NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Final appraisal document

Palforzia for treating peanut allergy in children and young people

1 Recommendations

1.1 Palforzia is recommended, within its marketing authorisation, as an option for treating peanut allergy in children aged 4 to 17. Palforzia may be continued in patients aged 18 years or older. Palforzia should be used in conjunction 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.

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2 Information about Palforzia

Marketing authorisation indication

2.1 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 aged 18 years or older. Palforzia should be used in conjunction with a peanut-avoidant diet'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics.

Price

2.3 The list price of Palforzia is £[redacted] per day. A flat price is applied for each Palforzia dose (range 0.5 to 300 mg).

3 Committee discussion

The appraisal committee considered evidence submitted by Aimmune Therapeutics UK Ltd, a review of this submission by the evidence review group (ERG), and responses from stakeholders. See the committee papers for full details of the evidence.

Clinical need and treatment pathway

Peanut allergy burdens patients and their carers

3.1 Peanut allergy is one of the most common food allergies in children, affecting between 0.5% and 2% of children in the UK. Severe reactions, notably anaphylaxis, can be life threatening, although deaths from peanut allergy-related anaphylaxis are very rare in the UK. Symptoms can have a rapid onset. They can include angioedema (facial swelling), respiratory symptoms (wheezing), conjunctivitis, oral allergy syndrome (lip or tongue swelling), rhinitis (blocked nose) and urticaria (blotchy red rash). It is not possible to predict the likelihood or severity of future allergic reactions

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based on previous reactions. Patient experts explained that peanut allergy affects 'all aspects of daily life' and 'can cause extreme anxiety' for children and young people with the allergy and their carers. It can have implications for shopping and preparing food, weaning infants, eating out, travelling, seasonal events, education, socialising and work. Parents may experience anxiety, in particular around the time their children start secondary school or leave home. The committee concluded that peanut allergy burdens patients and their carers.

There is a need for preventive treatment options for peanut allergy

3.2 The goal of treatment for peanut allergy is preventive, that is, to reduce the frequency and severity of allergic reactions and improve quality of life, to lessen anxiety and to normalise activities of daily living. The main preventive strategy for peanut allergy is strictly avoiding peanuts and being ready to respond to an emergency. Symptomatic treatment of mild reactions to accidental peanut exposure includes antihistamines, while severe anaphylactic reactions need emergency treatment including self-administered adrenaline. Clinical experts explained that strictly avoiding peanuts cannot be considered the only option, and active preventive treatments are needed to reduce the risks of accidental peanut exposure. They noted that most accidental exposures involve less than 300 mg of peanut protein. Tolerating this amount, equivalent to roughly 1.5 peanuts, would give 'bite protection' from small accidental exposures to peanut and would be a 'meaningful outcome'. Tolerating 1000 mg of peanut protein is considered to be 'highly clinically significant'. The committee concluded that clinicians and people affected by peanut allergy 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.

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Lifetime treatment with Palforzia or regularly including peanuts in the diet is needed to maintain tolerance

3.3 Palforzia is an oral immunotherapy, consisting of peanut protein, as a defatted powder of *Arachis hypogaea L*. It is given through a 'structured dosing' approach, starting from a dose level as low as 0.5 mg, and gradually increasing. This allows people to build tolerance to peanut protein over time. Strict peanut avoidance and emergency preparedness continue during treatment. The experts explained that Palforzia allows for precise and reproducible dosing of 'minuscule amounts' of peanut protein, which is not possible with dietary peanut. However, according to the clinical experts, once people tolerate higher doses of peanut protein, they 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. Yet, it also states that no recommendation can be made about the duration of treatment beyond 24 months, and that the effect of stopping treatment on maintenance of clinical efficacy has not been evaluated. 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. They added that whether or not people keep peanuts in their diet after Palforzia treatment may be linked to taste aversion, motivation, adverse effects, restrictions around meals and exercise, and support received. The patient experts anticipated that people will be highly motivated to include peanuts in their diet after committing to Palforzia treatment, but noted that some may be averse to the taste of peanuts. Moreover, there may be psychological stress and anxiety associated with eating a food that people have diligently avoided and greatly feared for many years. The patient experts explained that people with peanut allergy and their carers may require additional psychological support during the transition. The committee concluded that people would need lifetime treatment with

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Palforzia or to regularly include peanuts in their diet to maintain tolerance to peanuts.

