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Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2487

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

Aimmune Therapeutics

09 September 2022

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission

defatted powder of Arachis hypogaea L., semen (Palforzia®) is not recommended for use within NHSScotland.

Indication under review: 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.

Palforzia®, compared with placebo, increased the proportion of patients aged 4 to 17 years with peanut allergy who could tolerate, with no more than mild symptoms, a single dose of at least 1,000mg peanut protein (2,043mg cumulative).

The submitting company did not present a sufficiently robust economic analysis to gain acceptance by SMC.

The submitting company has indicated their intention to make a resubmission.

Chairman
Scottish Medicines Consortium

Published 10 October 2022

Indication

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.[1]

Dosing Information

Palforzia® is given in three sequential phases: initial dose escalation, up-dosing, and maintenance. Initial dose escalation comprises a series of single oral doses of 0.5mg, 1mg, 1.5mg, 3mg and 6mg administered sequentially on a single day in a health care setting that can manage potentially severe allergic reactions. The period of observation after each dose is 20 to 30 minutes and for the final dose is 60 minutes. Treatment must be discontinued if symptoms requiring medical intervention occur. Patients who tolerate at least the 3mg single dose must return to the healthcare setting for initiation of up-dosing the following day, if possible or within four days. The up-dosing phase comprises 11 dose levels (3mg, 6mg, 12mg, 20mg, 40mg, 80mg, 120mg, 160mg, 200mg, 240mg, 300mg), each taken for 2 weeks, with the first daily dose at each dose level taken in the healthcare setting followed by 60 minutes of observation and subsequent doses taken at home with a meal at the same time each day. After completion of all levels of up-dosing, maintenance dosing is 300mg orally each day. There is no information on treatment beyond 24 months. Dose adjustments to manage intercurrent and adverse events are in the summary of product characteristics (SPC). Palforzia® should not be taken on an empty stomach. The powder should be emptied onto a few spoonfuls of refrigerated or room temperature semisolid food and mixed well. Liquids must not be used.

Palforzia® should be administered under the supervision of a healthcare professional qualified in the diagnosis and treatment of allergic diseases. Initial dose escalation and the first dose of each new up-dosing level must be administered under supervision in a healthcare setting that can manage severe allergic reactions. Self-injectable adrenaline must be available to the patient at all times.[1]

Product availability date

1 January 2021

Summary of evidence on comparative efficacy

Palforzia®, defatted powder of *Arachis hypogaea L.,* semen (peanuts), is an oral allergen-specific immunotherapy that modifies the patient's immunologic response to peanut. It comprises increasing amounts of the allergen, peanut protein, administered to patients to raise the threshold and decrease the severity of allergic responses to the allergen. The precise mechanism of desensitisation provided by Palforzia® is not fully understood.[1,2]

Two double-blind phase III studies (PALISADE and ARTEMIS) recruited children and adolescents (4 to 17 years) with peanut allergy. PALISADE also included adults (18 to 55 years). At screening, patients had serum immunoglobulin E (IgE) concentration ≥0.35kUA/L to peanut and / or a skin prick test wheal diameter of ≥3mm to peanut compared with control. They also had dose-limiting symptoms (allergic reaction with type I hypersensitivity symptoms) after consuming a single dose of peanut protein ≤100mg in PALISADE and ≤300mg in ARTEMIS (144mg and 444mg cumulative, respectively) in the screening double-blind, placebo-controlled food challenge (DBPCFC). In PALISADE, randomisation was stratified by region (Europe or North America) and by age (4 to 17 years or 18 to 55 years). In both studies, patients were randomised in a 3:1 ratio to receive the licensed dose regimen of Palforzia® or placebo, with maintenance for 24 to 28 weeks in PALISADE and 12 to 16 weeks in ARTEMIS. All patients continued their peanut avoidance diet. In European analyses, the primary outcome in both studies was the proportion of patients aged 4 to 17 years who tolerated, with no more than mild symptoms, a single highest dose of 1,000mg peanut protein (2,043mg cumulative) at the study exit DBPCFC. This was assessed in the intention-to-treat population, which comprised all randomised patients who received at least one dose of study treatment.[2-4]

