PALFORZIA® Instruction Manual for Healthcare Professionals

Risk minimisation information for PALFORZIA®▼ (defatted powder of *Arachis hypogaea L.*, semen (peanuts))

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

PALFORZIA® HCP Instruction Manual_UK version 1.0_October 2024.

Indication:

▼PALFORZIA is indicated for the treatment of patients aged 4 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.

Reporting side effects

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See **back page** for how to report adverse reactions.

Welcome

This document is designed to provide healthcare professionals with important risk minimisation information for PALFORZIA.

Please refer to the PALFORZIA Summary of Product Characteristics (SmPC) and/or submit a medical information request to **MedInfo-EU@stallergenesgreer.com** if you have any further questions about this medicine.

Contents

Summary of key risks

PALFORZIA has two known risks: **Anaphylaxis** and **Eosinophilic oesophagitis (EoE)**.

It is important that your patients and their caregivers are appropriately educated and prepared to identify and manage these risks.

Your patients and their caregivers should be aware of :

- Symptoms to watch out for
- When to use their/their child's adrenaline autoinjectors
- When to contact you or emergency services
- What the common co-factors associated with these risks are and how they can be managed or avoided

Anaphylaxis

Anaphylaxis is defined as a severe, potentially life-threatening systemic hypersensitivity reaction, characterised by being rapid in onset with life-threatening airway, breathing, or circulatory problems that is usually, though not always, associated with skin and mucosal changes. Patients with an IgE-mediated food allergy who receive oral immunotherapy may experience Anaphylaxis.

Treatment with PALFORZIA should not be initiated in a patient who has had severe or life-threatening anaphylaxis within the previous 60 days.

Anaphylaxis can involve any of the severe adverse reactons listed below.

- Difficulty swallowing
- Difficulty breathing
- Changes in voice or feeling of fullness in the throat
- Dizziness or fainting
- Severe stomach cramps or pain
- Vomiting
- Diarrhoea
- Severe flushing or itching of the skin

These reactions require immediate treatment, including the use of adrenaline and subsequent medical evaluation.

Eosinophilic oesophagitis

Patients with an IgE-mediated food allergy who receive oral immunotherapy may develop **Eosinophilic oesophagitis (EoE)**.

EoE can involve any of the following symptoms:

- Upper or lower abdominal pain
- Heartburn
- Chest pain
- Vomiting or nausea
- Dysphagia
- Reduced appetite
- Gastroesophageal reflux

For chronic/recurrent GI symptoms, the potential for a diagnosis of EoE should be considered. In patients who experience severe or persistent GI symptoms, treatment must be discontinued and a diagnosis of EoE should be considered.

Summary of key risks continued

It is essential that your patients and their caregivers are able to quickly recognise these symptoms, judge their severity, and know to treat severe adverse reactions with adrenaline and contact emergency services. In the emergency department, treatment should follow the anaphylaxis guidelines.

To facilitate emergency treatment of severe adverse reactions, please ensure that your patients and their caregivers are equipped with and trained on the use of adrenaline autoinjectors.

It is important that your patients and their caregivers know to contact you or another health care professional if they experience any of these reactions and before administering the next dose of PALFORZIA if symptoms of an escalating or persistent allergic reaction occur.

PALFORZIA

Treatment overview

Treatment overview

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

Self-injectable adrenaline (epinephrine) should be available to the patient or carer for any other dose. Two auto-injectors should be carried at all times.

Contraindications

- Current severe or uncontrolled asthma
- 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
- Hypersensitivity to any of the excipients (microcrystalline cellulose, partially pre-gelatinised maize starch, colloidal anhydrous silica, magnesium stearate)
- Do not initiate PALFORZIA treatment in a patient who has had severe or life-threatening anaphylaxis within the previous 60 days.

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

Dosing

Treatment with PALFORZIA is administered in 3 sequential phases: Initial Dose Escalation, Up-dosing, and Maintenance.

The dose configurations for each phase of dosing are provided in detail in the **SmPC.**

Preparation, administration and storage of PALFORZIA

Proper preparation and administration of PALFORZIA are critical in all treatment phases. The following guidance should be used for in-office and at-home dosing.

The powder must be taken orally after mixing with an age-appropriate soft food that the patient isn't allergic to.

The entire volume of the prepared mixture should be consumed promptly, but can be refrigerated for up to 8 hours if necessary.

Unused PALFORZIA, including prepared mixtures not consumed within 8 hours, must be disposed of in accordance with local requirements.

Opened capsule(s) or sachet must be disposed of promptly.

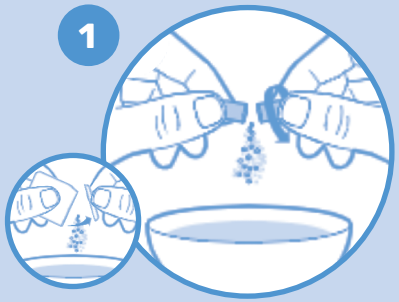
Hands should be washed immediately after handling PALFORZIA capsule(s) or sachet.

Each dose taken at home should be consumed daily with a meal at approximately the same time each day, preferably in the evening. Patients must not take their dose within 2 hours of going to sleep.

PALFORZIA should be stored somewhere cool (below 25°C), dry and out of the sight and reach of children.

Instructions to prepare and administer a dose

IMPORTANT: Capsules should not be swallowed whole.

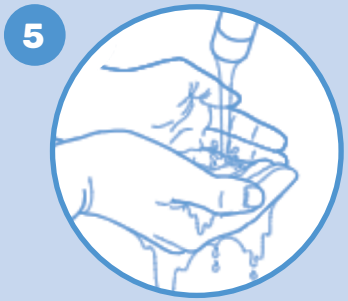


Open capsule(s) or sachet and empty the entire dose of PALFORZIA powder onto a few spoonfuls of refrigerated or room temperature semisolid food (e.g. rice-pudding, fruit puree or yoghurt). Do not use liquid (e.g. milk, water, juice) to prepare.

