ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PALFORZIA 0.5 mg oral powder in capsules for opening
PALFORZIA 1 mg oral powder in capsules for opening
PALFORZIA 10 mg oral powder in capsules for opening
PALFORZIA 20 mg oral powder in capsules for opening
PALFORZIA 100 mg oral powder in capsules for opening
PALFORZIA 300 mg oral powder in sachet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PALFORZIA 0.5 mg oral powder in capsules for opening

Each capsule contains 0.5 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

PALFORZIA 1 mg oral powder in capsules for opening

Each capsule contains 1 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

PALFORZIA 10 mg oral powder in capsules for opening

Each capsule contains 10 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

PALFORZIA 20 mg oral powder in capsules for opening

Each capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

PALFORZIA 100 mg oral powder in capsules for opening

Each capsule contains 100 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

PALFORZIA 300 mg oral powder in sachet

Each sachet contains 300 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral powder in capsules for opening
Oral powder in sachet

PALFORZIA 0.5 mg oral powder in capsules for opening

White to beige oral powder in white opaque hard capsules (16 x 6 mm).

PALFORZIA 1 mg oral powder in capsules for opening

White to beige oral powder in red opaque hard capsules (16 x 6 mm).

PALFORZIA 10 mg oral powder in capsules for opening

White to beige oral powder in blue opaque hard capsules (23 x 9 mm).

PALFORZIA 20 mg oral powder in capsules for opening

White to beige oral powder in white opaque hard capsules (23 x 9 mm).

PALFORZIA 100 mg oral powder in capsules for opening

White to beige oral powder in red opaque hard capsules (23 x 9 mm).

PALFORZIA 300 mg oral powder in sachet

White to beige oral powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PALFORZIA is indicated for the treatment of patients aged 1 to 17 years with a confirmed diagnosis of peanut allergy. PALFORZIA may be continued in patients 18 years of age and older.

PALFORZIA should be used in conjunction with a peanut-avoidant diet.

4.2 Posology and method of administration

This medicinal product should be administered under the supervision of a health care professional qualified in the diagnosis and treatment of allergic diseases.

Initial dose escalation and the first dose of each new up-dosing level are to be administered in a health care setting prepared to manage potential severe allergic reactions.

Self-injectable adrenaline (epinephrine) must be available to the patient at all times.

Posology

Treatment is administered in 3 sequential phases: Initial dose escalation, up-dosing, and maintenance.

For each dose level during up-dosing, the doses given in clinic and at home should be from the same batch to avoid variations in the potency range (see section 4.4).

The dose configurations for each phase of dosing are provided in Table 1, Table 2, Table 3, Table 4 and Table 5.

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

Initial dose escalation phase

Initial dose escalation is administered on a single day under the supervision of a health care professional in a health care setting with the ability to manage potentially severe allergic reactions, including anaphylaxis.

Initial dose escalation is administered in sequential order on a single day beginning at 0.5 mg and completing with 3 mg for patients aged 1 to 3 years and with 6 mg for patients aged 4 to 17 years (see Tables 1 and 2).

Table 1: Dose and capsule presentation for initial dose escalation for patients aged 1 to 3 years old

Dose	Capsule presentation per dose
0.5 mg	1 × 0.5 mg capsule
1 mg	1 × 1 mg capsule
1.5 mg	1 × 0.5 mg capsule + 1 × 1 mg capsule
3 mg	3 × 1 mg capsules

Table 2: Dose and capsule presentation for initial dose escalation for patients aged 4 to 17 years old

Dose	Capsule presentation per dose
0.5 mg	1 × 0.5 mg capsule
1 mg	1 × 1 mg capsule
1.5 mg	1 × 0.5 mg capsule + 1 × 1 mg capsule
3 mg	3 × 1 mg capsules
6 mg	6 × 1 mg capsules

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

Each dose should be separated by an observation period of 20 to 30 minutes.

No dose level should be omitted.

Patients must be observed after the last dose for at least 60 minutes until suitable for discharge.

Treatment must be discontinued if symptoms requiring medical intervention (e.g., use of adrenaline) occur with any dose during initial dose escalation.

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) during initial dose escalation must return to the health care setting for initiation of up-dosing.

If possible, up-dosing should begin the day after initial dose escalation.

If the patient is unable to begin up-dosing within 4 days, 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 1 to 3 years old
The up-dosing phase consists of 12 dose levels and is initiated at a 1 mg dose (level 0) and up-dosed to level 11 (see Table 3).

Patients 4 to 17 years old
The up-dosing phase consists of 11 dose levels and is initiated at a 3 mg dose (level 1) and up-dosed to level 11 (see Table 4).

The first dose of each new up-dosing level is administered under the supervision of a health care professional in a health care setting with the ability to manage potentially severe allergic reactions, including anaphylaxis. Patients should be observed for at least 60 minutes after administering the first dose of a new up-dosing level until suitable for discharge.

If the patient tolerates the first dose of the increased dose level, the patient may continue that dose level at home.

All the dose levels in Tables 3 and 4 must be administered in sequential order at 2-week intervals if tolerated. No dose level should be omitted. Patients must not progress through up-dosing more rapidly than shown in Tables 3 and 4.

Table 3: Daily dosing configuration for up-dosing in patient aged 1 to 3 years old

Dose level	**Total daily dose**	**Presentation of dose (capsule colour)**	**Dose duration (weeks)**
0	1 mg	1 x 1 mg capsule (red)	2
1	3 mg	3 × 1 mg capsules (red)	2
2	6 mg	6 × 1 mg capsules (red)	2
3	12 mg	2 × 1 mg capsules (red) 1 × 10 mg capsule (blue)	2
4	20 mg	1 × 20 mg capsule (white)	2
5	40 mg	2 × 20 mg capsules (white)	2
6	80 mg	4 × 20 mg capsules (white)	2
7	120 mg	1 × 20 mg capsule (white) 1 × 100 mg capsule (red)	2
8	160 mg	3 × 20 mg capsules (white) 1 × 100 mg capsule (red)	2
9	200 mg	2 × 100 mg capsules (red)	2
10	240 mg	2 × 20 mg capsules (white) 2 × 100 mg capsules (red)	2
11	300 mg	1 × 300 mg sachet	2

Table 4: Daily dosing configuration for up-dosing in patients aged 4 to 17 years old

Dose level	Total daily dose	Presentation of dose (capsule colour)	Dose duration (weeks)
1	3 mg	3 × 1 mg capsules (red)	2
2	6 mg	6 × 1 mg capsules (red)	2
3	12 mg	2 × 1 mg capsules (red) 1 × 10 mg capsule (blue)	2
4	20 mg	1 × 20 mg capsule (white)	2
5	40 mg	2 × 20 mg capsules (white)	2
6	80 mg	4 × 20 mg capsules (white)	2
7	120 mg	1 × 20 mg capsule (white) 1 × 100 mg capsule (red)	2
8	160 mg	3 × 20 mg capsules (white) 1 × 100 mg capsule (red)	2
9	200 mg	2 × 100 mg capsules (red)	2
10	240 mg	2 × 20 mg capsules (white) 2 × 100 mg capsules (red)	2
11	300 mg	1 × 300 mg sachet	2

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 consumed in the clinic.

Care should be taken to ensure that patients have only one dose level in their possession at any time.

Dose modification or discontinuation should be considered for patients who do not tolerate up-dosing as described in Tables 3 and 4 (see *Dose modification instructions*).

Maintenance therapy

All dose levels of up-dosing must be completed before starting maintenance.

The maintenance dose is 300 mg daily.

Table 5: Daily dosing configuration for maintenance

Presentation of dose	Total daily dose
1 × 300 mg sachet	300 mg

Daily maintenance is required to maintain the tolerability and clinical effects of PALFORZIA.

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

Efficacy data currently are available for up to 12 months of treatment for ages 1 to 3 years. No recommendation can be made about the duration of treatment beyond 12 months.

Stopping treatment will likely not maintain achieved efficacy.

If treatment is stopped, patients must continue to carry self-injectable adrenaline at all times.