In both studies, European analyses of the primary outcome and the first three key secondary outcomes, tested in a hierarchy detailed in Table 1, were significantly improved with Palforzia®, compared with placebo. PALISADE had a fourth key secondary outcome, proportion of adults (18 to 55 years) who could tolerate a peanut protein dose of at least 1,000mg (2,043mg cumulative) at exit DBPCFC, and this was not significantly different with Palforzia® compared with placebo: 34% versus 14%, with a difference of 20% (95% CI: -7.7% to 47%), p=0.16.[2]

Table 1: Primary and Selected Key Secondary Outcomes of PALISADE[a] and ARTEMIS in Patients aged 4 to 17 years.[2]

	PALISADE[a] (ARC003)		**ARTEMIS (ARC010)**	
	Palforzia®	**Placebo**	**Palforzia®**	**Placebo**
	N=372	**N=124**	**N=132**	**N=43**
Response[b] at 1,000mg peanut protein	50%	2.4%	58%	2.3%
Difference (95% CI)	48% (38%, 58%), p<0.001		56% (44%, 65%), p<0.001	
Response[b] at 600mg peanut protein	67%	4.0%	68%	9.3%
Difference (95% CI)	63% (53%, 73%), p<0.001		59% (44%, 69%), p<0.001	
Response[b] at 300mg peanut protein	77%	8.1%	74%	16%
Difference (95% CI)	68% (59%, 78%), p<0.001		57% (41%, 69%), p<0.001	
Maximum symptom severity[c]	p<0.001		p<0.001	
None	38%	2.4%	36%	0
Mild	32%	28%	42%	37%
Moderate	25%	59%	18%	46%
Severe or higher	5.1%	10%	4.5%	16%

(a) European analyses in paediatric subgroup, aged 4 to 17 years; (b) Response = able to tolerate a single dose of peanut protein with no more than mild symptoms (i.e. no dose-limiting symptoms) at exit double-blind placebo-controlled food challenge (DBPCFC); (c) Maximum symptom severity at any challenge dose of peanut protein during exit DBPCFC; CI = confidence interval.

Patients in PALISADE who had placebo, or had Palforzia® and tolerated at least 300mg of peanut protein at exit DBPCFC, could enter an open-label phase III study (ARC004). Patients previously treated with placebo (Group 1) received the licensed dose regimen of Palforzia® and patients who

had Palforzia® (Group 2) were assigned to sequential cohorts with increasing dose intervals during Palforzia® maintenance, as detailed in Table 2 below. Desensitisation rates at study exit DBPCFC were assessed in completers (that is, patients who had at least one dose of study treatment and an exit DBPCFC) aged 4 to 17 years. These rates were generally higher in groups with continuous once daily dosing of Palforzia® (Group 1 and Group 2, cohorts 1 and 3A) than in the groups with extended dosing intervals (Group 2, cohorts 2, 3B and 3C). The highest response rate at every peanut protein challenge dose was in cohort 3A, which had the longest Palforzia® once daily dosing schedule (56 weeks). The European regulatory review noted that there was progressive desensitisation over time in patients who had received Palforzia® 300mg daily for up to 18 months, with no indication of a plateaued response.[2]

Table 2: ARC-004 Desensitisation Response at Exit DBPCFC in Completers aged 4 to 17 years.[2]

Dose that could be tolerated	Group 1	Group 2				
		Cohort 1	Cohort 2	Cohort 3A	Cohort 3B	Cohort 3C
	N=72	N=103	N=38	N=26	N=22	N=21
300mg	71 (99%)	101 (98%)	36 (95%)	26 (100%)	18 (82%)	19 (90%)
600mg	62 (86%)	92 (89%)	27 (71%)	25 (96%)	17 (77%)	16 (76%)
1,000mg	52 (72%)	83 (81%)	22 (58%)	25 (96%)	15 (68%)	14 (67%)
2,000mg	37 (51%)	50 (48%)	14 (37%)	21 (81%)	10 (46%)	9 (43%)

