Briefing Paper for Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee (APC)

NICE Technology Appraisals: Local implementation

NICE TA Guidance	Palforzia for treating peanut allergy in children and young people (NICE TA 769)		
Available at	https://www.nice.org.uk/guidance/ta769		
Date of issue	2 February 2022	**Implementation deadline**	2 May 2022

Medicine details	
Name, brand name	Palforzia ▼
Manufacturer	Aimmune Therapeutics UK Limited
Licensed indication	**4.1 Therapeutic indications [accessed on 12 April 2022 16:22]** 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.
Formulation	White to beige oral powder in capsules for opening or sachet. **[accessed on 12 April 2022 16:22]**
Usual dosage	**Posology [accessed on 12 April 2022 16:22]** Treatment with PALFORZIA is administered in 3 sequential phases: **<u>Initial dose escalation</u>** • 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 6 mg (see Table 1). **Table 1: Dose and capsule presentation for initial dose escalation**

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

• 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 3 mg single dose PALFORZIA 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.
- Up-dosing consists of 11 dose levels and is initiated at a 3 mg dose (see Table 2).
- 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 Table 2 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 Table 2.

Table 2: Daily dosing configuration for up-dosing

Dose level	Total daily dose	Presentation of dose (capsule colour)	Dose duration (weeks)	
1	3 mg	3 × 1 mg capsules (red)	2	42
2	6 mg	6 × 1 mg capsules (red)	2	84
3	12 mg	2 × 1 mg capsules (red) 1 × 10 mg capsule (blue)	2	42
4	20 mg	1 × 20 mg capsule (white)	2	14
5	40 mg	2 × 20 mg capsules (white)	2	28
6	80 mg	4 × 20 mg capsules (white)	2	56
7	120 mg	1 × 20 mg capsule (white) 1 × 100 mg capsule (red)	2	28
8	160 mg	3 × 20 mg capsules (white) 1 × 100 mg capsule (red)	2	56
9	200 mg	2 × 100 mg capsules (red)	2	28
10	240 mg	2 × 20 mg capsules (white) 2 × 100 mg capsules (red)	2	56
11	300 mg	1 × 300 mg sachet	2	14

- 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 Table 2 **Maintenance therapy** • All dose levels of up-dosing must be completed before starting maintenance. • The maintenance dose of PALFORZIA is 300 mg daily. **Table 3: 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 with PALFORZIA.** No recommendation can be made about the duration of treatment beyond 24 months. • The effect of stopping treatment on maintenance of clinical efficacy has not been evaluated. • If treatment with PALFORZIA is stopped, patients must continue to carry self-injectable adrenaline at all times.
NICE recommended dosage/schedule	As above

Disease and potential patient group

Brief description of disease

www.patient.co.uk
Nuts and peanuts can cause allergic reactions, which are sometimes severe. A severe reaction to nuts is called anaphylaxis and can be life-threatening. Symptoms often start quickly, within an hour of coming into contact with a nut, and sometimes within minutes. If you have a nut allergy, avoiding foods that contain nuts will prevent an allergic reaction. But, if you do come into contact with nuts, and a reaction starts then treating it quickly is important. If you have a severe allergic reaction, if available, give yourself an adrenaline (epinephrine) injection straightaway and call an ambulance. If you are well prepared and take action quickly the risk of suffering any serious problems is small.

Potential patient numbers per 100,000 & per CCG

NICE resource template accessed 13 April 2022 12:52

Patient numbers	Local assumption future practice - activity year 1	Local assumption future practice - activity year 2	Local assumption future practice - activity year 3	Local assumption future practice - activity year 4	Local assumption future practice - activity year 5
	0.44%	0.89%	1.50%	1.80%	2.11%
Per 100,000	1	2	4	5	5

	Surrey Heartlands CCG	12	25	41	50	58

SUMMARY

NICE recommendation

1. Recommendations

1.1. Palforzia is recommended, within its marketing authorisation, as an option for treating peanut allergy in children aged 4 to 17. It can be continued in people who turn 18 while on treatment. Palforzia should be used with a peanut-avoidant diet.

Why the committee made these recommendations

For people with peanut allergy, strictly avoiding peanuts and being ready to respond to an emergency are the main ways to protect against reactions to accidental exposure.

Clinical trial evidence shows that Palforzia improves tolerance to peanut protein compared with placebo when precise amounts are used in a food challenge test. And it is likely that Palforzia improves people's quality of life once they are having a stable dose. People are likely to need to take Palforzia or regularly include peanuts in their diet to maintain the tolerance they gained. It is uncertain how long people would continue treatment, but few are likely to need to continue Palforzia for the rest of their lives.