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 or for practical reasons for patient management. Allergic reactions, including gastrointestinal reactions, that are severe, recurrent, bothersome, or last longer than 90 minutes during up-dosing or maintenance should be actively managed with dose modifications. Clinical judgment should be used to determine the best course of action on a patient by patient basis. This can include maintaining the dose level for longer than 2 weeks, reducing, or withholding PALFORZIA doses.

Management of consecutive missed doses

Missed doses of PALFORZIA may pose a significant risk to patients due to potential loss of desensitisation. The guidelines in Table 6 are to be used for managing missed doses.

Table 6: Management of consecutive missed doses

Consecutive missed doses	**Action**
1 to 2 days	Patients may resume treatment at the same dose level at home.
3 to 4 days	Patients may resume treatment 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 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 or to discontinue treatment completely.

Following a dose reduction due to missed doses, up-dosing should be resumed as described in Tables 3 and 4.

Special populations

Elderly

The safety and efficacy of PALFORZIA therapy initiated in patients aged over 17 years has not been established.

Paediatric population

The safety and efficacy of PALFORZIA therapy in paediatric patients with peanut allergy below the age of 1 year have not been established. No data are available.

Method of administration

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

Capsules are not to be ingested. Inhalation of the powder must be avoided.

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.

The entire dose of PALFORZIA powder should be emptied onto a few spoonfuls of refrigerated or room temperature semisolid food (e.g., fruit puree, yogurt, rice-pudding) and mixed well. Liquid (e.g., milk, water, juice) must not be used.

Hands should be washed immediately after handling PALFORZIA capsule(s) or sachets.

Each dose taken at home should be consumed daily with a meal at approximately the same time each day, preferably in the evening. PALFORZIA should not be taken on an empty stomach or after fasting.

Alcohol should not be taken for 2 hours before or 2 hours after a dose (see section 4.4, Table 7).

PALFORZIA should not be taken within 2 hours of bedtime to facilitate the detection of allergic reactions and ensure their appropriate management (see section 4.4).

4.3 Contraindications

- Current severe or uncontrolled asthma (see section 5.1)
- A history of food protein-induced enterocolitis syndrome (FPIES) in the past 12 months (applicable for patients aged 1-3 years, see section 5.1)
- A history of failure to thrive (applicable for patients aged 1-3 years, see section 5.1)
- A history of, or current, eosinophilic oesophagitis (EoE); other eosinophilic gastrointestinal disease; chronic, recurrent, or severe gastroesophageal reflux disease (GERD); dysphagia
- A history of, or current, severe mast cell disorder
- Severe or life-threatening anaphylaxis within 60 days before initiating treatment
- Hypersensitivity to any of the excipients listed in section 6.1

4.4 Special warnings and precautions for use

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.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Adrenaline

Self-injectable adrenaline must be prescribed to patients receiving this medicinal product. Patients must be instructed to carry self-injectable adrenaline at all times. 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 until they have been evaluated by a physician.

PALFORZIA may not be suitable for patients who are taking medications that can inhibit or potentiate the effect of adrenaline (see the SmPC of adrenaline for further information).

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

Dose modifications should be considered for patients who experience moderate or severe adverse allergic reactions to PALFORZIA. For dose modification instructions, see section 4.2.

PALFORZIA can cause systemic allergic reactions including anaphylaxis, which may be life-threatening.

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. Any reaction must be treated promptly (e.g., with self-administration of intramuscular adrenaline) in case a severe adverse reaction develops 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. Table 7 provides guidance on recommended actions to mitigate the risks associated with co-factors whilst on treatment.

Table 7: Guidelines on management of co-factors

Modifiable co-factors	**Recommended action to be taken**
Hot bath or shower	Hot showers or baths should be avoided immediately prior to or following 3 hours of treatment.
Exercise	Exercise should be avoided immediately prior to or for 3 hours following treatment. After strenuous exercise signs of a hypermetabolic state (e.g., flushing, sweating, rapid breathing, rapid heart rate) must have subsided before taking a dose.
Fasting or empty stomach	Each dose should be consumed with a meal.
Alcohol (including medicinal products containing alcohol)	Alcohol should not be taken for 2 hours before or 2 hours after a dose.
Intake of non-steroidal anti-inflammatory medicinal products	The potential for allergic reactions to occur if taking non-steroidal anti-inflammatory medicinal products whilst on PALFORZIA treatment should be considered.
Non-modifiable co-factors	
Intercurrent illness	Patients and/or caregivers should be instructed to seek medical advice before taking their next dose of PALFORZIA.
Exacerbation of asthma	
Menstruation	Withholding or decreasing the PALFORZIA dose temporarily should be considered based on individual patient needs.
Stress	
Fatigue or sleep deprivation	

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 (see section 5.1).

Asthma

In patients with asthma, treatment may only be initiated when the asthma status is controlled. Treatment 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 considered. This medicinal product has not been studied in patients on long-term systemic corticosteroid therapy.

Concomitant illnesses

This medicinal product 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.

Gastro-intestinal adverse reactions including eosinophilic oesophagitis (EoE)

If patients develop chronic or recurrent gastrointestinal symptoms, dose modification may be considered (see section 4.2). EoE has been reported in association with PALFORZIA (see section 4.8). For chronic/recurrent gastrointestinal symptoms, especially upper gastrointestinal symptoms (nausea, vomiting, dysphagia) in all age groups, or food refusal and failure to thrive especially assessed in toddlers and younger patients (ages 1 to 3 years), the potential for a diagnosis of IgE- or non-IgE-mediated gastrointestinal diseases such as EoE should be considered. Additionally, FPIES, a food-associated non-IgE mediated gastrointestinal disease that may occur in toddlers, should be considered in any toddler with significant food associated GI 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

This medicinal product 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 potential for severe allergic reactions may be enhanced.

Oral inflammation or wounds

Patients with acute severe inflammation of the mouth or oesophagus, or with oral wounds may be at greater risk of severe systemic allergic reactions following ingestion of peanut protein. Initiation of treatment should be postponed in these patients and ongoing treatment should be temporarily interrupted to allow healing of the oral cavity.

Chronic urticaria

Chronic urticaria, especially in the presence of severe exacerbations may confound the safety assessment of treatment.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Interactions with other medicinal products are not expected.

Severe allergic reactions may be treated with adrenaline (see section 4.4). Please refer to the SmPC for adrenaline for further information on medicinal products that may potentiate or inhibit the effects of adrenaline.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no data from defatted powder of *Arachis hypogaea L.*, semen (peanuts) in pregnant women.

Initiation of treatment is not recommended during pregnancy.

Treatment with this medicinal product may cause anaphylaxis, which is a risk to pregnant women. 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 oral immunotherapy (OIT) on the immune system of the mother and foetus during pregnancy is unknown.

For patients who are established on OIT and become pregnant, the benefits of remaining on OIT and retaining desensitisation should be weighed against the risks of an anaphylactic reaction while remaining on OIT.

Breast-feeding

Peanut allergens have been found in human milk after consumption of peanuts. There are no data available on the effects of PALFORZIA on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for treatment 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 defatted powder of *Arachis hypogaea L.*, semen (peanuts) on fertility.

4.7 Effects on ability to drive and use machines

PALFORZIA has 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, cycle, or use machines.

4.8 Undesirable effects

Summary of the safety profile for ages 1 to 3 years

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 initial dose escalation (15.3 %) and maintenance (34.5 %).

5.1% of subjects discontinued treatment due to 1 or more adverse reaction.

Summary of the safety profile for ages 4 to 17 years

The most common adverse reactions (of any severity) are abdominal pain (49.5%), throat irritation (41.4%), pruritus (33.9%), nausea (33.3%), urticaria (28.7%), vomiting (28.5%), oral pruritus (26.0%), abdominal pain upper (22.9%), and abdominal discomfort (22.8%).

The incidence of adverse reactions was higher during up-dosing (85.9%) than initial dose escalation (45.7%) and maintenance (57.9%).

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.

11.2% of subjects discontinued treatment due to 1 or more adverse reactions.

Overall, the safety profile in 1-3 year old subjects was consistent with that seen in 4-17 year old subjects. However, all severe adverse reactions were diagnosed in subjects aged 4 – 17 years.