Mix well.

Consume the entire volume of the prepared mixture promptly.

Dispose of the opened capsule(s) or sachet.



Wash hands immediately after handling PALFORZIA capsule(s) or sachet.

Dispose of all unused PALFORZIA.

Treatment overview

Initial dose escalation

Initial Dose Escalation (IDE) 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.

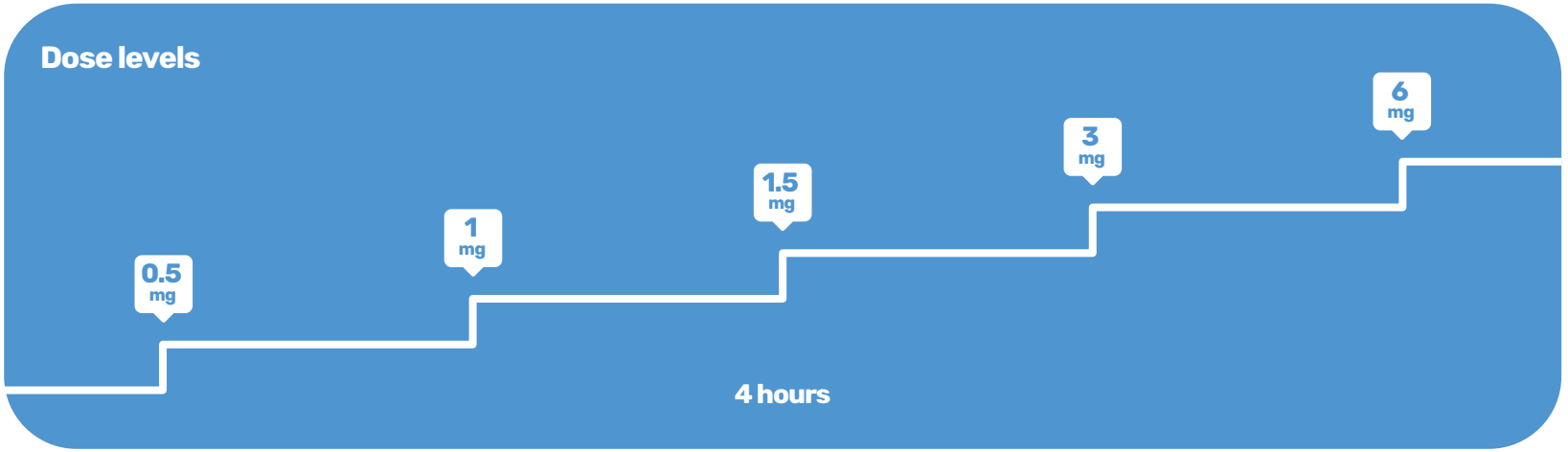
Initial Dose Escalation is administered in sequential order on a single day beginning at 0.5 and completeing with 6 mg if tolerated.

Summary

- Takes place at the clinic
- Typically lasts ~4 hours
- Consists of 5 sequential dose escalations (no dose level should be omitted)
- Each dose should be administered sequentially (if tolerated) separated by an observation period of 20-30 minutes
- Observe patients after final dose for at least 60 minutes

Safety considerations

- **Discontinue treatment with PALFORZIA for patients who are unable to tolerate doses up to and including the 3mg dose during IDE**
- Patients who tolerate at least the 3mg single dose of PALFORZIA during Initial Dose Escalation must return to the healthcare setting for initiation of Up-dosing the next day, if possible
- Repeat Initial Dose Escalation in a healthcare setting if the patient is unable to begin Up-dosing within 4 days
- **Please refer to SmPC for more information**



Assessing symptom severity during IDE

The following protocol was used to assess dose tolerability and next steps during Initial Dose Escalation phase in the PALISADE trial (Vickery et al. 2018)

No symptoms or mild oral/pharyngeal pruritus symptoms only	Other mild symptoms	Moderate symptoms	Severe symptoms
Time to next dose: 30 mins **Next dose:** Advanced to next level	**Time to next dose:** Advanced to next level within 30 to 60 minutes; or treated with antihistamine and then resumed dose escalation within 60 min of last dose provided that the patient had no or only minimal residual signs or symptoms. If however the subject required a second medication (e.g. adrenaline or a beta-agonist) to treat the symptoms, or more than 2 doses of an antihistamine, Initial Dose Escalation was discontinued.	**Occurring at ≤3 mg:** Treat as indicated for moderate reactions; stop Up-dosing and discontinue PALFORZIA. **Occurring at 6 mg:** Treat as indicated for moderate reactions; patient could continue with Up-dosing the next day.	Treat as indicated for severe reactions; discontinue PALFORZIA.

Dose modifications are not appropriate during Initial Dose Escalation.

Up-dosing

Initial Dose Escalation must be completed before starting Up-dosing.