The most likely cost-effectiveness estimates are within the range that NICE normally considers an acceptable use of NHS resources. Also, additional benefits of Palforzia may not have been captured in the cost-effectiveness results. So, Palforzia is recommended.

Cost implications*

Cost of product: The list price of Palforzia is £10.12 per day. A flat price is applied for each Palforzia dose (range 0.5 mg to 300 mg).

Annual cost per patient:

	Cost of phase (plus VAT)
Initial dose escalation (Single day)	13 x £10.12 = £131.56 *(plus VAT)*
Up-dosing phase (22 weeks)	448 x £10.12 = £4,533.76 *(plus VAT)*
	Total cost for induction phase = £4,665.32 *(plus VAT)*
Maintenance therapy (remainder of 1st year)	*£2,125.20 (plus VAT) for 1st 12 months*

1st year treatment (including initial escalation, up-dosing and maintenance) = £6,790.52 (plus VAT)
2nd year treatment (at maintenance phase) = £3,693.80 (plus VAT)

Costs over time

The table below shows the number of patients from Surrey Heartlands CCG (using the NICE resource template) expected to be initiated on Palforzia over the next 5 years. The NICE resource template makes assumptions about the number of patients that may discontinue treatment each year.

The costs below show the costs of treatment and the number of patients each year to year 5. This would not include those patients that continue on treatment from the previous year. The costs to the health economy are for the whole CCG and not per place.

Patient numbers	Local assumption future practice - activity year 1	Local assumption future practice - activity year 2	Local assumption future practice - activity year 3	Local assumption future practice - activity year 4	Local assumption future practice - activity year 5
	0.44%	0.89%	1.50%	1.80%	2.11%
Surrey Heartlands CCG	12	25	41	50	58
Treatment cost (year 1)	**£81,486**	**£169,763**	**£278,411**	**£339,526**	**£393,850**

Has dose escalation been considered as part of the NICE costing template?

- *Not available*

Availability of PAS and details (if appropriate):

- Price as above and in NICE guidance. No commercially confidential PAS price

Availability of homecare service (if appropriate):

- *None*

**NICE funding requirements are based on Quality Adjusted Life Years (QALY) threshold. If there is evidence that the incremental cost rises above this threshold in the future, the APC may reconsider the commissioning status.*

Alternative treatments and cost per patient (per year / per month as appropriate)

Other NICE recommended products:

No comparative product available.
www.openprescribing.net
However, an analysis of Surrey Heartlands CCG prescribing for Adrenaline Autoinjectors for the last 12 months is as follows:

across NHS SURREY HEARTLANDS CCG

	Jan '22	Financial YTD (Apr '21—Jan '22)
Cost (£)	56,813	599,801
Items	755	8,322

In line with the license for Palforzia, all patients should continue to carry adrenaline autoinjectors during treatment. Although an assumption could be made that there would be a reduction in usage of the adrenaline autoinjectors over time, there is no mention of this assumption in the NICE guidance.
Also adrenaline autoinjectors are prescribed for other indications and not just for peanut allergies so the above information may not only be related to prescribing for peanut allergy.

Options not reviewed by NICE but used in standard practice:
None

Impact to patients

- Patients and parents/carers/guardians would welcome this innovative treatment.
- Patients would welcome a treatment option that would reduce the risks of accidental peanut exposure and improve quality of life of children with peanut allergy and their carers.
- Commitment to attend hospital to receive a comprehensive dosing regimen for 6 months to receive Palforzia. (Initial hospital attendance followed by a hospital attendance every 2 weeks for dose titration (up-dosing))
- Treatment with Palforzia increases the risk of an anaphylactic reaction as an adverse event of treatment.
- www.nice.org.uk Clinical experts consider that patients can start to include peanuts in their diet to maintain their tolerance instead of continuing treatment with Palforzia. This is not reflected in the marketing authorisation for Palforzia, which notes that daily maintenance is required to maintain the tolerance and clinical effects of Palforzia. The clinical experts explained that people not regularly including peanuts in their diet after Palforzia treatment may lose tolerance and will need to return to strictly avoiding peanuts and being prepared for emergencies.
- Potential for raised stress and anxiety associated with adding a food to the patient's diet that that they have avoided.

www.medicines.org.uk

Management of consecutive missed doses

Missed doses of PALFORZIA may pose a significant risk to patients due to potential loss of desensitisation.