Tabulated list of adverse reactions

Table 8 is based on data from the placebo-controlled clinical studies and post-marketing experience. Listed adverse reactions are divided into groups according to the MedDRA system organ class and frequency. Frequency categories are defined as: 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), and very rare (< 1/10 000). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 8: Tabulated list of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reaction**
Immune system disorders	*Very common*	Anaphylactic reaction
	Not known	Hypersensitivity*

MedDRA system organ class	Frequency	Adverse reaction
Respiratory, thoracic, and mediastinal disorders	*Very common*	Cough Throat irritation Throat tightness Rhinitis allergic Oropharyngeal pain Sneezing Nasal congestion
	Common	Dyspnoea Wheezing Dysphonia Throat clearing Pharyngeal paraesthesia
Gastrointestinal disorders	*Very common*	Vomiting Abdominal pain Nausea Oral pruritus Paraesthesia oral
	Common	Dyspepsia Diarrhoea Dysphagia Salivary hypersecretion Cheilitis Mouth swelling Mouth ulceration Eosinophilic oesophagitis**
General disorders and administration site conditions	*Common*	Chest discomfort Swelling face Flushing Fatigue Sensation of foreign body
Nervous system disorders	*Common*	Headache
Psychiatric disorders	*Common*	Anxiety
Skin and subcutaneous tissue disorders	*Very common*	Pruritus Urticaria Rash
	Common	Angioedema Eczema
Eye disorders	*Common*	Eye pruritus Eye swelling Lacrimation increased Conjunctivitis allergic
Ear and labyrinth disorders	*Common*	Ear pruritus

*cases of hypersensitivity have been reported during post-marketing experience.
**based on placebo-controlled clinical studies and open-label follow-on studies - not observed in 1-3 year old subjects.

Description of selected adverse reactions

Systemic allergic reactions (anaphylactic 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 and the term anaphylaxis is used to distinguish anaphylactic reaction events that were severe. Systemic allergic reactions were milder in the 1 to 3 years age group.

For ages 1 to 3 years
Systemic allergic reactions of any severity were reported in 8.2% of subjects treated with PALFORZIA, including 0% during initial dose escalation, 2.0% during up-dosing, and 6.9% during maintenance. Out of the 9 total systemic allergic reactions (occurring in 8 subjects), 3 were related to study drug. Of the PALFORZIA-treated population, 7.1% of subjects reported a single episode of systemic allergic reaction and 1.0% reported two or more systemic allergic reactions. The most commonly reported symptoms of systemic allergic reactions were cough and urticaria, followed by throat irritation and wheezing.

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 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, pruritis, 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.

Adrenaline use

For ages 1 to 3 years
In the safety population, 11.2% of subjects reported at least one episode of adrenaline use for any reason and in 2.1% of subjects adrenaline was used for symptoms that were considered related to study drug. In 92.3% of the adrenaline usage events, a single dose of adrenaline was used, and 84.6% of adrenaline usage was for events of mild to moderate severity.

For ages 4 to 17 years
In the 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.

Eosinophilic oesophagitis (EoE)

In all clinical studies, 1.2% of subjects, aged 1 to 17 years, were diagnosed with biopsy-confirmed eosinophilic oesophagitis while receiving PALFORZIA compared with 0% of subjects receiving placebo. After discontinuation of treatment, symptomatic improvement was reported in 73% of subjects. In 7 subjects with available follow-up biopsy results, eosinophilic oesophagitis was resolved

in 57% of subjects and improved in 43% of subjects. All events were diagnosed in subjects aged 4 – 17 years.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 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 event of anaphylaxis at home, patients should self-administer intramuscular adrenaline and follow-up with an emergency medical evaluation. In an emergency department, the anaphylaxis guidelines should be followed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Allergen, allergen extracts, ATC code: V01AA08

Mechanism of action

The precise mechanism of desensitisation provided by defatted powder of *Arachis hypogaea L.*, semen (peanuts) is not fully understood.

A summary of immunoglobulin values reported for subjects aged 1 to 3 years treated with PALFORZIA for 12 months in the POSEIDON study is provided in Table 9.

Table 9: Change over time in immunoglobulin values in POSEIDON (ITT population, PALFORZIA subjects, 1-3 years)

Parameter	Statistic	Screening DBPCFC	Exit DBPCFC
ps-IgE (kUA/L)	n	87	76
	Geometric mean (SD) [1]	7.04 (6.712)	3.33 (7.713)
	Q1, Q3	2.3, 33.5	1.0, 19.8
ps-IgG4 (mgA/L)	n	85	76
	Geometric mean (SD) [1]	385.773 (3.8797)	3396.998 (4.5179)
	Q1, Q3	120.0, 910.0	1205.0, 11200.0
ps-IgE/ IgG4	n	85	76
	Geometric mean (SD) [1]	0.02 (5.540)	0.00 (5.407)
	Q1, Q3	0.0, 0.0	0.0, 0.0

[1] Geometric means were calculated by computing the mean on the log10 scale and converting the mean to the original scale by calculating the antilog.

ITT, intent-to-treat; ps, peanut specific; Q1, Q3, first quartile, third quartile; DBPCFC, double-blind, placebo-controlled food challenge; SD, standard deviation.

A summary of immunoglobulin values reported for subjects aged 4 to 17 years treated with PALFORZIA for 12 months in the PALISADE study is provided in Table 10.

Table 10: Change over time in immunoglobulin values in PALISADE (ITT population, PALFORZIA subjects, 4-17 years)

Parameter	Statistic	Screening DBPCFC	End of up-dosing	Exit DBPCFC
ps-IgE (kUA/L)	n	372	305	272
	Geometric mean (SD) [1]	51.40 (5.965)	101.33 (8.134)	48.61 (7.799)
	Q1, Q3	18.6, 194.3	28.8, 491.0	12.2, 259.0
ps-IgG4 (mgA/L)	n	353	305	274
	Geometric mean (SD) [1]	0.538 (3.4655)	3.341 (4.0450)	5.557 (4.4633)
	Q1, Q3	0.22, 1.21	1.72, 8.79	2.50, 14.70
ps-IgE/ IgG4	n	353	305	272
	Geometric mean (SD) [1]	97.36 (5.053)	30.32 (4.640)	8.76 (5.261)
	Q1, Q3	36.2, 310.0	11.6, 88.4	2.3, 26.3

[1] Geometric means were calculated by computing the mean on the $\log_{10}$ scale and converting the mean to the original scale by calculating the antilog.

ITT, intent-to-treat; ps, peanut specific; Q1, Q3, first quartile, third quartile; DBPCFC, double-blind, placebo-controlled food challenge; SD, standard deviation.

In the ARTEMIS study, the geometric mean (SD) peanut specific IgE of the PALFORZIA group was 30.55 (7.794) kUA/L at the screening double-blind, placebo-controlled food challenge (DBPCFC), increasing to 44.28 (10.850) kUA/L at the end of Up-Dosing, thereafter decreasing to 28.92 (9.908) kUA/L at the exit DBPCFC (following 3 months of PALFORZIA maintenance dosing at 300 mg daily). The geometric LS (least squares) mean ratio (exit/screening) was 1.18, 95% confidence interval (CI) (0.97, 1.44).

Immunologic parameters in long-term maintenance

The sustained effects of PALFORZIA treatment on the immunologic parameters peanut-specific IgE, IgG4 and the IgE/IgG4 ratio for subjects who completed 12 and 18 months of PALFORZIA maintenance treatment with the ongoing therapeutic dose (300 mg daily) through participation in both PALISADE and the open-label follow-on study ARC004 are provided in Table 11.

Table 11: Immunologic parameters following continued maintenance at study exit (PALISADE and ARC004 completer populations, 4-17 years)

	PALISADE	ARC004	
	6-month maintenance	12-month maintenance	18-month maintenance
n, Geometric Mean (SD) [1]			
ps-IgE kUA/L	272	96	26
	48.61 (7.799)	27.87 (6.831)	13.42 (9.670)
ps-IgG4 mgA/L	274	89	25
	5.557 (4.4633)	5.875 (4.3605)	8.900 (3.1294)
ps-IgE/IgG4	272	89	25
	8.76 (5.261)	4.55 (6.189)	1.55 (5.462)

[1] Geometric means were calculated by computing the mean on the $\log_{10}$ scale and converting the mean to the original scale by calculating the antilog.