Strict peanut avoidance is the most appropriate comparator

3.4 Palforzia is used 'in conjunction with a peanut-avoidant diet', in line with its marketing authorisation. The company selected strict peanut avoidance as the only comparator for Palforzia. The committee agreed, concluding that strict peanut avoidance was the most appropriate comparator for Palforzia.

Clinical evidence

An oral food challenge is clinically relevant and an appropriate surrogate end point

3.5 The committee recalled that one of the treatment goals is to reduce the risks associated with accidental peanut exposure (section 3.2). Reactions to accidental exposures are uncommon, with one study suggesting an annual incidence of around 12%. Therefore, clinical trials use oral food challenges as a surrogate end point. In an oral food challenge, people are given increasing doses of precise amounts of peanut protein to assess their tolerance to the allergen. Their maximum tolerated dose, or 'tolerability threshold', is the highest dose tolerated with no more than mild symptoms. Having some tolerance to peanut protein can protect from risks of accidental exposure to peanut. The committee recalled that tolerating 1000 mg peanut protein is considered clinically significant. The committee agreed that tolerance to peanut protein measured during oral food challenge is clinically relevant, and reflects an appropriate surrogate end point for assessing the efficacy of Palforzia.

Palforzia was studied in 2 phase 3 trials that are generalisable to NHS practice

3.6 Palforzia was studied in 2 randomised controlled trials conducted in North America and Europe, including the UK. All people had peanut allergy confirmed by peanut-specific IgE reactivity and skin prick test. All

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participants had an entry food challenge at screening to select people who had dose-limiting symptoms to peanut protein at a dose of 100 mg or less in PALISADE, and 300 mg or less in ARTEMIS. PALISADE enrolled people aged 4 to 55 years (N=496), and ARTEMIS enrolled people aged 4 to 17 years (N=175). People were randomised to receive Palforzia while avoiding peanuts, or placebo while avoiding peanuts. Treatment with Palforzia was given in 3 phases:

- An 'escalation phase', which consisted of 5 dose levels (0.5 mg to 6 mg), all given on day 1 of treatment.
- An 'up-dosing phase', which had 11 dose levels lasting 2 weeks each (3 mg to 300 mg).
- A 'maintenance phase', in which people received 300 mg once daily for 24 to 28 weeks in PALISADE and 12 weeks in ARTEMIS.

Peanut desensitisation was measured in an exit food challenge at the end of maintenance treatment. The primary end point in ARTEMIS and PALISADE in Europe was the proportion of people who tolerated at least 1000 mg peanut protein with no more than mild symptoms, while in PALISADE in North America it was the proportion of people who tolerated at least 600 mg peanut protein. People completing maintenance treatment and tolerating at least 300 mg peanut protein in the food challenge could enrol in PALISADE follow-on, an open-label observational study, and continue the Palforzia maintenance dose for a further 28 to 56 weeks, after which there was an additional food challenge. The clinical experts explained that the baseline characteristics of people enrolled in PALISADE and ARTEMIS aligned with those of people with peanut allergy seen in NHS practice. They also explained that people in NHS practice would follow the same dosing schedule as in the trials. The committee concluded that PALISADE and ARTEMIS are generalisable to NHS practice.

