u>Packs for up-dosing:</u>

Level 0 (1 mg):	16 capsules of 1mg (corresponds to 16 doses) [A]
Level 1 (3 mg):	48 capsules of 1 mg (corresponds to 16 doses) [A]
Level 2 (6 mg):	96 capsules of 1 mg (corresponds to 16 doses) [A]
Level 3 (12 mg):	32 capsules of 1 mg, 16 capsules of 10 mg (corresponds to 16 doses) [A]
Level 4 (20 mg):	16 capsules of 20 mg (corresponds to 16 doses) [A]
Level 5 (40 mg):	32 capsules of 20 mg (corresponds to 16 doses) [A]
Level 6 (80 mg):	64 capsules of 20 mg (corresponds to 16 doses) [A]
Level 7 (120 mg):	16 capsules of 20 mg, 16 capsules of 100 mg (corresponds to 16 doses) [A]
Level 8 (160 mg):	48 capsules of 20 mg, 16 capsules of 100 mg (corresponds to 16 doses) [A]
Level 9 (200 mg):	32 capsules of 100 mg (corresponds to 16 doses) [A]
Level 10 (240 mg):	32 capsules of 20 mg, 32 capsules of 100 mg (corresponds to 16 doses) [A]
Level 11 (300 mg):	15 sachets of 300 mg (corresponds to 15 doses) [A]

Packs for maintenance therapy:

30 sachets of 300 mg (corresponds to 30 doses) [A]

Marketing authorisation holder

Stallergenes AG, 8305 Dietlikon

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