Clinical efficacy

In all PALFORZIA clinical studies, efficacy was measured using a DBPCFC. This food challenge was performed according to the Practical Allergy (PRACTALL) guidelines with modification to include a 600 mg protein dose (between the 300 mg and 1 000 mg challenge doses).

The efficacy of PALFORZIA was assessed in 3 randomised, double-blind, placebo-controlled, multicentre, phase 3 pivotal studies PALISADE, ARTEMIS and POSEIDON. Each study recruited subjects with a documented history of peanut allergy. Subjects with a severe or life-threatening anaphylaxis event within 60 days of study entry and those with severe or uncontrolled asthma were excluded from the studies. Additionally subjects with current or a history of FPIES, or other recurrent gastrointestinal symptoms or failure to thrive were excluded in 1-3 year old population (POSEIDON).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 1 mg on day 2, subjects underwent up-dosing for 20-40 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. Subjects then underwent 6 months (PALISADE and POSEIDON) or 3 months (ARTEMIS) of maintenance immunotherapy with 300 mg PALFORZIA or placebo until the end of the study when subjects completed an exit DBPCFC to assess desensitisation to peanut.

PALISADE recruited subjects aged 4 to 55 years in Europe and North America. A total of 750 subjects aged 4 to 17 years were screened and 499 were randomly assigned (3:1) to study treatment (374 to PALFORZIA and 125 to placebo). The primary efficacy analysis population consisted of 496 subjects aged 4 to 17 years who received at least one dose of study treatment. In this study, eligible subjects were those sensitive to ≤ 100 mg of peanut protein at the screening DBPCFC. Of the subjects treated with PALFORZIA in the primary analysis population, 72% had a medical history of allergic rhinitis, 66% reported multiple food allergies, 63% had a medical history of atopic dermatitis, and 53% had a present or previous diagnosis of asthma. The median age of subjects was 9 years. More than half of the subjects were male (56%) and most subjects were white (78%).

ARTEMIS recruited subjects aged 4 to 17 years of age in Europe. A total of 175 subjects aged 4 to 17 years were randomly assigned (3:1) to study treatment (132 to PALFORZIA and 43 to placebo). The primary efficacy analysis population consisted of 175 subjects aged 4 to 17 years who received at least one dose of study treatment. In this study, eligible subjects were those sensitive to ≤ 300 mg of peanut protein at the screening DBPCFC. Of the subjects treated with PALFORZIA in the primary analysis group, 61% reported multiple food allergies, 59% had a medical history of atopic dermatitis, 48% had a medical history of allergic rhinitis, and 42% had a present or previous diagnosis of asthma. The median age of subjects was 8.0 years. More than half of the subjects were male (52%) and most subjects were white (82%).

POSEIDON recruited subjects aged 1 to 3 years in Europe and North America. A total of 289 subjects were screened and 146 were randomly assigned (2:1) to study treatment (98 to PALFORZIA and 48 to placebo). The primary efficacy analysis population consisted of 146 subjects who received at least one dose of study treatment. In this study, eligible subjects were those sensitive to > 3 mg and ≤ 300 mg of peanut protein at the screening DBPCFC. Of the subjects treated with PALFORZIA in the primary analysis population, 13.3% had a medical history of allergic rhinitis, 72.4% reported multiple food allergies other than peanut, 63.3% had a medical history of atopic dermatitis, and 8.2% had a present or previous diagnosis of asthma. The median age of subjects was 2 years. More than half of the subjects were male (58.2%) and most subjects were white (67.1%).

Efficacy data

The primary efficacy endpoint in all 3 studies PALISADE, ARTEMIS and POSEIDON was the proportion of subjects 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 (desensitisation response rate). Key secondary endpoints 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. In addition, the highest tolerated dose at the exit double-blind, placebo-controlled food challenge DBPCFC was included as a pre-specified exploratory endpoint.

Desensitisation response rates

The summary of desensitisation response rates for efficacy endpoints for the intention to treat (ITT) population in all 3 studies PALISADE, ARTEMIS and POSEIDON are provided in Table 12. Subjects without an exit DBPCFC were counted as non-responders.

Table 12: PALISADE, ARTEMIS and POSEIDON: Summary of desensitisation response rates for primary, key secondary efficacy endpoints (ITT population, 1-17 years)

	PALISADE		**ARTEMIS**		**POSEIDON**	
Endpoint	**PALFORZIA N = 372**	**Placebo N = 124**	**PALFORZIA N = 132**	**Placebo N = 43**	**PALFORZIA N = 98**	**Placebo N = 48**
Primary efficacy endpoint						
Response rate: proportion of subjects who tolerated 1 000 mg peanut protein (95% CI) [1][2]	50.3% (45.2, 55.3)	2.4% (0.8, 6.9)	58.3% (49.4, 66.8)	2.3% (0.1, 12.3)	68.4% (58.2, 77.4)	4.2% (0.5, 14.3)
P-value [3]	< 0.0001		< 0.0001		< 0.0001	
Key secondary efficacy endpoints						
Response rate: proportion of subjects who tolerated 600 mg peanut protein (95% CI) [2][4]	67.2% (62.3, 71.8)	4.0% (1.7, 9.1)	68.2% (59.5, 76.0)	9.3% (2.6, 22.1)	73.5% (63.6, 81.9)	6.3% (1.3, 17.2)
P-value [3]	< 0.0001		< 0.0001		< 0.0001	
Response rate: proportion of subjects who tolerated 300 mg peanut protein (95% CI) [2]	76.6% (72.1, 80.6)	8.1% (4.4, 14.2)	73.5% (65.1, 80.8)	16.3% (6.8, 30.7)	79.6% (70.3, 87.1)	22.9% (12.0, 37.3)
P-value [3]	< 0.0001		< 0.0001		< 0.0001	

[1] Desensitisation response rate after single dose of 1 000 mg was the primary efficacy endpoint for PALISADE and ARTEMIS and a key secondary efficacy endpoint for POSEIDON.

[2] PALISADE: Based on Wilson (score) confidence limits, ARTEMIS: Based on exact Clopper-Pearson interval, POSEIDON: Based on exact Clopper-Pearson intervals.

[3] PALISADE: 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.
POSEIDON: Based on Farrington-Manning confidence limits.

[4] Desensitisation response rate after single dose of 600 mg was the primary efficacy endpoint for POSEIDON and a key secondary efficacy endpoint for PALISADE and ARTEMIS.

CI, confidence interval

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 4 to 17 years.

Sustained efficacy

Sustained efficacy has been demonstrated in 103 subjects and 26 subjects who completed 12 and 18 months 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 can be made by comparing the response rates for the 12-month and 18-month maintenance cohorts in ARC004 with those who completed PALISADE (see Table 13).

Table 13: Percentage of challenge doses tolerated following continued maintenance during exit DBPCFC (PALISADE and ARC004 completer populations, 4-17 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	na [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.
DBPCFC, double-blind, placebo-controlled food challenge; CI confidence interval; na, not applicable.

5.2 Pharmacokinetic properties

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.

5.3 Preclinical safety data

Non-clinical studies with defatted powder of *Arachis hypogaea L.*, semen (peanuts) have not been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

PALFORZIA 0.5 mg, 1 mg, 10 mg, 20 mg oral powder in capsules for opening

Microcrystalline cellulose
Partially pre-gelatinised maize starch
Colloidal anhydrous silica
Magnesium stearate

PALFORZIA 100 mg oral powder in capsules for opening and PALFORZIA 300 mg oral powder in sachet

Microcrystalline cellulose
Colloidal anhydrous silica
Magnesium stearate

Capsule shells

0.5 mg capsule (white)
Hydroxypropyl methylcellulose, titanium dioxide (E 171), grey SW 5014 (ink).

1 mg capsule (red)
Hydroxypropyl methylcellulose, red iron oxide (E 172), titanium dioxide (E 171), white TEK SW 0012 (ink).