DBPCFC = double-blind placebo-controlled food challenge.
Group 1 (n=102): licensed dose regimen of Palforzia®, with maintenance (300mg daily) for 24 to 28 weeks
Group 2, cohort 1 (n=112): 300mg daily for 28 weeks
Group 2, cohort 2 (n=48): 300mg on alternate days for 4 weeks, then twice weekly for 24 weeks
Group 2, cohort 3A (n=31): 300mg daily for 56 weeks
Group 2, cohort 3B (n=31): 300mg daily for 28 weeks, then alternate days for 4 weeks, then twice weekly for 24 weeks
Group 2, cohort 3C (n=34): 300mg daily for 28 weeks, then alternate days for 4 weeks, then twice weekly for 24 weeks, then once weekly for 28 weeks.

Health related quality of life was assessed using the Food Allergy Quality of Life Questionnaire (FAQLQ) and Food Allergy Independent Measure (FAIM) total scores at baseline and exit. Across the PALISADE and ARTEMIS studies, there were no consistent clinically meaningful differences between Palforzia® and placebo for these outcomes. In ARC004, within the subgroup of patients treated with Palforzia® for approximately one and half years, a change from baseline of at least 0.5 points in FAQLQ total score (which was suggested to be clinically relevant) was self-reported by 60% (21/35) of patients aged 8-12 years and by 55% (10/18) of patients aged 13-17 years, with caregiver-reported figures of 51% (21/41) and 41% (7/17) in the respective age groups.[5]

Summary of evidence on comparative safety

The European regulatory review noted that overall the safety profile of Palforzia® was predictable and manageable. Most adverse events were related to allergic reactions, with systemic allergic reactions and eosinophilic oesophagitis key concerns and less severe gastrointestinal events more common.[2]

In a pooled analysis of phase III placebo-controlled studies (PALISADE, ARTEMIS and a safety study, RAMSES), within the Palforzia® and placebo groups adverse events were reported by 98% (823/841) and 93% (311/335) of patients, respectively, during the initial dose escalation and up-

dosing period. These were treatment-related in 89% and 57% of patients and led to study discontinuation in 11% and 2.4% of patients, respectively. During the maintenance dosing phase (part of PALISADE and ARTEMIS only) within the Palforzia® and placebo groups, rates of adverse events were 87% (270/310) versus 80% (94/118) in PALISADE and 88% (95/108) versus 78% (32/41) in ARTEMIS. These were treatment-related in 51% versus 22% and 53% versus 12%, respectively. In the maintenance phases, four patients discontinued treatment: all in the PALISADE Palforzia® group.[2]

In pooled analysis of placebo-controlled studies (PALISADE, ARTEMIS and RAMSES), systemic allergic reactions were more common with Palforzia® than placebo during the initial dose escalation and up-dosing period, 9.2% (77/841) versus 3.3% (11/335), and during maintenance in PALISADE, 8.7% (27/310) versus 1.7% (2/118), and ARTEMIS, 7.4% (8/108) versus 2.4% (1/41). Overall, in an integrated analysis of all patients given Palforzia® in these studies and follow-on studies (ARC004 and ARC011), 15% (143/944) of patients had a systemic allergic reaction including 0.6% during initial dose escalation, 8.7% during up-dosing, and 9.9% during maintenance. In this population, anaphylaxis (defined as severe systemic allergic reaction) was reported in 10 patients (1.1%): 4 patients in up-dosing and 6 patients in maintenance. [2]