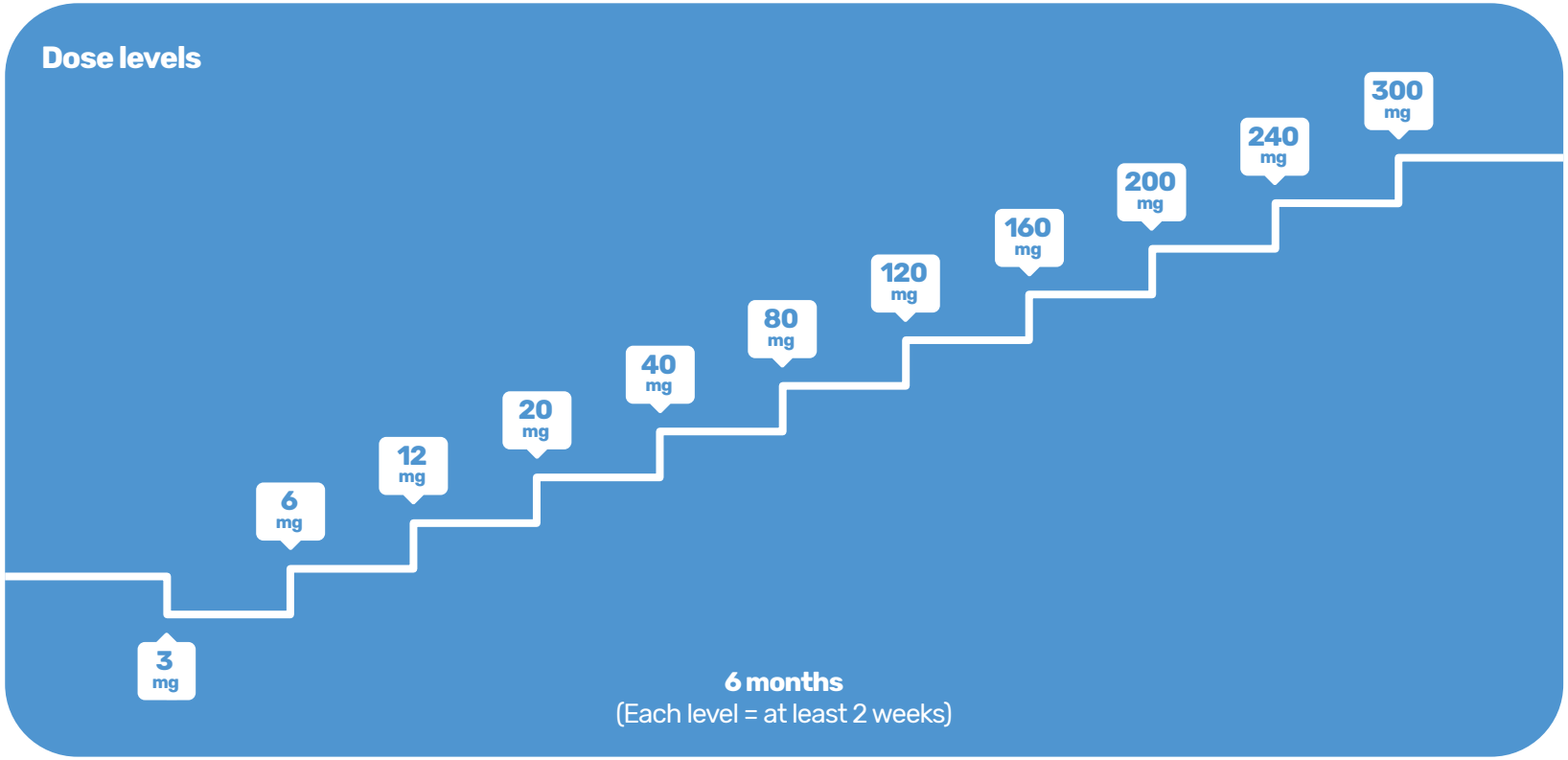
Up-dosing consists of 11 dose levels and is initiated at a 3 mg daily dose (Level 1).

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.

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

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

At each dose-level during Up-dosing, it is important that the dose you give your patient in clinic and the doses they take at home are from the same batch to avoid variations in potency range.



Summary

- Takes place in office and at home
- Consists of 11 dose levels and is initiated at a 3mg daily dose
- No dose level should be omitted
- Each dose level is administered daily and increased sequentially in 2-week intervals, if tolerated
- Observe patients for at least 60 minutes after each dose

No more than 1 dose should be consumed per day. Instruct patients not to take a dose at home on the day of a scheduled office visit.

Instruct patient to return to the health care setting every 2 weeks for each subsequent assessment for a new Up-dosing level.

An Up-dosing dose level can be maintained for longer than 2 weeks if a patient is unable to progress to the next level because of allergy symptoms or for practical reasons for patient management.

Ensure that your patients only have one dose level in their possession at any one time. This may involve asking that they discard unused doses of a different dose level.

Ensure that the doses given in clinic and those that will be given at home come from the same Up-dosing pack.

For children, instruct parents/caregivers to ensure that:

- All doses of PALFORZIA are given by an adult.
- Children should be observed for about 1 hour after dosing to monitor for any symptoms of an allergic reaction.

Safety considerations

Discontinue PALFORZIA treatment for:

- Patients unable to comply with the daily dosing requirements

  EoE is a known risk of OIT. Consider discontinuation of PALFORZIA referral to a gastroenterologist for diagnosis of EoE in patients who experience severe or persistent gastrointestinal symptoms, including dysphagia, gastroesophageal reflux, chest pain or abdominal pain.

Do not omit a dose level from the Up-dosing schedule.

Do not escalate Up-dosing faster than every 2 weeks.