10 mg capsule (blue)
Hydroxypropyl methylcellulose, FD&C Blue #1 (E 133), red iron oxide (E 172), black iron oxide (E 172), titanium dioxide (E 171), white SW 0012 (ink).

20 mg capsule (white)
Hydroxypropyl methylcellulose, titanium dioxide (E 171), grey TEK SW 5014 (ink).

100 mg capsule (red)
Hydroxypropyl methylcellulose, red iron oxide (E 172), titanium dioxide (E 171), white SW 0012 (ink).

6.2 Incompatibilities

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

6.3 Shelf life

Initial dose escalation pack: 2 years
All packs except initial dose escalation pack: 3 years

After mixing a daily dose of PALFORZIA with age-appropriate soft-food, the entire volume of the prepared mixture should be consumed promptly, but if necessary, can be refrigerated for up to 8 hours.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Initial dose escalation pack

PVC:PCTFE/Aluminium blister containing 13 capsules (2 x 0.5 mg + 11 x 1 mg) in 5 single-dose blisters.

2-week packs

Each 2-week pack contains additional doses in case of need.

Name/Capsule or Sachet strength	Pack contents by dose level (daily dose)
PALFORZIA 1 mg oral powder in capsules for opening	**Level 0 (1 mg daily) - 1 to 3 years:** 16 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains one 1 mg capsule **Level 1 (3 mg daily):** 48 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains three 1 mg capsules **Level 2 (6 mg daily):** 96 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains six 1 mg capsules
PALFORZIA 10 mg PALFORZIA 1 mg oral powder in capsules for opening	**Level 3 (12 mg daily):** 48 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains one 10 mg capsule and two 1 mg capsules
PALFORZIA 20 mg oral powder in capsules for opening	**Level 4 (20 mg daily):** 16 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains one 20 mg capsule **Level 5 (40 mg daily):** 32 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains two 20 mg capsules **Level 6 (80 mg daily):** 64 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains four 20 mg capsules
PALFORZIA 100 mg oral powder in capsules for opening	**Level 9 (200 mg daily):** 32 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains two 100 mg capsules
PALFORZIA 100 mg PALFORZIA 20 mg oral powder in capsules for opening	**Level 7 (120 mg daily):** 32 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains one 100 mg capsule and one 20 mg capsule **Level 8 (160 mg daily):** 64 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains one 100 mg capsule and three 20 mg capsules **Level 10 (240 mg daily)**: 64 capsules in PVC:PCTFE/Aluminium blisters in a carton Each blister-well contains two 100 mg capsules and two 20 mg capsules
PALFORZIA 300 mg oral powder in sachet	**Level 11 (300 mg daily):** 15 PET/Aluminium/mLLDPE foil sachets in a carton

Maintenance pack

Each pack of PALFORZIA 300 mg oral powder contains 30 PET/Aluminium/mLLDPE foil sachets in a carton.

6.6 Special precautions for disposal

Disposal

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

Unused medicinal product or waste material includes opened capsule(s) (i.e., empty or contained powder that was not used) or sachet(s), and prepared mixtures not consumed within 8 hours.

7. MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

8. MARKETING AUTHORISATION NUMBERS

EU/1/20/1495/001
EU/1/20/1495/002
EU/1/20/1495/003
EU/1/20/1495/004
EU/1/20/1495/005
EU/1/20/1495/006
EU/1/20/1495/007
EU/1/20/1495/008
EU/1/20/1495/009
EU/1/20/1495/010
EU/1/20/1495/011
EU/1/20/1495/012
EU/1/20/1495/013
EU/1/20/1495/014

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17 December 2020
Date of latest renewal:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Golden Peanut Company, LLC
(also known as Golden Peanut and Tree Nuts)
Specialty Products Division
3886 Martin Luther King Jr. Boulevard
Blakely, Georgia 39823
United States

Name and address of the manufacturer responsible for batch release

Millmount Health Limited
Block 7, City North Business Campus
Stamullen
Co Meath
Ireland

STALLERGENES
6, rue Alexis de Tocqueville
92160 ANTONY
France

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Key messages of the additional risk minimisation measures

Healthcare professional educational materials:

- The Summary of Product Characteristics
- Healthcare professional educational materials:

These materials consist of print and on-line materials and video resources including an instruction manual. The instruction manual is a reference document which details the appropriate use of PALFORZIA and will include the following information:

- Treatment overview
    - Summary of relevant background information and overview of the three dosing phases (initial dose escalation, up-dosing and maintenance)
    - Explanation of dose preparation and administration
    - When to consider dose modifications and management of missed doses
- Safety overview
    - Summary of risks of anaphylaxis and eosinophilic oesophagitis with focus on the identification of symptoms, management, and mitigation of known risks (including - co-factors which may precipitate systemic allergic reactions)
    - Summary of common side effects with focus on severity, frequency, and management
    - Explanation of requisite treatment adherence with focus on daily dosing, peanut avoidance, and appropriate prescription and use of emergency adrenaline
    - Appropriate referral to SmPC for additional information
    - Country-specific guidance on how and when to report adverse events

Patient and parent/caregiver educational materials:

- Package leaflet
- Patient and parent/caregiver educational materials:

These consist of a collection of print and on-line materials and video resources that will be developed in lay terms to an appropriate reading age for the following audiences: patients aged 1-6, 7-11, and 12-17 years old, and parents/caregivers. Materials will include the following information:

- Treatment overview
    - Brief explanation as to what PALFORZIA is used for, which patients are suitable to be treated with PALFORZIA, and who should not take the medicine
    - Summary of relevant background information and overview of the three dosing phases (initial dose escalation, up-dosing, and maintenance)
    - How to safely prepare, administer, and (if necessary) store doses and dispose of unused doses
- Safety overview
    - Summary of risks of anaphylaxis and eosinophilic oesophagitis with focus on the identification of symptoms, management, and mitigation of known risks (including co-factors which may precipitate systemic allergic reactions)
    - Summary of common side effects with focus on severity, frequency, and management
    - Explanation of requisite treatment adherence with focus on daily dosing, peanut avoidance, and appropriate use of emergency adrenaline
    - Appropriate referral to package leaflet for additional information
    - Description of how and when to report side effects to a healthcare professional

Patient card

- To be given to a patient by the prescribing physician when PALFORZIA treatment is initiated
- Patients will be instructed to carry the card on their person at all times

- Warning for healthcare professionals treating the patient at any time, including in emergency situations, that the patient is peanut-allergic and that they are using PALFORZIA
- Warning that if anaphylaxis is suspected to administer a dose of adrenaline and to contact emergency services
- Description of the symptoms of anaphylaxis and when to contact a healthcare professional
- Emergency contact details for the patient
- Contact details of the PALFORZIA prescriber

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON FOR INITIAL DOSE ESCALATION (PHYSICIAN / CLINIC USE ONLY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 0.5 mg oral powder in capsules for opening
Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each 0.5 mg capsule contains 0.5 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 1 mg capsule contains 1 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 1.5 mg dose comprises 1 × 1 mg capsule + 1 × 0.5 mg capsule.

Each 3 mg dose comprises 3 × 1 mg capsules.