Eosinophilic oesophagitis is another key concern. Across the clinical study programme, biopsy-confirmed eosinophilic oesophagitis was reported by 1% (12/1,217) of patients receiving Palforzia® and no patients (0/443) receiving placebo. Other gastrointestinal adverse events were more common. These were reported at higher rates with Palforzia® compared with placebo: abdominal pain (52% versus 24% in PALISADE; 67% versus 44% in ARTEMIS; and 52% versus 20% in RAMSES), vomiting (41% versus 24%; 40% versus 23%; and 39% versus 17%), nausea (39% versus 23%; 44% versus 26%: and 34% versus 12%), oral pruritus (41% versus 16%; 21% versus 2.3%; and 15% versus 3.0%) and oral paraesthesia (18% versus 6.5%; 39% versus 21%; and 14% versus 5.4%). Other common adverse events included throat irritation (41% versus 27%; 43% versus 19%; and 46% versus 18%), throat tightness (23% versus 6.5%; 7.6% versus 2.3%; and 10% versus 1.2%), pruritus (41% versus 27%; 51% versus 33%; and 37% versus 24%) and urticaria (38% versus 24%; 36% versus 21%; and 26% versus 21%).[3,4,6] In contrast to systemic allergic reaction rates, which appear constant over time, rates of common adverse events appeared to decrease over time. The proportion of patients with an adverse event decreased over time during maintenance from 76% for 0 to 13 weeks to 51% for > 52 weeks, with treatment-related adverse events decreasing from 47% to 19%.[2]

Summary of clinical effectiveness issues

Peanut allergy is an IgE-mediated type I hypersensitivity reaction. It is a potentially serious condition associated with severe allergic reactions, including life-threatening anaphylaxis and death. It usually presents early in life and continues into adulthood for the majority (80%) of patients. Severity of the allergic reactions can be influenced by several factors, including history of anaphylaxis to peanut, comorbidities, concurrent medications and exercise. Teenagers and young adults with risk-taking behaviour (such as failure to avoid triggers, forgetting to carry an adrenaline auto-injector and alcohol use) may be at particular risk of severe or fatal anaphylaxis. The current

standard of care is peanut avoidance and treatment for allergic reactions due to peanut exposure. Patients, their families, teachers and friends must be educated to recognise and manage allergy symptoms, including the use of rescue medications, such as intramuscular adrenaline (for example, via auto-injector), which is the fist-line treatment for severe systemic allergic reactions. There are no licensed therapeutic options for desensitising individuals with peanut allergy.[2]

Palforzia® is the first oral allergen-specific immunotherapy licensed in the UK for desensitisation treatment in patients with peanut allergy.

In two double-blind phase III studies, Palforzia® was associated with increases of 48% to 56% ,over placebo, in the proportion of patients aged 4 to 17 years who could tolerate, with no more than mild symptoms, a single dose of at least 1,000mg peanut protein (cumulative 2,043mg). There were also reductions in maximum symptom severity with Palforzia®. These results were considered clinically meaningful. In an open-label follow-on study there was continued desensitisation with once daily maintenance dosing, which appeared superior to Palforzia® maintenance with longer dosing intervals.[2-4]

The incidence of systemic allergic reactions was greater with Palforzia® compared with placebo during initial dose escalation, up-dosing and maintenance.[2]

During the European regulatory review, subgroup analyses of the primary outcome of PALISADE and ARTEMIS by age were consistent with the primary analyses, however, the size of treatment difference appears less for the smaller groups: age 12-17 years and adults. A single dose of peanut protein of 1,000mg was tolerated by 52% to 60% of patients aged 4-11 years, 45% to 46% of patients aged 12-17 years and 34% of patients aged 18-55 years at exit DBPCFC. Patients aged 12-17 years had twice as many systemic allergic reactions including anaphylaxis as adverse events than patients aged 4-11 years, 22% versus 12%, with 2% versus 0.5% having anaphylaxis. The increased risk of systemic allergic reactions in adolescents could not be solely explained by risk taking behaviour as teenagers in the placebo-arm did not experience these events. Additional analyses of adverse events suggest that older age (12-17 years versus 4-11 years) and increasing baseline levels of peanut-specific IgE may be more likely to be associated with systemic allergic reactions, adrenaline use and discontinuation due to persistent gastrointestinal adverse events.[2]

Overall, approximately 22% of patients discontinued Palforzia® early, with about half of these due to adverse events. During the European regulatory review, it was noted that the majority of other discontinuations were also likely to be related to Palforzia® and that most patients who withdrew consent had mild or moderate adverse events around the time of the withdrawal. Across the entire population of 1,182 Palforzia®-treated patients aged 4 to 55 years, 43% discontinued treatment, with 14% due to adverse event or symptom and 21% withdrew consent.[2]