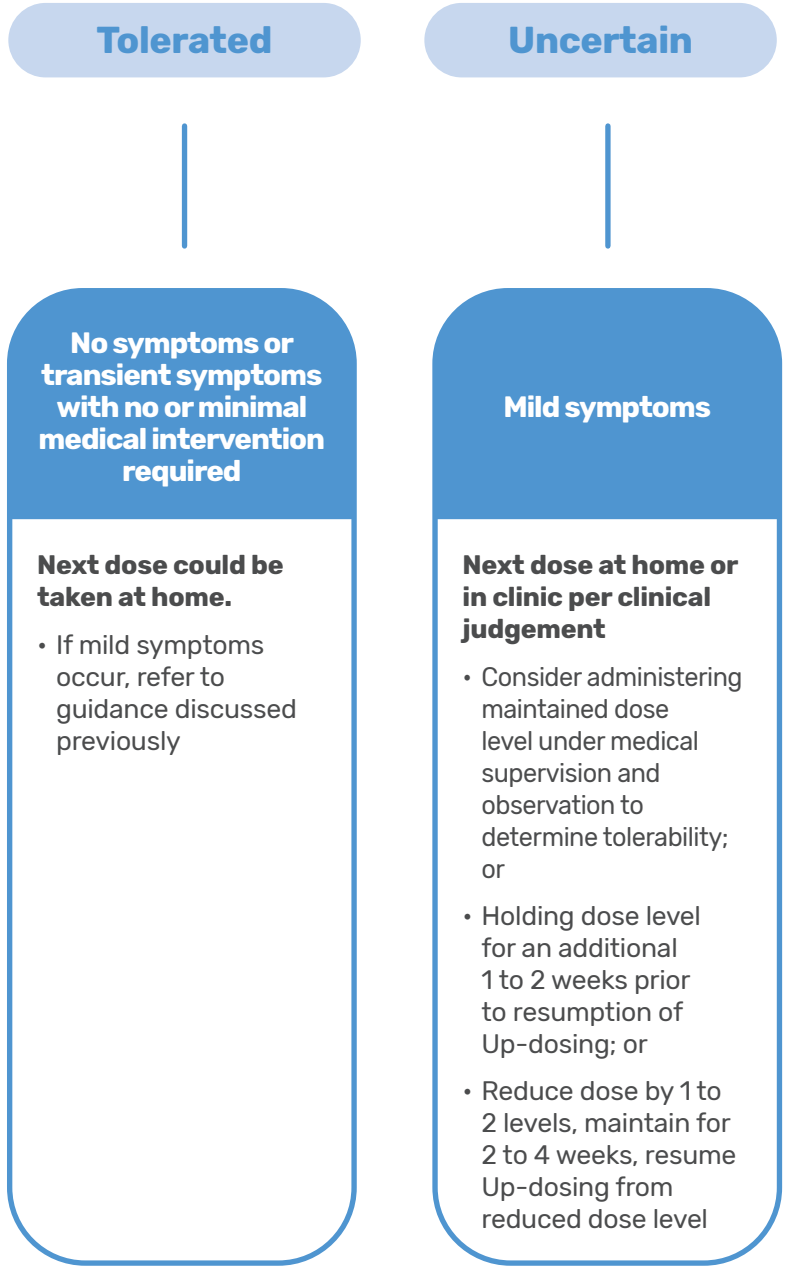
Treatment should be temporarily withheld if the patient is experiencing an acute asthma exacerbation.

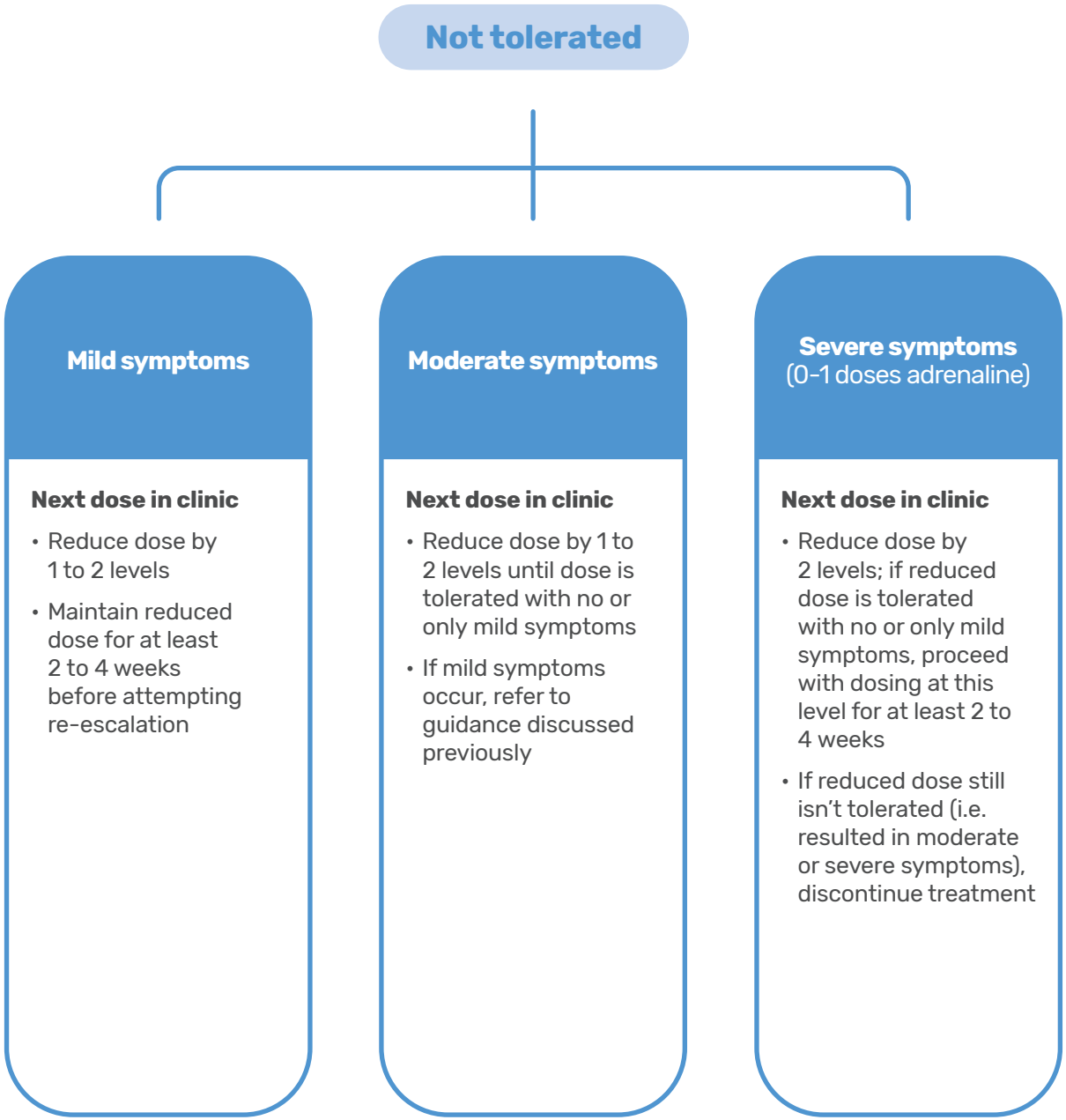
Patients who have recurrent asthma exacerbations should be re-evaluated and discontinuation considered.