Each 6 mg dose comprises 6 × 1 mg capsules.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

Each pack of 13 capsules for initial dose escalation contains 2 capsules of 0.5 mg and 11 capsules of 1 mg
5 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use. The dose of 6 mg must not be used for patients 1 to 3 years old.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Initial dose escalation
Physician use only

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
5-DOSE BLISTER STRIP

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 0.5 mg oral powder in capsules for opening
Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

0.5 mg → 1 mg → 1.5 mg → 3 mg → 6 mg - MUST BE USED FOR 4 to 17 years olds only (4 to 17 years)
0.5 mg → 1 mg → 1.5 mg → 3 mg (1 to 3 years)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 0 - 1 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 1 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 1 mg dose comprises 1 × 1 mg capsule

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

16 capsules
16 doses

5. METHOD AND ROUTE OF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 0 (1 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

For children 1 to 3 years old only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/014

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 0 (1 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 0 – 1 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 0 (1 mg daily)

LEVEL 0 (1 MG DAILY)PARTICULARS TO APPEAR ON THE OUTER PACKAGING OUTER CARTON (LEVEL 1 - 3 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 1 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 3 mg dose comprises 3 × 1 mg capsules

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

48 capsules
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 1 (3 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 1 (3 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 1 - 3 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 1 (3 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 2 - 6 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 1 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 6 mg dose comprises 6 × 1 mg capsules.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

96 capsules
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 2 (6 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/003

13. BATCH NUMBER<, DONATION AND PRODUCT CODES>

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 2 (6 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 2 - 6 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 2 (6 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 3 - 12 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 10 mg oral powder in capsules for opening
Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each 10 mg capsule contains 10 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 1 mg capsule contains 1 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 12 mg dose comprises 1 × 10 mg capsule + 2 × 1 mg capsules

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

48 capsules (16 capsules of 10 mg, 32 capsules of 1 mg)
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 3 (12 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 3 (12 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 3 - 12 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 10 mg oral powder in capsules for opening
Palforzia 1 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 3 (12 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 4 – 20 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 20 mg dose comprises 1 × 20 mg capsule

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

16 capsules
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 4 (20 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/005

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 4 (20 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 4 - 20 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 4 (20 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 5 - 40 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 40 mg dose comprises 2 × 20 mg capsules

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

32 capsules
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 5 (40 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/006

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 5 (40 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 5 – 40 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 5 (40 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 6 - 80 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 80 mg dose comprises 4 × 20 mg capsules

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

64 capsules
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 6 (80 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/007

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 6 (80 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 6 - 80 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 6 (80 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 7 - 120 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each 100 mg capsule contains 100 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 20 mg capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 120 mg dose comprises 1 × 100 mg capsule + 1 × 20 mg capsule

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

32 capsules (16 capsules of 100 mg, 16 capsules of 20 mg)
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 7 (120 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/008

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 7 (120 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 7 - 120 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 7 (120 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 8 - 160 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each 100 mg capsule contains 100 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 20 mg capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 160 mg dose comprises 1 × 100 mg capsule + 3 × 20 mg capsules

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

64 capsules (16 capsules of 100 mg, 48 capsules of 20 mg)
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 8 (160 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/009

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 8 (160 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 8 - 160 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 8 (160 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 9 - 200 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each capsule contains 100 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 200 mg dose comprises 2 × 100 mg capsules

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

32 capsules
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 9 (200 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/011

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 9 (200 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 9 - 200 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 9 (200 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 10 – 240 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each 100 mg capsule contains 100 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 20 mg capsule contains 20 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

Each 240 mg dose comprises 2 × 100 mg capsules + 2 × 20 mg capsules.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in capsules for opening

64 capsules (32 capsules of 100 mg, 32 capsules of 20 mg)
16 doses

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix capsule contents with soft food before administration.
Do not ingest capsules.

Level 10 (240 mg daily)

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/010

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 10 (240 mg daily)

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
BLISTER STRIPS (LEVEL 10 - 240 MG DAILY)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 100 mg oral powder in capsules for opening
Palforzia 20 mg oral powder in capsules for opening
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. NAME OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Level 10 (240 mg daily)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING
OUTER CARTON (LEVEL 11 - 300 MG DAILY / Maintenance)

1. NAME OF THE MEDICINAL PRODUCT

Palforzia 300 mg oral powder in sachet
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

2. STATEMENT OF ACTIVE SUBSTANCE

Each sachet contains 300 mg peanut protein as defatted powder of *Arachis hypogaea L.*, semen (peanuts).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Oral powder in sachet

15 sachets
30 sachets

5. METHOD AND ROUTEOF ADMINISTRATION

Read the package leaflet before use.
Oral use. Mix sachet contents with soft food before administration.

Level 11 (300 mg daily)
Maintenance

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store below 25°C.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

STALLERGENES
6 rue Alexis de Tocqueville
92160 Antony
France

12. MARKETING AUTHORISATION NUMBER

EU/1/20/1495/012 15 sachets
EU/1/20/1495/013 30 sachets

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Palforzia level 11 (300 mg)
Palforzia 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Not applicable.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
SACHETS (LEVEL 11 – 300 MG DAILY / Maintenance)

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Palforzia 300 mg oral powder in sachet
defatted powder of *Arachis hypogaea L.*, semen (peanuts)
Oral use

2. METHOD OF ADMINISTRATION

Read the package leaflet before use.
Mix contents of sachet with soft food before adminstration.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

300 mg

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

PALFORZIA 0.5 mg oral powder in capsules for opening
PALFORZIA 1 mg oral powder in capsules for opening
PALFORZIA 10 mg oral powder in capsules for opening
PALFORZIA 20 mg oral powder in capsules for opening
PALFORZIA 100 mg oral powder in capsules for opening
PALFORZIA 300 mg oral powder in sachet
defatted powder of *Arachis hypogaea L.*, semen (peanuts)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What PALFORZIA is and what it is used for

PALFORZIA contains peanut protein from defatted powder of peanut seed. It belongs to a class of medicines called food allergens. It is a treatment for people who are allergic to peanuts (*Arachis hypogaea L.*).

PALFORZIA is intended for children and young people aged from 1 to 17 years and those who become adults whilst on treatment.

PALFORZIA works in people with peanut allergy by gradually increasing the body's ability to tolerate small amounts of peanut (desensitisation). PALFORZIA can help reduce the severity of allergic reactions after coming into contact with peanut.

PALFORZIA is not effective against any other nut or food allergies.

You must continue to strictly avoid eating peanuts while taking PALFORZIA.

2. What you need to know before you take PALFORZIA

Do not take PALFORZIA

- if you are allergic to any of the excipients (other ingredients) in this medicine (listed in section 6).
- if you have severe asthma or if your asthma is not under control (as assessed by a doctor).
- if you have had a condition called 'food protein-induced enterocolitis syndrome (FPIES)', in the past 12 months (applicable for young children aged 1-3 years)
- if you have ever had a problem with growing or developing as you should i.e. 'failure to thrive' (applicable for young children aged 1-3 years)
- if you have ever had a problem swallowing or long term problems with your digestive system.
- if you have ever had a severe mast cell disorder (as assessed by a doctor).
- if you had severe or life-threatening anaphylaxis within 60 days before starting treatment.

Warnings and precautions

Talk to your doctor before taking PALFORZIA and tell your doctor about any medical conditions that you have.

You must not take any peanut or peanut containing food in your diet whilst taking PALFORZIA.

It is important to keep a record of the batch number of your PALFORZIA. So, every time you get a new package of PALFORZIA, note down the date and the batch number (which is on the packaging after "Lot") and keep this information in a safe place.

PALFORZIA does not treat the symptoms of peanut allergy and you must not take PALFORZIA during an allergic reaction.

Your doctor will advise the best time to start treatment depending on any medical conditions that you have.

PALFORZIA contains the substance that patients with peanut allergy react to. Allergic reactions to PALFORZIA may occur during treatment. These reactions mostly occur during the first two hours after taking a PALFORZIA dose and are usually mild or moderate but occasionally can be severe. Patients aged 12 years or older and/or with high sensitivity to peanut may be at higher risk of experiencing allergic symptoms during treatment.

Stop taking PALFORZIA and get medical treatment straight away if you have any of the following symptoms:
- Trouble breathing
- Throat tightness or feeling of fullness in throat
- Trouble swallowing
- Change in voice
- Dizziness or fainting or feeling of impending doom
- Severe stomach cramps or pain, vomiting or diarrhoea
- Severe flushing or itching of the skin
- Worsening of asthma or of any other breathing condition
- Heartburn, difficult swallowing, pain with swallowing, stomach pain or chest pain that does not go away or worsens

Certain conditions or factors can increase the likelihood of an allergic reaction. These include:
- Worsening of asthma
- Having an open sore or other damage to the lining of the mouth or the passage leading from the mouth to the stomach (oesophagus)
- Exercising

- Having a hot bath or shower
- Being very tired or missing sleep
- For women, having your period
- Taking certain pain medications such as aspirin or ibuprofen
- Drinking alcohol
- Being stressed
- Taking PALFORZIA on an empty stomach
- Having an illness such as a cold or flu or other viral infections

There are actions you should take to avoid some of these factors from affecting you. These factors include: exercise, having a hot bath or shower, drinking alcohol, or taking this medicine on an empty stomach. See the sections on 'PALFORZIA with food, drink and alcohol' and 'Dosing instructions' for advice on what to do about these.