Impact to primary care prescribers

- There may be a potential for shared care for maintenance once our allergy specialists have more experience of this treatment.
- Primary care prescribers should ensure that patient medication records include any medicine for which prescribing remains the responsibility of secondary or tertiary care. This will ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

Impact to secondary care

- Intensive regimen for initiation and up-dosing which NICE state ….'extending into delivering oral immunotherapy would demand additional investment, particularly in capacity and training of staff'.
- There is a need during up-dosing to observe the patient for 60 minutes after the initial dose in that up-dosing level and so there would need to be capacity to undertake this observation for 11 attendances every 2 weeks, in an outpatient setting.

www.nice.org.uk

- Palforzia needs to be delivered under the care of a specialist healthcare professional qualified in the diagnosis and treatment of allergic diseases (stated in the Summary of Product Characteristics (SmPC)) and therefore, the capacity to offer Palforzia treatment in England is likely to be restricted to a small number of specialist secondary and tertiary paediatric allergy services. Not all specialist allergy clinics are expected to be able to deliver Palforzia treatment. There are expected to be around 20 clinic providers in England during each of the first 5 years of Palforzia being available that can offer the treatment.

Impact to CCGs

www.nice.org.uk

- This technology is commissioned by clinical commissioning groups. It is expected to be provided in allergy clinics within NHS hospital trusts.
- Administrative costs for first 6 months of treatment (12 appointments with 1st appointment as a day case and subsequent 11 appointments as outpatient attendances)
- The resource impact template and report model an uptake level that is low. This is based on treatment with Palforzia involving several risks for the patient (strict peanut avoidance and emergency preparedness continue during treatment) and requiring extensive monitoring from carers who are often risk averse. In addition to this the uptake of Palforzia is also expected to be affected by capacity within food allergy clinics during the next five years.
- It is assumed that no new allergy centres are likely to open during the next 5 years.

Implementation

- Capacity in clinics to provide this treatment to this cohort of patients could be an issue for specialist colleagues.
- Educational risk materials available as follows: https://www.medicines.org.uk/emc/product/12197/rmms
    - Caregiver safety educational booklet
    - HCP instruction manual
    - Patient Alert Card
    - Patient safety educational booklet (12 – 17 years old)
    - Patient safety educational booklet (4-6 years old)
    - Patient safety educational booklet (7-11 years old)

Recommendation to APC

PbRe: No

Recommended traffic light status (see attached guidelines):

- RED traffic light status proposed with a view to consider shared care for maintenance with primary care once our specialist colleagues have more experience.

Additional comments:
Sussex Commissioners:

- Red traffic light status
- New product with a complex dose regimen and therefore patients should be managed and maintained by the specialist.
- Decision could be reviewed in time once further clinical experience is gained.

South West London Commissioners:

- Red traffic light status until more experience is obtained, with a view to review in the future when there is a bit more experience with its use.

References:

1 www.nice.org.uk [accessed on 13 April 2022]
2 www.medicines.org.uk [accessed on 13 April 2022]

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Declaration of Interest None Date: 13 April 2022

Reviewed by:

Name, Designation, Organisation

Declaration of Interest:

XXXX

Date: XXXX

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1	*13 April 2022*	*Clare Johns*	*Draft V1*	*Out for consultation*
v.2				
v.3				

APPENDIX 1
Information taken directly from the NICE resource template for reference

NICE resource impact template [accessed 13 April 2022 12:21]

Administration costs - fall within the first year of treatment therefore applied to all people who start treatment				
Phase of treatment	**Tariff description**	**Tariff**	**Number of attendances**	**Total cost of treatment**
Initial dose escalation	National Tariff 2021/22 Daycase rate for HRG code WH05Z Allergy or Adverse Allergic Reaction.	£325	1	**£325**
Up-dosing	National Schedule of NHS Costs Year: 2019-20 - Outpatient Attendances DataService code 255, Paediatric Clinical Immunology and Allergy Service. Consultant-led, follow-up appointment.	£238.37	11	**£2,622**
			12	**£2,947**

Monitoring costs - for children receiving Palforzia				
	Tariff description	**Tariff**	**Number of attendances**	**Total cost of treatment**

Year 1 of treatment	National Schedule of NHS Costs Year : 2019-20 - Outpatient Attendances DataService code 255, Paediatric Clinical Immunology and Allergy Service. Consultant-led, follow-up appointment.	£238.37	1	**£238**
From year 2 of treatment	National Schedule of NHS Costs Year : 2019-20 - Outpatient Attendances DataService code 255, Paediatric Clinical Immunology and Allergy Service. Consultant-led, follow-up appointment.	£238.37	4	**£953**