The European regulatory review noted that a proportion of patients (20% to 35% in ARTEMIS) could not tolerate a single dose of 300mg peanut protein (equivalent to about one peanut) despite receiving maintenance, and continuation of treatment in this subgroup may not be reasonable.[2]

Palforzia® is not licensed for initiation in adults, although treatment commenced before 18 years can be continued in adults.[1,2] There is limited information in patients reaching 18 years of age while receiving Palforzia®, with only 51 of these patients in the clinical study programme. Efficacy

data are available for only 26 patients who have received Palforzia® treatment for a maximum of two years. There is limited information on Palforzia® treatment beyond two years or the consequences of stopping treatment with respect to maintenance of clinical efficacy, disease modification or risks of rebound. This may be provided by the ongoing open-label long-term study, ARC008.[2]

The complexity of Palforzia® treatment (including dose modification for intercurrent events like stress, alcohol consumption, viral illness, menses or others) may be associated with risks and difficulties in compliance in real-life settings. The potential for significant adverse events could affect patient compliance, especially in adolescents. Careful selection and appropriate education of patients would be required to ensure compliance with treatment and necessary precautions. Palforzia® treatment requires commitment, active participation and shared-decision making between the patient, their family and the treating physician. Therefore, it may not be suitable for all patients with peanut allergy.[2]

Clinical experts consulted by SMC considered Palforzia® is a therapeutic advance in the treatment of children with peanut allergy as it raises the threshold and reduces the severity of allergic reactions upon accidental exposure to peanuts. However, it would not be suitable for all patients. They noted that Palforzia® would be used in addition to current standard of care including peanut avoidance diets. The clinical experts noted that the introduction of this treatment could have service impacts, including staff resource and potential reorganisation of services.

Summary of comparative health economic evidence

The company submitted a cost-utility analysis of Palforzia® for the treatment of patients aged 4 to 17 years with a confirmed diagnosis of peanut allergy. Strict avoidance of peanuts (together with symptomatic treatments and emergency medication if exposure occurs) is the only other indicated strategy and was the sole comparator in the model.

A Markov model was implemented for the base case analysis. The model structure separated out costs and outcomes according to different levels of desensitisation to peanut protein. Several health states were included to capture differences in adverse event rates, reactions to accidental exposure to peanuts and utilities between different peanut tolerance levels.

The model covered a 90-year lifetime horizon and captured five phases of treatment: escalation, up-dosing, maintenance, extension, and extrapolation. Patients entered the model in the 'up-dosing' health state. After maintenance, health states were based on the amount of peanut protein tolerated in an oral food challenge. Tolerance based health states were set at <300mg, 300mg, 600mg, 1,000mg, and 2,000mg. Post treatment maintenance phase, it was assumed that level of desensitisation to peanut protein may change over time, therefore patients could move between different levels of tolerance to peanut protein.

In the model, people who tolerate at least 300mg peanut protein in the oral food challenge after approximately two years of treatment could either: stay on Palforzia® lifelong and continue avoiding peanuts; start including peanuts in their diet permanently; or start including peanuts in

their diet, but then switch back to avoiding peanuts. In the absence of long term evidence, an assumption of 5% of individuals continuing on Palforzia® for their entire lifetime was applied in the base case.

Key effectiveness and safety data were based on the PALISADE study and the ARC004 extension study. This included input parameters for baseline demographics, probability of tolerating a dose of peanut protein, probabilities of changing tolerated dose of peanut protein, discontinuation, compliance, treatment related anaphylactic reactions and treatment related adverse events.

The company conducted a separate quality of life (QoL) survey to estimate utility values in children and adolescents with peanut allergy as well as their carers. Both the adult and youth based versions of the EuroQol-5D (EQ-5D) were used to elicit utilities. Caregiver utilities and proxy-reported values were not included in the base case.

Acquisition and administration costs for Palforzia® were included in the analysis, as were the costs associated with adrenaline autoinjectors and high-dose antihistamines. Unit costs for routine monitoring, food challenge testing, and managing adverse events were included in the analysis. The base case analysis presented by the submitting company produced an incremental cost-effectiveness ratio (ICER) of £18,162 versus avoidance only. This results from an estimated quality adjusted life year (QALY) gain of 0.716 and an estimated difference in costs of £13,003 for Palforzia®.

Table 3: Base-case results for Palforzia® versus peanut avoidance

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER incremental (£/QALY)
Palforzia®	23,329	26.8	20.195	13,003	0.000	0.716	18,162
Avoidance only	10,326	26.8	19.480				

ICER: incremental cost-effectiveness ratio; LYG: life-years gained; QALY: quality-adjusted life-year.

The company provided probabilistic sensitivity analysis (PSA), deterministic sensitivity analysis (DSA) and scenario analysis. In the DSA, a range of parameters were tested including time horizon, discounting rate, health state costs, utility values and adverse event costs. The factors with the greatest impact on the ICER were the utility value associated with <300mg, proportion of patients transitioning to 'regular inclusion of peanut in diet', utility of peanut in diet and health state cost for tolerated dose <300mg.

The company also conducted scenario analyses to test the impact of several assumptions. Table 4 below contains some of the results from scenario analyses.

Table 4: Selected scenario analysis

		ICER vs avoidance only
	Base case	*£18,162*
1	Time Horizon : 5 years	£75,952
2	Time Horizon: 20 years	£26,780
3	Clinical effectiveness inputs : ARTEMIS trial	£19,122

4	Long term outcomes: higher proportion staying on treatment and lower proportion transition to RIPD beyond year 2	£28,770
5	Long term outcomes: higher proportion staying on treatment, lower proportion transition to RIPD and higher proportion revert to total avoidance beyond year 2	£54,835
6	Inclusion of carers utility	£15,505
7	Pooled utility values excluding Palforzia®-treated participants	£21,543
8	Treatment discontinuation (for MTD <300) before two years	£18,079
9	A food challenge in 20% of patients who completed two years of Palforzia® treatment	£17,907

ICER: Incremental cost-effectiveness ratio, RIPD: Regular inclusion of peanut in diet, MTD: Maximum tolerated dose

There were some limitations with the analysis which include the following:

- There is uncertainty regarding the duration of treatment with Palforzia® and longer term outcomes after treatment discontinuation. Duration of treatment in the model was two years, which is consistent with the period for which efficacy data are currently available. The effect of stopping treatment on maintenance of clinical efficacy has not been evaluated. In the base case analysis, it was assumed that 5% of individuals would continue on Palforzia® for their entire lives. If a higher proportion of patients were to continue on Palforzia® lifelong as a preferred alternative to regular inclusion of peanuts in diet (e.g. taste aversion), this would lead to a substantial increase in ICER (scenarios 4 and 5). Responses from SMC clinical experts agreed long-term outcomes are uncertain but generally indicated the proportion of patients who would continue on treatment may be higher than 5%.

- Beyond two years, people tolerating at least 300mg peanut protein could alternatively either start including peanuts in their diet permanently or start including peanuts in their diet, but later switch back to completely avoiding peanuts. In the base case, it was assumed that 95% of individuals would include peanuts in diet, but during next 2 years a proportion of these patients would drop out and revert to avoidance. There is a high degree of uncertainty regarding the proportion of individuals who would include peanuts in their diet, the proportion who would revert to avoidance only and the rate at which this occurs after cessation of Palforzia®.

- There is uncertainty regarding the utility values for people with peanut allergies. The company elicited utilities by means of a separate survey study which included both self-reported and proxy-reported utilities. Utility values were a key driver in the one-way sensitivity analysis and varying the source in the scenario analysis led to ICERs ranging between £15k and £21.5k. In the base case analysis, utilities based on self-reported data from young people who had not had prior treatment were used. However, it may be appropriate to include carer utilities as well.

- The model does not account for any service setup costs associated with introducing Palforzia®. Treatment with Palforzia® is expected to be resource intensive with food allergy clinics being reconfigured or newly setup to build capacity in providing oral immunotherapies.
- It is unclear whether all patients would require a food challenge test before starting Palforzia® to confirm diagnosis of a peanut allergy. The base case assumed only 50% of patients would need a test, however it's plausible that a greater number of patients would require it in an unscreened population.

Due to the limitations outlined above, the economic case has not been demonstrated.

Summary of patient and carer involvement

The following information reflects the views of the specified Patient Groups.

- We received patient group submissions from Allergy UK and Anaphylaxis UK, which are both registered charities.
- Allergy UK has received 32% pharmaceutical company funding in the past two years, including from the submitting company. Anaphylaxis UK has received 11% pharmaceutical company funding in the past two years, including from the submitting company.
- Peanut allergy affects around 2% (1 in 50) of children in the UK and has been increasing in recent decades. Living with peanut allergy can have a detrimental impact on the individual's quality of life as well as the psychological wellbeing of both carers and their families. The biggest challenges of living with this condition are the impact on every day quality of life including shopping and preparing food, eating out, travelling, family life, leisure activities, education and career. More support is required for individuals and their families to help reduce the psychosocial burden of food allergy.
- Current treatments are inadequate because the only current way to manage serious allergy is complete avoidance of the allergen and carrying two adrenaline auto-injectors as emergency treatment in case of accidental exposure. There is a need for treatments and therapies to reduce the risk of severe allergic reactions should the allergenic food be accidentally ingested.
- This new medicine is important to patients and carers because it may reduce the burden of managing all of the implications of living with a serious allergy due to decreased risk of a serious allergic reaction. However, with novel therapies such as the proposed treatment there is a need to manage expectations amongst both HCPs and patients and their families. Adequate patient information to help inform choice and manage these expectations is required.

Additional information: guidelines and protocols

In 2017, the British Society for Allergy and Clinical Immunology (BSACI) published BSACI guideline for the diagnosis and management of peanut and tree nut allergy. This recommends that patients should be provided with a comprehensive management plan including avoidance advice, patient specific emergency medication and an emergency treatment plan, and training in administration of emergency medication. It notes that regular retraining is required. As part of the management plans for children, all staff within the school and early years setting require appropriate training in managing an allergic reaction. The guideline notes that clinical trials of peanut oral immunotherapy have shown promising results and are ongoing.[7]

In 2011, the National Institute for Health and Care Excellence (NICE) published clinical guideline number 116: Food allergy in under 19s: assessment and diagnosis. This provided guidance on allergen avoidance and referral to secondary services.[8]

Additional information: comparators

There is no active comparator.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost year (£)
Palforzia®	**Dose escalation**: sequential single oral doses of 0.5mg, 1mg, 1.5mg, 3mg and 6mg on Day 1 **Up-dosing**: sequential oral daily doses for two weeks of 3mg, 6mg, 12mg, 20mg, 40mg, 80mg, 120mg, 160mg, 200mg, 240mg, 300mg **Maintenance**: 300mg orally once daily	£3,684

Costs from MIMS online, accessed 08/09/22. Costs calculated using the full cost of capsules assuming wastage.

Additional information: budget impact

The submitting company estimated there would be 4,983 patients eligible for treatment with Palforzia® in year 1 rising to 5,069 in Year 5. The estimated uptake rate was 0.2% in year 1 and 2.2% in year 5 with a discontinuation. This resulted in 10 patients estimated to receive treatment in year 1 rising to 110 patients in year 5.
SMC is unable to publish the submitting company's budget impact estimates due to commercial in confidence issues.

*Other data were also assessed but remain confidential.**

References

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2. European Medicines Association (EMA). Defatted powder of Arachis hypogaea L., semen (peanuts) oral powder in capsules for opening or in sachets (Palforzia®), EMA/583336/2020, 15 October 2020. www.ema.europa.eu

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6. Clinicaltrials.gov. Record for NCT03126227 (ARC007, RAMSES)

7. Stiefel G, Anagnostou K, Boyle RJ, et al. BSACI guideline for the diagnosis and management of peanut and tree nut allergy. Clin Exp Allergy 2017; 47(6): 719-739.

8. National Institute for Health and Care Excellence (NICE). Clinical guideline number 116: Food allergy in under 19s: assessment and diagnosis, 23 February 2011.

This assessment is based on data submitted by the applicant company up to and including 22 August 2022.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in

determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.