For all other conditions or factors listed above, contact your doctor for advice if you experience allergic reactions during any of these.

Your doctor will prescribe adrenaline for you to self-inject, which you must have with you at all times in case you have a severe allergic reaction. Your doctor will tell you how to recognise an allergic reaction and teach you when and how to use the adrenaline. Talk to your doctor and read the adrenaline package leaflet if you have any questions about its use.

If you use adrenaline, do not take any further doses of PALFORZIA and seek emergency medical care immediately afterwards.

Desensitisation to peanut with PALFORZIA takes time. The ability to tolerate gradually increasing small amounts of peanut has been shown after completion of all up-dosing levels of PALFORZIA and after at least 3 months of maintenance therapy and this continues to improve over time.

You must take PALFORZIA every day to maintain the desensitisation it provides. Missing any doses can lead to an increased risk of allergic reactions.

PALFORZIA treatment may not work in all patients.

Children and adolescents

PALFORZIA is intended for children and young people aged 1 to 17 years and those who become adults whilst on treatment.

Do not give this medicine to children aged less than 1 year because it is not known if PALFORZIA is safe and effective in this age group.

Other medicines and PALFORZIA

Tell your doctor if you are taking, have recently taken, or might take any other medicines.

PALFORZIA with food, drink and alcohol

PALFORZIA should not be mixed with liquid (e.g., water, milk, juice, soup, smoothie).

Do not drink alcohol or medicines containing alcohol 2 hours before and 2 hours after taking PALFORZIA as this may increase the likelihood of an allergic reaction.

Pregnancy, breast-feeding and fertility

Do not start treatment with PALFORZIA if you are pregnant or planning to become pregnant.

If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines

PALFORZIA may have a small effect on your ability to drive, cycle or operate machinery. Exercise caution for 2 hours after taking a dose of PALFORZIA in case you have an allergic reaction which affects your ability to drive, cycle, or use machinery. Wait until all symptoms of such allergic reactions have gone away before driving, cycling, going to the playground or using machinery.

3. How to take PALFORZIA

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

PALFORZIA is prescribed by doctors who are experienced in the diagnosis and treatment of allergy and allergic reactions, including anaphylaxis.

How should I take PALFORZIA?

Dosing

There are 3 phases of treatment with PALFORZIA: initial dose escalation, up-dosing, and maintenance. You must complete these treatment phases in the order that your doctor has prescribed. During the initial dose escalation and up-dosing phases, the dose of PALFORZIA is increased in a precise way. During the maintenance phase, you take the same dose of PALFORZIA each day.

You should take PALFORZIA every day to maintain your level of desensitisation to peanuts.

Tell your doctor on the day of each clinic visit if you are feeling unwell or if you feel your asthma is less controlled.

Initial dose escalation

You will be treated with the first doses (initial dose escalation) of PALFORZIA over about 4 to 5 hours in your doctor’s clinic.

Patients 1 to 3 years old:
On the first day you will be treated with 0.5 mg, 1 mg, 1.5 mg and 3 mg of PALFORZIA.

Patients 4 to 17 years old:
On the first day you will be treated with 0.5 mg, 1 mg, 1.5 mg, 3 mg, and 6 mg of PALFORZIA.

Up-dosing

If you tolerate the initial dose-escalation phase, you will be asked to return to your doctor’s clinic on another day (usually the next day) to start the up-dosing phase.

The first dose of each up-dosing level is given to you by your doctor in a clinic. If you tolerate the first dose of a new dose level, your doctor will ask you to continue to take that dose every day at home for about 2 weeks. You will be observed for at least 60 minutes after the administering the first dose of a new up-dosing level until suitable for discharge.

Patients 1 to 3 years old:
There are 12 different dose levels of up-dosing, starting with PALFORZIA 1 mg (level 0) and increasing to PALFORZIA 300 mg (level 11).

The up-dosing levels are shown in the table below:

Daily dose	**Dose level**	**Presentation of dose**
1 mg	level 0	1 × 1 mg capsules (red)
3 mg	level 1	3 × 1 mg capsules (red)
6 mg	level 2	6 × 1 mg capsules (red)
12 mg	level 3	2 × 1 mg capsules (red) and 1 × 10 mg capsule (blue)
20 mg	level 4	1 × 20 mg capsule (white)
40 mg	level 5	2 × 20 mg capsules (white)
80 mg	level 6	4 × 20 mg capsules (white)
120 mg	level 7	1 × 20 mg capsule (white) and 1 × 100 mg capsule (red)
160 mg	level 8	3 × 20 mg capsules (white) and 1 × 100 mg capsule (red)
200 mg	level 9	2 × 100 mg capsules (red)
240 mg	level 10	2 × 20 mg capsules (white) and 2 × 100 mg capsules (red)
300 mg	level 11	1 × 300 mg sachet

You must have completed all 12 up-dosing levels before you can start maintenance treatment. It will take at least 24 weeks to complete all up-dosing levels.

Patients 4 to 17 years old:
There are 11 different dose levels of up-dosing, starting with PALFORZIA 3 mg (level 1) and increasing to PALFORZIA 300 mg (level 11).

The up-dosing levels are shown in the table below:

Daily dose	**Dose level**	**Presentation of dose**
3 mg	level 1	3 × 1 mg capsules (red)
6 mg	level 2	6 × 1 mg capsules (red)
12 mg	level 3	2 × 1 mg capsules (red) and 1 × 10 mg capsule (blue)
20 mg	level 4	1 × 20 mg capsule (white)
40 mg	level 5	2 × 20 mg capsules (white)
80 mg	level 6	4 × 20 mg capsules (white)
120 mg	level 7	1 × 20 mg capsule (white) and 1 × 100 mg capsule (red)
160 mg	level 8	3 × 20 mg capsules (white) and 1 × 100 mg capsule (red)
200 mg	level 9	2 × 100 mg capsules (red)
240 mg	level 10	2 × 20 mg capsules (white) and 2 × 100 mg capsules (red)
300 mg	level 11	1 × 300 mg sachet

You must have completed all 11 up-dosing levels before you can start maintenance treatment. It will take at least 22 weeks to complete all up-dosing levels.

During the up-dosing phase, your doctor will see you about every 2 weeks to assess you for a new up-dosing level.

Maintenance dosing

If you are able tolerate level 11 (300 mg) of the up-dosing phase, your doctor will ask you to continue taking PALFORZIA at a 300 mg dose every day as maintenance therapy.

Preparation for use

PALFORZIA is available either in capsules or sachets. Empty the powder from PALFORZIA capsules or sachets.

Do not swallow PALFORZIA capsules.

Open the daily dose of PALFORZIA.
- To open a capsule gently pull the two ends of the capsule apart over a bowl with soft food and empty the powder into the bowl by rolling each half of the capsule between the finger and thumb. Tap the ends of each half capsule to make sure that all the powder is emptied.
- To open a sachet carefully cut or tear along the top along the line indicated. Tip the sachet upside down over a bowl with soft food and tap the sachet to make sure that all the powder is emptied.

Empty the full dose of PALFORZIA oral powder on to a small amount of soft food to which you are not allergic such as fruit puree, yogurt, or rice-pudding. Make sure you are not allergic to the food used for mixing.

The food used for mixing should be cool and no warmer than room temperature.

Mix well.

Use just enough food to mix with PALFORZIA so you can eat it all in a few spoonfuls to take the full dose.

Take PALFORZIA immediately after mixing. However, if needed, you can mix PALFORZIA with food and keep it in a refrigerator for up to 8 hours before taking. If it is not used within 8 hours, throw it away and prepare a new dose.

Handling instructions

Do not breathe in PALFORZIA powder as this could cause breathing problems (worsening of asthma) or cause an allergic reaction.

Wash your hands immediately after handling PALFORZIA capsules or sachets.