Assessing symptom severity

The first dose of each new Up-dosing level is administered under the supervision of a healthcare professional in a healthcare setting with the ability to manage potentially severe allergic reactions, including anaphylaxis.

- If the first dose is tolerated, the patient may continue that dose level at home
- If the first dose is not tolerated, consider dose modification or discontinuation




Not tolerated
Mild symptoms
Next dose in clinic
• Reduce dose by 1 to 2 levels
• Maintain reduced dose for at least 2 to 4 weeks before attempting re-escalation
Moderate symptoms
Next dose in clinic
• Reduce dose by 1 to 2 levels until dose is tolerated with no or only mild symptoms
• If mild symptoms occur, refer to guidance discussed previously
Severe symptoms
(0-1 doses adrenaline)
Next dose in clinic
• Reduce dose by 2 levels; if reduced dose is tolerated with no or only mild symptoms, proceed with dosing at this level for at least 2 to 4 weeks
• If reduced dose still isn't tolerated (i.e. resulted in moderate or severe symptoms), discontinue treatment

Maintenance dosing

All doses of Up-dosing must be completed before starting Maintenance dosing.

The Maintenance dose of PALFORZIA is 300 mg daily.

Continued daily treatment is required to maintain the tolerability and clinical effects of PALFORZIA.

Efficacy and safety data are currently available for up to 24 months of treatment with PALFORZIA and the effects of stopping treatment on clinical efficacy has not been evaluated.

When your patients reach Maintenance dosing, consider scheduling routine check-ups with them to monitor their progress on therapy.

Continued long term, daily use of the 300 mg ongoing therapeutic dose is required to maintain the desensitisation effects of PALFORZIA.

If treatment with PALFORZIA is stopped, please ensure your patients and their caregivers know to continue carrying their adrenaline autoinjectors at all times.

Management of consecutive missed doses

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 judgement.

5 to 14 days

- Patients may resume Up-dosing with PALFORZIA under medical supervision in a health care setting at a dose of 50% or less of the last tolerated dose.

Greater then 14 days

- Patient compliance should be evaluated and it should be considered to re-start up-dosing at 3mg under supervision in a health care setting or to discontinue treatment completely.

Dose modification instructions

Dose modifications are not appropriate during initial dose escalation. Treatment must be discontinued in any patients who cannot tolerate at least the 3 mg single dose of PALFORZIA, or who require medical intervention (e.g. use of adrenaline) at any dose, during initial dose escalation.

Consider dose modification or discontinuation for patients who do not tolerate Up-dosing.

Temporary dose modification of PALFORZIA may be required for patients who experience allergic reactions during Up-dosing or Maintenance, for patients who miss doses, or for practical reasons of individual 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. Use clinical judgment to determine the best course of action on a patient by patient basis, which can include maintaining the dose level for longer than 2 weeks, reducing, withholding, or discontinuing PALFORZIA doses.

Understanding PALFORZIA doses

PALFORZIA Up-dosing is broken into 11 steps.

At each step, the daily dose of PALFORZIA is slightly increased.

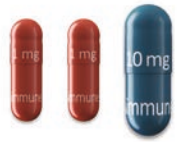
For the first 10 steps, the doses come in capsules of different shapes, sizes and colours which are grouped together in separate blisters. At the 11th step, and during Maintenance dosing, the daily dose comes in a sachet.

This is what the capsules and sachet will look like at each Up-dosing step.

Step 1
(3 mg daily dose)

Step 2
(6 mg daily dose)

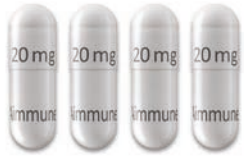
Step 3
(12 mg daily dose)



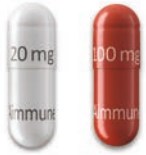
Step 4
(20 mg daily dose)

Step 5
(40 mg daily dose)

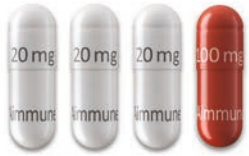
Step 6
(80 mg daily dose)



Step 7
(120 mg daily dose)

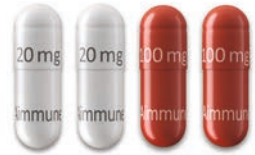


Step 8
(160 mg daily dose)



Step 9
(200 mg daily dose)

Step 10
(240 mg daily dose)



Step 11
(300 mg daily dose)

Patient and caregiver education

It is essential that your patients and their caregivers understand what PALFORZIA treatment involves, the key safety considerations and warnings, and how to use the drug safely.

To facilitate this, handbooks similar to this one with complementary short videos and a 'Patient Alert' wallet card have been developed for patients aged 4-6, 7-11 and 12-17 years. A separate handbook has also been developed for caregivers.

Please provide these materials to your patients and their families when they have been prescribed PALFORZIA and encourage them to read them and discuss any questions they may have with you.

All patient and caregiver handbooks and videos can be accessed on the following website:

www.aimmune.co.uk

Commitment to therapy

Compliance and adherence to treatment is required to maintain the effects and tolerability of PALFORZIA.

Currently, efficacy and safety data are available for up to 24 months of PALFORZIA treatment. No recommendation can be made about the duration of treatment beyond 24 months.

PALFORZIA is a long-term, daily treatment that has associated risk and requires commitment from both the patient, their caregivers and families. It is not appropriate for all peanut-allergic individuals.

The desensitisation response to PALFORZIA is achieved gradually over the first year of treatment in most patients. Studies have shown that clinically relevant desensitisation may be achieved in the majority of patients following the completion of all Up-dosing levels and after at least 3 months of Maintenance with the ongoing therapeutic dose (see section 5.1 of the SmPC for additional details). Continued long-term daily use of the 300 mg ongoing therapeutic dose is required to maintain the desensitisation effects of PALFORZIA.

As with any immunotherapy treatment, clinically meaningful desensitisation may not occur in all patients (see section 5.1 of the SmPC for additional details).

It is imperative that prescribers of PALFORZIA and prospective patients/their caregivers are provided with sufficient information to make an informed and shared decision as to whether this treatment it appropriate for them.

PALFORZIA

Safety overview

Overview

Common adverse reactions

The most common adverse reactions (of any severity) reported in PALFORZIA clinical trials were abdominal pain, throat irritation, general pruritus, nausea, vomiting, urticaria, oral pruritus, abdominal discomfort, and upper abdominal pain.

The incidence and maximum severity of adverse reactions peaked during Up-dosing and decreased with Maintenance dosing.

Symptoms recorded in a clinical setting typically occurred shortly after dosing (median onset 4 to 8 minutes) and resolved within 15 to 30 minutes.

10.5% of trial participants discontinued trial drug due to 1 or more adverse events; the most common of which were abdominal pain, vomiting, nausea and systemic allergic reactions.

Please see the full PALFORZIA SmPC for additional information of adverse reactions.

Special warnings

If patients have asthma, it should be well controlled prior to initiation of therapy. Patients should not have active wheezing, a flare of atopic disease (e.g. atopic dermatitis) or suspected intercurrent illness prior to initiation of therapy.

Please see accompanying full SmPC for additional information.

Systemic allergic reactions including anaphylaxis

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 must be educated to recognise the signs, symptoms and severity of allergic reactions. Your patients and their caregivers should be appropriately trained to provide prompt emergency treatment (including treatment with adrenaline) and to seek immediate medical attention in the event of severe allergic reactions. In the event of an escalating or persistent allergic reaction, patients and their caregivers should be instructed to contact you or a healthcare professional before administering the next dose of PALFORZIA.

Adrenaline

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

PALFORZIA may not be suitable for patients who are taking medications that can inhibit or potentiate the effect of adrenaline such as beta blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), calcium channel blockers, or tricyclic antidepressants.

Eosinophilic oesophagitis

Biopsy-confirmed eosinophilic oesophagitis (EoE) was reported in 12 subjects (1%) who received PALFORZIA during the entire PALFORZIA clinical trial programme (including phase 2 subjects). Symptomatic improvement was reported in all 12 subjects after discontinuation of PALFORZIA.

Discontinue PALFORZIA and consider referral to a gastroenterologist for diagnosis of EoE in patients who experience severe or persistent gastrointestinal symptoms, including dysphagia, vomiting, nausea, gastroesophageal reflux, chest pain, or abdominal pain.

Asthma

Uncontrolled asthma is a risk factor for a serious outcome, including death, in anaphylaxis. Ensure patients with asthma have their asthma under control prior to initiation of PALFORZIA. PALFORZIA should be temporarily withheld if the patient is experiencing an acute asthma exacerbation. Following resolution of the exacerbation, resumption of PALFORZIA should be undertaken cautiously. Re-evaluate patients who have recurrent asthma exacerbations and consider discontinuation of PALFORZIA.

Gastrointestinal adverse reactions

Gastrointestinal adverse reactions were commonly reported in PALFORZIA-treated subjects, and dose modification should be considered for patients who report these reactions. For severe or persistent gastrointestinal symptoms consider a diagnosis of eosinophilic esophagitis.

Pregnancy and lactation

There are no data from the use of PALFORZIA in pregnant or lactating women.

Initiation of treatment with PALFORZIA is not recommended during pregnancy.

For patients who are established on PALFORZIA treatment and become pregnant, the benefits of remaining on treatment should be weighed against the risks of an adverse reaction.

Please contact Aimmune Therapeutics using the details on the back page of this handbook if any of your patients become pregnant while taking PALFORZIA so that they can be added to the PALFORZIA pregnancy registry.

Management of co-factors

Patients may be more likely to experience allergy symptoms after dosing and/or anaphylaxis in the presence of co-factors which may be modifiable (e.g. exercise shortly before or after dosing) or non-modifiable (e.g. intercurrent illness).

Not all patients may be affected by co-factors but please ensure you counsel all patients on the importance of identifying and, where possible, managing co-factors.

On an individual basis and when needed, adjust the time of dosing 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.

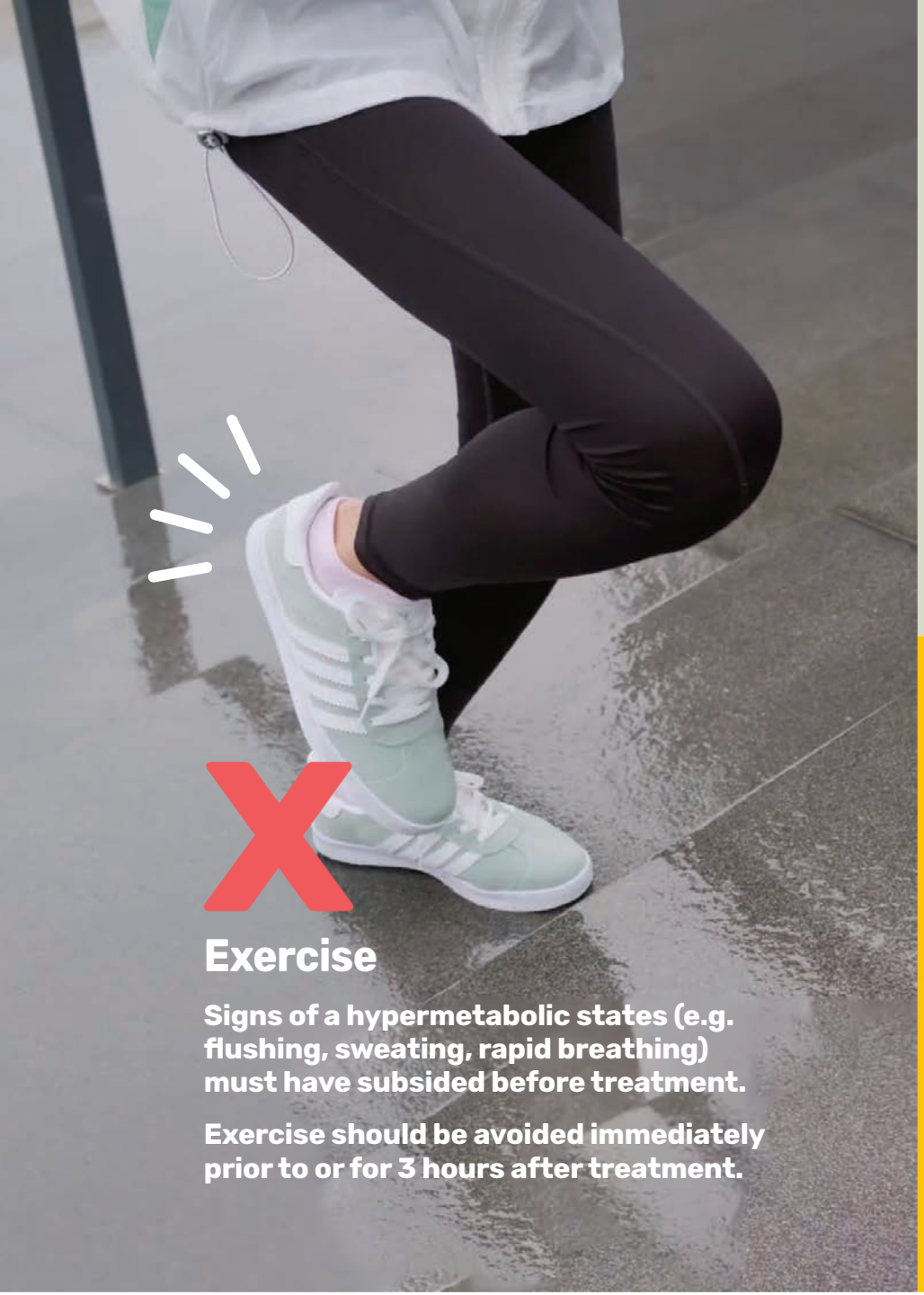
Modifiable co-factors

Fasting or empty stomach

Patients should not take a dose on an empty stomach or while they are fasted. They should be instructed to take PALFORZIA with a meal.

Hot bath or shower

Patients should avoid having a hot bath or shower immediately prior to treatment or for 3 hours after.



Exercise

Signs of a hypermetabolic states (e.g. flushing, sweating, rapid breathing) must have subsided before treatment.

Exercise should be avoided immediately prior to or for 3 hours after treatment.

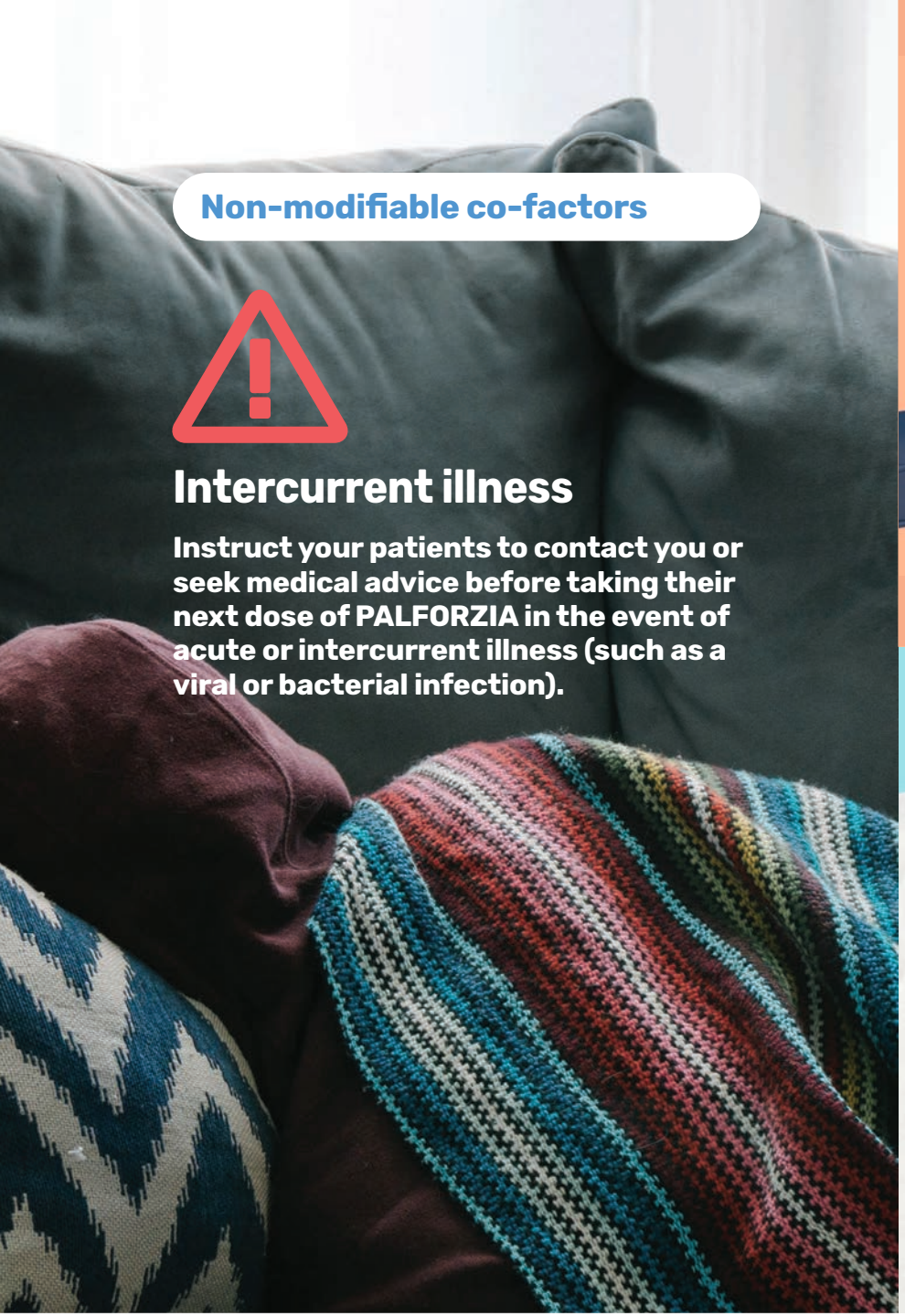
Alcohol

Patients should not consume alcohol 2 hours prior to or following treatment.

Non-steroidal anti-inflammatory medicines

Additional consideration and caution should be used if the patient is taking NSAID medicines.

Non-modifiable co-factors



Intercurrent illness

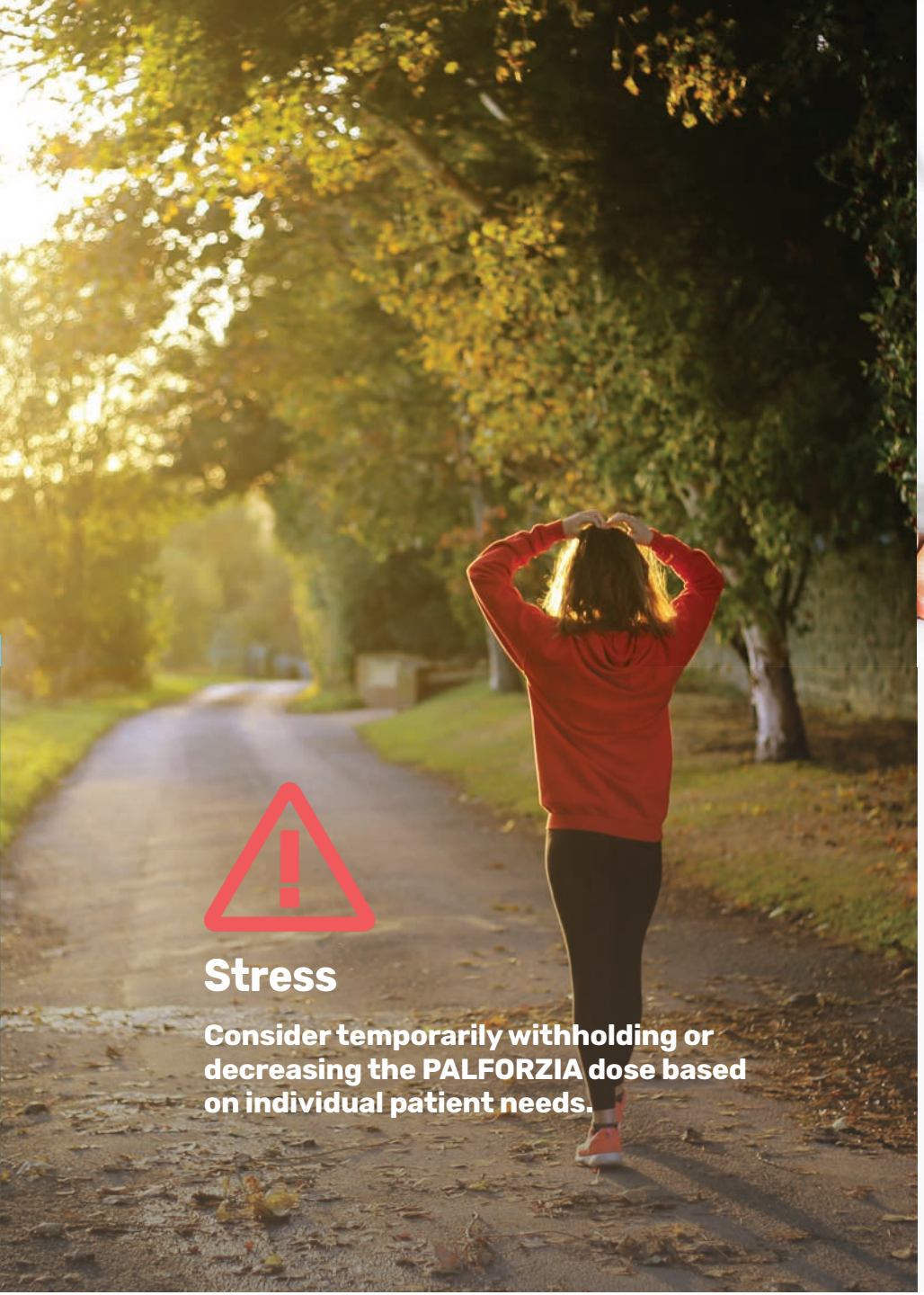
Instruct your patients to contact you or seek medical advice before taking their next dose of PALFORZIA in the event of acute or intercurrent illness (such as a viral or bacterial infection).

Exacerbation of asthma

Instruct your patients to contact you or seek medical advice before taking their next dose of PALFORZIA in the event of exacerbation of asthma.

Menstruation

Consider temporarily withholding or decreasing the PALFORZIA dose based on individual patient needs.



Stress

Consider temporarily withholding or decreasing the PALFORZIA dose based on individual patient needs.

Fatigue or sleep deprivation

Consider temporarily withholding or decreasing the PALFORZIA dose based on individual patient needs.

Contact information

Stallergenes UK Ltd

30 Old Bailey

London

EC4M 7AU

Medical information and safety reporting

Email: MedInfo-EU@stallergenesgreer.com

Tel: +44 (0)800 0487 217

Healthcare professionals are asked to report any suspected adverse reactions via https://yellowcard.mhra.gov.uk/the-yellow-card-scheme/

STALLERGENES GREER

PALFORZIA® Patient Educational booklet (12-17)_UK version 2.0_October 2024.