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Palforzia improves tolerance to peanut protein compared with placebo

3.7 Compared with placebo, Palforzia increased the proportion of people who could tolerate at least 1,000 mg peanut protein. Among people aged 4 to 17 years, the proportion of people tolerating at least 1,000 mg peanut protein was:

- 50.3% of people randomised to Palforzia versus 2.4% of people randomised to placebo in PALISADE (absolute treatment difference 48.7%; 95% confidence interval: 38.0% to 57.7%; p<0.0001)
- 58.3% versus 2.3% of people, respectively, in ARTEMIS (absolute treatment difference 56.0%; 95% confidence interval: 44.1% to 65.2%; p<0.0001).

These findings were supported by the key secondary outcomes of tolerating at least 600 mg or at least 300 mg peanut protein. The committee concluded that Palforzia improved tolerance to peanut protein in people aged 4 to 17 years with peanut allergy compared with placebo.

There is no direct clinical trial evidence that Palforzia reduces the frequency and severity of reactions to accidental peanut exposure

3.8 The committee recalled that reactions to accidental peanut exposure are rare (see section 3.5). It noted that these reactions, including severe anaphylactic reactions needing treatment with adrenaline, infrequently occurred in the Palforzia trials. It also noted that there was no proven differences in this outcome between the Palforzia and placebo groups. The company considers the exact rates to be confidential so they cannot be reported here. The committee appreciated that avoiding anaphylaxis from accidental exposure to peanuts is a goal of treatment with Palforzia, but also that treatment with Palforzia increases the risk of anaphylactic reactions as an adverse event of treatment (see section 3.9). A clinical expert noted that while there is no direct evidence that Palforzia 'prevents anaphylaxis' following accidental exposure, there is evidence from clinical trials that the maximum severity of symptoms at the exit oral food challenge was lower with Palforzia than with placebo. The committee

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concluded that there is no direct clinical trial evidence that Palforzia reduces the frequency and severity of reactions to accidental peanut exposure.

Palforzia may increase the risk of treatment-related anaphylactic reactions, but the risk of severe anaphylaxis is low

3.9 People who had Palforzia had more adverse events affecting the gastrointestinal tract, respiratory tract, skin, and immune system than those who received placebo. Severe or serious treatment-emergent adverse events were rare. The committee noted that mild and moderate anaphylactic reactions as an adverse event of treatment (not because of accidental peanut exposure) were more common with Palforzia than with placebo, but severe anaphylactic reactions were rare – only 1 patient in the Palforzia group and 2 patients in the placebo group had severe anaphylaxis in PALISADE, and none in ARTEMIS. In both trials, more people on Palforzia stopped treatment because of treatment-emergent adverse events than did people taking placebo. The committee concluded that Palforzia may increase the risk of treatment-related reactions, although the risk of severe anaphylaxis is low.

The committee would prefer a meta-analysis, but this would not have a meaningful impact on the results

3.10 The company explained that it attempted a meta-analysis of Palforzia clinical trial data but did not consider it robust because of differences in study design between PALISADE and ARTEMIS. These differences included trial location (North America and Europe versus Europe only), age of participants (4 to 55 years versus 4 to 17 years), severity of peanut allergy (reactions to 100 mg or less versus 300 mg or less in the entry food challenge test), and duration of maintenance treatment (24 to 28 weeks versus 12 weeks). The ERG explained that despite these differences, the company could have done a network meta-analysis, a simple meta-analysis, or used individual participant data. The ERG also noted that the company did not consider a phase 2 study, the ARC001

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trial. The company explained that it excluded this study because it had only 55 participants and was done solely in the USA. The ERG accepted that including this study would not add much insight. The committee agreed with the ERG that despite differences between trials, there were several ways in which the company could have done a meta-analysis of trial data. It noted that meta-analysis would have allowed it to assess heterogeneity and uncertainty in the treatment effect. The committee concluded that it would have preferred to have seen the results of a meta-analysis, but accepted this would be unlikely to have any meaningful impact on the results presented.

Cost-effectiveness evidence

The company's economic model is suitable for decision making

3.11 The company used a Markov state transition model to estimate the cost effectiveness of Palforzia plus avoiding peanuts compared with avoiding peanuts only. The model structure had 5 phases: escalation, up-dosing, maintenance, extension, and extrapolation. After maintenance, health states were based on the amount of peanut protein tolerated in an oral food challenge. Simulated people who tolerated 300 mg or more peanut protein could also move to an 'include peanuts in diet' health state. From all health states, people could move to 'spontaneous tolerance' with the lifetime probability of 5%, or 'death' health states. The committee concluded that the model structure and health states were reasonable, and suitable for decision-making.

It is reasonable to assume no survival benefit from Palforzia

3.12 The model assumed that peanut allergy does not increase the risk of death compared with that of the general population. The company modelled the risk of death from UK life tables for the general population. The company assumed that Palforzia had no effect on the risk of dying. All gains in quality-adjusted life years (QALYs) were from improvements in quality of life for patients and their carers. The committee recalled that deaths from peanut allergy are very rare in the UK. However, the

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committee considered it possible that Palforzia could decrease that risk and noted that the assumption of no survival gain may be conservative (see section 3.22). The committee concluded that it is reasonable to assume no survival benefit of Palforzia in the model.

The model does not reflect that in the NHS some people may need an oral food challenge before starting Palforzia

3.13 The company based its model on results from PALISADE; ARTEMIS was used in a scenario analysis. In PALISADE, everyone had an oral food challenge before they entered the trial to confirm they were sensitive to less than 100 mg peanut protein. However, the company and the ERG models excluded an oral food challenge before starting Palforzia. The committee noted that the company's trial results for people with confirmed severe peanut allergy may not apply to an unscreened NHS population, some of whom might have developed tolerance spontaneously, or be sensitive to higher doses of peanut protein than people in the trial. The British Society of Allergy and Clinical Immunology 'strongly recommended' doing a food challenge before starting Palforzia in the NHS to confirm whether a peanut allergy is still present, and to determine its severity. The clinical experts explained that re-testing for peanut allergy with a skin prick test and/or IgE testing already forms part of routine care to check for tolerance that sometimes develops spontaneously. It is also done to remind teenagers of their allergy – older children may not have experienced a reaction to peanuts since they were much younger and may not remember being allergic. The clinical experts noted that up to half of people may need a food challenge to determine whether they are suitable for treatment with Palforzia. They also noted that people with recent severe reactions to small amounts of peanut protein from accidental exposure would not need a food challenge. The committee acknowledged that the model did not include a food challenge before starting treatment with Palforzia. The committee concluded that the model

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does not reflect the likely need for oral food challenge before starting Palforzia in the NHS.

The model does not reflect that most people would not need an oral food challenge after Palforzia treatment in NHS practice

3.14 The company and ERG models included a single oral food challenge for people taking Palforzia, at around 2 years, and none for people avoiding peanuts only. The clinical experts confirmed that people who avoid peanuts are not usually offered food challenges in NHS practice. They also confirmed that if a food challenge were needed after Palforzia, they would offer one only after 1 to 2 years of treatment. They explained that fewer than 20% of people would need a food challenge to determine tolerance after treatment with Palforzia. This is because taking maintenance doses of Palforzia is a de facto food challenge, and if people take 300 mg Palforzia every day, they will be able to tolerate the same amount of peanut protein. Therefore, most people could start including peanuts in their diets without the oral food challenge. The committee concluded that the model does not reflect that most people would not need an oral food challenge after Palforzia treatment in NHS practice.

Few people are likely to continue treatment with Palforzia lifelong in NHS practice, and the model overestimates this

3.15 In the model, people who tolerate at least 300 mg peanut protein in the oral food challenge after approximately 2 years of treatment can:

- stay on Palforzia lifelong and continue avoiding peanuts
- start including peanuts in their diet permanently
- start including peanuts in their diet, but then switch back to avoiding peanuts.

The company estimated the likelihood of being in each of these 3 groups based on a consensus clinical opinion. The company considers these estimates confidential so they cannot be reported here. The ERG

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acknowledged that the company used reasonable methods to reach these estimates but highlighted that they are not evidence based and are uncertain. The patient experts explained that people who have committed to 2 years' treatment with Palforzia will be highly motivated to maintain tolerance, start dietary peanuts and adhere to a diet that includes peanuts. The clinical experts agreed that most people would be happy to start including peanuts in their diet, although some may then stop. The clinical experts explained that only people with borderline tolerance to 300 mg peanut protein may need to continue treatment with Palforzia. They expected this would be fewer than 5% of people who had completed maintenance treatment with Palforzia. The committee noted that this proportion was lower than the company assumed in its model. The committee concluded that fewer people than modelled are likely to continue treatment with Palforzia lifelong in NHS practice.

Utility values

The utility values for people with peanut allergy are uncertain

3.16 The company conducted a de novo utility study to estimate quality of life in children and young people with peanut allergy using the EQ-5D-Y (the youth EQ-5D), and for their carers using EQ-5D. The company pooled data from various sources and populations to obtain utility estimates, including:

- 38 online surveys completed by young people aged 12 to 17 with peanut allergy themselves ('self-reported utilities'), none of whom had prior treatment with Palforzia
- 62 online surveys completed by carers on behalf of their children aged 4 to 11 with peanut allergy ('proxy-reported utilities'); none of the children had prior treatment with Palforzia
- 50 interviews with carers reporting utilities on behalf of their children aged 4 to 11 with peanut allergy; none of the children had prior treatment with Palforzia

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- 7 ‘Palforzia surveys’: surveys among people who have had prior treatment with Palforzia, of which 2 were self-reported by young people aged 12 to 17, and 5 were proxy-reported by parents of children aged 4 to 11 with peanut allergy.

The company pooled data from all these populations and sources (N=157) to inform its cost-effectiveness modelling. The ERG preferred to use only self-reported data from young people who had not had prior treatment with Palforzia (N=38). The ERG was concerned that carers may project some of the negative impact on their own quality of life when reporting proxy utility values for children. This risks double counting the negative impact on carers, because the company included carer disutility separately in its model (see section 3.17). Furthermore, the ERG explained that the company’s survey among people who have had Palforzia, or their carers, may have been biased, because they might have not remembered what their (or their children’s) quality of life was before or during the treatment. The committee noted the large difference between the utility values estimated by the company and the ERG. It agreed with the ERG that utility values from the Palforzia survey were not plausible. It also noted that the difference between the company and ERG approaches seemed to be driven mainly by differences in methods of data collection, rather than whether utilities were self- or proxy-reported. The committee agreed it was unclear which utility values better reflected quality of life of people with peanut allergy in NHS practice. The committee concluded that the utility values were uncertain and agreed to consider both the ERG-preferred approach and the pooled sample from all treatment-naïve people, that is, excluding those from the Palforzia survey (N=150).

The model adequately reflects utility values for carers of children with peanut allergy

3.17 The patient and clinical experts explained that carers often ‘carry the mental load’ of peanut allergy day-to-day. The model included carer

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disutility until people with peanut allergy reached 18 years of age. The utility values for carers were collected in company's de novo utility study, using EQ-5D (section 3.16). The company assumed that on average, there was more than 1 carer per child (the company considers the exact number to be confidential so it cannot be reported here). The ERG agreed it was reasonable to include carer quality of life in the model, but highlighted that the number of carers per child is uncertain. The committee noted that the number of carers per child assumed by the company was in line with other technology appraisals that included carers' quality of life. The committee concluded that including carers' quality of life in the model is appropriate, and that the methods used by the company to capture this were acceptable.

It is reasonable to assume the utility gains for children with peanut allergy and their carers can be realised without oral food challenge

3.18 The company and ERG assumed that treatment with Palforzia during escalation and up-dosing has a negative impact on quality of life of children with peanut allergy and their carers. However, once people start maintenance treatment, there is a small gain in quality of life compared with baseline. Any further gains are then realised only after the oral food challenge, and are linked to the tolerance level reached, with higher benefit related to higher tolerance levels. The ERG explained this is because utility values associated with a change in tolerance level are realised only after the results of a food challenge become known. Both the ERG and company models also assumed that people who avoid peanuts but do not take Palforzia do not have any oral food challenge and therefore have no gains in quality of life. That is, the model assumed they have the same baseline quality of life throughout the model time horizon. The clinical experts explained that people on Palforzia could have quality of life benefits without an oral food challenge because they know they can tolerate a 300 mg dose of peanut protein, and can start including peanuts in their diet. The committee recalled that tolerating 300 mg peanut protein

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gives 'bite protection' (section 3.2). It also recalled that taking maintenance doses of Palforzia is a de facto food challenge and people could start including peanuts in their diet after reaching tolerance to 300 mg peanut protein. The committee concluded that utility gains for children with peanut allergy and their carers related to Palforzia treatment can be realised without an oral food challenge.

Costs

The model should have included the costs related to setting up oral immunotherapy services in NHS food allergy clinics

3.19 The committee noted that treatment with Palforzia is resource intensive because patients must attend a clinic prepared to treat anaphylaxis for initial dose escalation and the first dose of each new up-dosing level. The ERG confirmed that the company's model captures costs related to staff time and resources needed to deliver Palforzia during these clinic visits. The clinical experts explained that food allergy clinics are mainly run as diagnostic services; extending into delivering oral immunotherapy would demand additional investment, particularly in capacity and training of staff. The company confirmed that its model did not include costs related to the 'set up' needed to provide oral immunotherapy in food allergy clinics. The committee noted that NICE's guide to the methods of technology appraisal specifies that 'if introduction of the technology requires changes in infrastructure, costs or savings should be included in the analysis'. The committee concluded that the model should have included all costs related to setting up oral immunotherapy treatment in NHS practice.

The costs of reactions to accidental peanut exposure and treatment-related adverse events are adequately captured in the model

3.20 The ERG's and company's final models included all treatment-related adverse events that could affect costs or benefits of Palforzia. Both assumed that an ambulance and accident and emergency visit may be needed for all anaphylactic reactions regardless of their severity or cause

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– that is, whether caused by Palforzia or accidental exposure to peanuts. The clinical experts agreed that all patients with anaphylaxis should receive the same care, regardless of cause. The committee concluded that the company and ERG captured the costs of reactions to accidental peanut exposure and treatment-related adverse events in their models.

Cost-effectiveness estimates

Palforzia is a cost-effective use of NHS resources

3.21 The committee noted that company and ERG base case models differed only in their approach to estimating utility values (see section 3.16). In a deterministic pairwise analysis, the company base case incremental cost-effectiveness ratio (ICER) was £23,745 per QALY gained compared with avoiding peanuts only. The ERG deterministic base case was £36,565 per QALY gained. Corresponding probabilistic ICERs were £25,940 and £39,716 per QALY gained, respectively, compared with avoiding peanuts only. However, the committee noted that neither the ERG nor company base cases fully captured its preferences that:

- up to 50% of people may need an oral food challenge before starting Palforzia in NHS practice to confirm peanut allergy (section 3.13)
- fewer than 20% of people would need an oral food challenge after Palforzia treatment to determine if they can start introducing peanuts into the diet, instead of continuing Palforzia (section 3.14)
- fewer than 5% of people would be expected to continue treatment with Palforzia lifelong in NHS practice (section 3.15)
- utility values for people with peanut allergy are highly uncertain; therefore, both the ERG-preferred utilities from only adolescent self-reported, treatment-naive sample (N=38) and pooled utilities from all people naive to treatment (N=150) should be considered (section 3.16)
- Palforzia can have a positive impact on quality of life of people with peanut allergy and their carers without an oral food challenge (section 3.17),

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- all costs related to setting up oral immunotherapy treatment in NHS practice should be included (section 3.19).

The committee therefore considered a number of scenario analyses done by the ERG. It noted that assuming a food challenge before starting treatment with Palforzia had a minimal impact on the ERG base case ICER, increasing it to £37,059 per QALY gained. Although it did not see a scenario assuming lower use of oral food challenge after treatment with Palforzia, it agreed it would also be likely to have a minimal impact on the ICERs. The committee noted that the choice of utility values and the proportion of people continuing treatment lifelong had the biggest impact on the cost-effectiveness estimates. Using utility values from the 150 treatment-naive people in the sample decreased the ERG base case ICER to £27,735 per QALY gained. Assuming nobody continues Palforzia lifelong decreased the ERG base case ICER to below £20,000 per QALY gained. The committee noted it did not see any scenario analyses assuming 5% people would continue Palforzia lifelong, but agreed that ICERs would slightly increase compared with scenarios assuming nobody continues Palforzia lifelong. When using utilities from the full sample of 150 treatment-naive people, the ICERs would be lower than £20,000 per QALY gained. The committee therefore agreed that the most plausible ICERs, when excluding the costs of setting up oral immunotherapy treatment in NHS practice, would be around £20,000 per QALY gained. The committee further noted it did not see any scenario analyses including all costs related to setting up oral immunotherapy treatment in NHS practice, in line with its preferred assumptions, and that it may be difficult to estimate the impact on the cost-effectiveness estimates. However, the committee agreed there may be some benefits of Palforzia not captured in the company and ERG models (section 3.22). It also recalled that peanut allergy is a burden for children and their carers (section 3.1). Therefore, the committee concluded that Palforzia is likely to be a cost-effective use of NHS resources, and therefore recommended it for routine NHS use.

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Innovation and equality

Palforzia is innovative and may have some benefits that are not adequately captured in the model

3.22 The committee agreed with the clinical experts and the company that Palforzia is a 'potential step change' in treating peanut allergy and as such is innovative. It further noted some potential benefits that may not have been captured in the modelling:

- The company's model assumed no survival benefit from Palforzia (section 3.12), so if even 1 death from anaphylaxis is prevented by Palforzia, this would be an additional benefit for people with peanut allergy and the NHS.
- Even if people do not continue to benefit from treatment for their whole life, for example if they return to avoiding peanuts later in life, they may still have benefited from treatment and peanut tolerance during important years as a young adult, when they are growing up, gaining independence and travelling.

The committee concluded that Palforzia is innovative and may have some benefits that were not adequately captured in the model, and took this into account in its decision-making.

There are no equalities issues that can be addressed in the guidance

3.23 The committee recalled that Palforzia has a marketing authorisation for treatment of peanut allergy in people aged 4 to 17 and those who turned 18 while on treatment (see section 2.1). This means most adults with peanut allergy will have no access to treatment. However, the committee noted that its remit only allows it to appraise a technology within its marketing authorisation.

3.24 The committee recalled that treatment with Palforzia is resource intensive because patients must attend a clinic prepared to treat anaphylaxis for initial dose escalation and the first dose of each new up-dosing level, in

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line with its marketing authorisation (see section 3.19). The patient and clinical experts explained that there may be unequal access to specialist allergy clinics in England because of geographic location or socioeconomic status. The committee considered these issues but noted they are related to implementing guidance in NHS practice and therefore outside of its remit. The committee concluded there are no equalities issues that can be addressed in the guidance.

4 Implementation

4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.

4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final appraisal document.

4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has peanut allergy and their carers and the doctor responsible for their care think that Palforzia is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Review of guidance

5.1 The guidance on this technology will be considered for review 3 years after publication. The guidance executive will decide whether the

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technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Amanda Adler
Chair, appraisal committee
November 2021

6 Appraisal committee members and NICE project team

Appraisal committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee B.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Catherine Spanswick
Technical lead

Ewa Rupniewska
Technical adviser

Daniel Davies, Jo Ekeledo

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Project managers

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