When your doctor has told you that an up-dosing level is complete, you must dispose of all remaining capsules or sachets from that pack (see section 5) before starting on a new level. This includes any extra doses that are provided in each pack, if not used.

Dosing instructions

Take PALFORZIA at about the same time every day with food, preferably as part of your evening meal. Do not take this medicine on an empty stomach.

Do not take PALFORZIA at home on the days that you visit your doctor for assessment as your doctor will give you PALFORZIA on these days.

Children should be given each dose of PALFORZIA by an adult and they should be watched for about 1 hour afterwards for any symptoms of an allergic reaction.

Do not take within 2 hours of bedtime.

Do not have a hot bath or shower just before or for 3 hours after taking PALFORZIA.

Do not exercise just before or for 3 hours after taking PALFORZIA.

If you have been exercising or have taken a hot bath or shower and are feeling hot, or you are sweating and your heart is beating fast, do not take PALFORZIA until you have cooled down and your heart rate (pulse) has returned to normal.

Do not take more than your individual total daily dose according to your current dose level of PALFORZIA in a single day.

If you take more PALFORZIA than you should

Taking PALFORZIA at doses more than those recommended increases the risk of allergic reactions.

In the case of severe reactions such as difficulty swallowing, difficulty breathing, changes in your voice, or a feeling of fullness in the throat, treat the reaction with adrenaline self-injector as instructed by your doctor and then contact a doctor immediately.

If you forget to take PALFORZIA

Do not take a double dose to make up for a forgotten dose.

Missed doses of PALFORZIA may cause you to lose the peanut tolerance you have built up and increase your risk of allergic reactions.

If you miss your dose of PALFORZIA for 1 to 2 days in a row, take the next dose at your normal scheduled time the next day.

If you miss your dose of PALFORZIA for 3 days in a row or longer, stop taking PALFORZIA and contact your doctor for advice on how to start your treatment again.

If you stop taking PALFORZIA

Stopping PALFORZIA may cause you to lose the peanut tolerance you have built up and increase your risk of allergic reactions.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Important side effects

PALFORZIA can cause severe allergic reactions that may be life-threatening. If you get any of the following symptoms, stop taking PALFORZIA, treat the reaction according to any instructions previously provided by your doctor, and then contact a doctor **immediately**.
- Trouble breathing
- Throat tightness or feeling of fullness in throat
- Trouble swallowing or speaking

- Changes in voice
- Dizziness or fainting or feeling of impending doom
- Severe stomach cramps or pain, vomiting, or diarrhoea
- Severe flushing or itching of the skin

PALFORZIA can cause problems with the stomach and digestive system including eosinophilic oesophagitis. This is a condition that affects the passage between the mouth and the stomach and affects up to 1 in 1 000 people. Symptoms of eosinophilic oesophagitis can include:
- Trouble swallowing
- Food stuck in throat
- Burning in chest, mouth, or throat
- Regurgitation
- Difficulty feeding
- Poor weight gain
- Loss of appetite

If you have these symptoms persistently, contact a doctor.

Other side effects

Very common (may affect up to 1 in 10 people)
- Severe allergic reaction
- Coughing
- Irritation in the throat
- Tightness in the throat
- Pain in the throat and mouth
- Rhinitis allergic (runny nose, sneezing, itchy nose, nasal discomfort)
- Sneezing
- Stuffy nose
- Vomiting
- Stomach pain
- Feeling sick in the stomach (nausea)
- Itchy mouth
- Tingling or numbness in the mouth
- Itching
- Rash
- Hives

Common (may affect up to 1 in 100 people)
- Shortness of breath
- Wheezing
- Hoarse voice
- Throat clearing
- Tingling or numbness in the throat
- Indigestion
- Difficulty swallowing
- Increased salivia in mouth
- Lips inflammation
- Diarrhoea
- Mouth swelling
- Sores in the mouth
- Chest discomfort
- Flushing
- Tiredness
- Swelling face
- Feeling of something stuck in throat
- Head pain

- Anxiety
- Swelling under the skin
- Eczema
- Itchy eyes
- Swollen eyes
- Increased tearing
- Conjunctivitis allergic (itchy eye, watery eye)
- Eye redness
- Itchy ears
- Symptoms of eosinophilic oesophagitis (trouble swallowing, food stuck in throat, burning in chest, mouth, or throat, regurgitation, difficulty feeding, poor weight gain, loss of appetite)*

*not observed in 1-3 year old subjects.

Frequency not known
- Hypersensitivity

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store PALFORZIA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the blister or sachet after EXP. The expiry date refers to the last day of that month.

Store below 25°C.

Do not use this medicine if you notice any hard lumps of powder that do not easily fall apart or if the powder is discoloured.

Do not throw away any medicines via household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What PALFORZIA contains

The active substance is peanut protein from defatted powder of peanut (*Arachis hypogaea L.*) seed.

The other ingredients are:

PALFORZIA 0.5 mg, 1 mg, 10 mg, 20 mg oral powder in capsules for opening
Partially pregelatinised maize starch, microcrystalline cellulose, colloidal anhydrous silica, magnesium stearate

PALFORZIA 100 mg oral powder in capsules for opening
Microcrystalline cellulose, colloidal anhydrous silica, magnesium stearate

PALFORZIA 300 mg oral powder in sachet
Microcrystalline cellulose, colloidal anhydrous silica, magnesium stearate

What PALFORZIA looks like and contents of the pack

White to beige oral powder in capsule for opening or sachet.

Initial dose escalation (see section 3)

Each carton contains 13 capsules in 5 single-dose blisters:
- 0.5 mg (1 × 0.5 mg capsule)
- 1 mg (1 × 1 mg capsule)
- 1.5 mg (1 × 0.5 mg capsule and 1 × 1 mg capsule)
- 3 mg (3 × 1 mg capsules)
- 6 mg (6 × 1 mg capsules)

Up-dosing phase (see section 3)

Name/Capsule or sachet strength	**Pack contents by dose level (daily dose)**
PALFORZIA 1 mg oral powder in capsules for opening	**Level 0 (1 mg daily) - 1 to 3 years** 16 capsules in blisters 16 doses (each blister-well contains 1 capsule of 1 mg) **Level 1 (3 mg daily):** 48 capsules in blisters 16 doses (each blister-well contains 3 capsules of 1 mg) **Level 2 (6 mg daily):** 96 capsules in blisters 16 doses (each blister-well contains 6 capsules of 1 mg)
PALFORZIA 10 mg PALFORZIA 1 mg oral powder in capsules for opening	**Level 3 (12 mg daily):** 48 capsules in blisters 16 doses (each blister-well contains 1 capsule of 10 mg + 2 capsules of 1 mg)
PALFORZIA 20 mg oral powder in capsules for opening	**Level 4 (20 mg daily):** 16 capsules in blisters 16 doses (each blister-well contains 1 capsule of 20 mg) **Level 5 (40 mg daily):** 32 capsules in blisters 16 doses (each blister-well contains 2 capsules of 20 mg) **Level 6 (80 mg daily):** 64 capsules in blisters 16 doses (each blister-well contains 4 capsules of 20 mg)
PALFORZIA 100 mg oral powder in capsules for opening	**Level 9 (200 mg daily):** 32 capsules in blisters 16 doses (each blister-well contains 2 capsules of 100 mg)

Name/Capsule or sachet strength	Pack contents by dose level (daily dose)
PALFORZIA 100 mg PALFORZIA 20 mg oral powder in capsules for opening	**Level 7 (120 mg daily):** 32 capsules in blisters 16 doses (each blister-well contains 1 capsule of 100 mg + 1 capsule of 20 mg) **Level 8 (160 mg daily):** 64 capsules in blisters 16 doses (each blister-well contains 1 capsule of 100 mg + 3 capsules of 20 mg) **Level 10 (240 mg daily)**: 64 capsules in blisters 16 doses (each blister-well contains 2 capsules of 100 mg + 2 capsules of 20 mg)
PALFORZIA 300 mg oral powder in sachet	**Level 11 (300 mg daily):** 15 sachets (300 mg sachet)

Maintenance dosing (see section 3)

Each carton contains 30 sachets of 300 mg.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu