A feasibility study to evaluate PDE MAX, a food for special medical purposes (FSMP) for use in the dietary management of Pyridoxine Dependent Epilepsy (PDE) with regards to acceptability, tolerability, adherence and effect on metabolic control.

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To evaluate product acceptability, tolerance and adherence during an 8-week intake of PDE MAX in patients with Pyridoxine Dependent Epilepsy.To evaluate the effects on metabolic control by comparing the changes from baseline after an 8-week intake...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON51235

Source
ToetsingOnline

Brief title
Evaluation of PDE Max

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym

ATQ (ALDH7A1) deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Vitaflo International Ltd
Source(s) of monetary or material Support: Bedrijf Vitaflo International

Intervention

Keyword: food for special medical purposes, Pyridoxine Dependent Epilepsy (PDE)

Outcome measures

Primary outcome

To evaluate the product acceptability, tolerance and adherence during an 8-week

intake of PDE MAX in patients with Pyridoxine Dependent Epilepsy.

Secondary outcome

To observe the changes from baseline, after an 8-week intake of PDE MAX, in PDE

biomarkers:

- Pipecolic acid in plasma
- 6-oxo-pipecolic acid in bloodspot, plasma and urine
- P6C in plasma and bloodspot
- αAASA in plasma and urine
- Amino acid profile in plasma
- Whole blood serotonin
- Pyridoxal phosphate in plasma
- Vitamers in plasma
- Organic acids in urine

• 2OPP in bloodspot, plasma and urine

The outcome of this assessment will be used to support regulatory submissions

by Vitaflo (International) Ltd. for the purpose of registration in any

geography for sale and/or reimbursement of the product as appropriate.

Study description

Background summary

Pyridoxine dependent epilepsy (PDE) is a rare (~1:350,000), inherited disorder characterised by recurrent and drug resistant seizures. The disorder is pyridoxine (vitamin B6) dependent and patients are treated with high doses of this, although they are not deficient. 75% of patients have intellectual developmental disability and/or delay, despite adequate seizure control from treatment. Best practice is for triple therapy: pyridoxine, arginine supplementation and lysine restriction.

There is often delayed diagnosis. 6-oxo-pipecolic acid has been identified as a novel biomarker that utilises current newborn screening techniques. Another biomarker has also recently been discovered, 2OPP.

There is currently no protein substitute designed specifically for PDE.
Patients are being offered a *best fit* diet based on another condition, Glutaric Aciduria Type 1 (GA1). The GA1 products are low in lysine but also low in tryptophan, which may cause a deficiency for PDE patients. Due to the restrictive nature of the low protein diet, PDE sufferers are also at an increased risk of micronutrient deficiencies.
Therefore, vitamins, minerals and trace elements are incorporated into PDE MAX, to adequately replace the micronutrients that would typically be consumed through dietary protein intake.

The study will recruit up to 15 participants aged one and above to evaluate PDE Max on acceptability and tolerance.

Study objective

To evaluate product acceptability, tolerance and adherence during an 8-week intake of PDE MAX in patients with Pyridoxine Dependent Epilepsy.
To evaluate the effects on metabolic control by comparing the changes from

baseline after an 8-week intake of PDE MAX in the biomarkers described in the secondary outcomes.

Study design

This is a prospective, feasibility study in up to 15 participants aged one (1) year and over of PDE MAX for the dietary management of Pyridoxine Dependent Epilepsy. Participants will be provided with an eight-week supply of PDE MAX and will be asked to complete a daily diary and short questionnaire to record information on the following:
• Adherence
• Gastrointestinal tolerance
• Palatability
• How the product is used

Blood and urine samples will be taken at the beginning and end of the study to measure several biochemical parameters. Physical and neurological assessments will be carried out by the local Metabolic Consultant at the beginning and end of the study. Routine monitoring of lysine levels will continue.

Patients can then continue to use PDE Max if deemed desirable by the physician, dietitian and patient. The patients will then be followed for 12 months according to routine care and data on growth, lysine levels and diet information will be collected to also assess use over the longer term.

Intervention

15 participants, aged one (1) year and above, will have a 3-day baseline period on their current dietary regimen and then for the next 53 days will add PDE MAX to their diet under the direction of a dietitian. Blood and urine samples will be taken at baseline and the end of the study for biomarker analysis. Participants or their parents/guardian will complete a daily diary on adherence and seizures throughout the study and a GI symptoms diary in weeks 1, 4 and 8.

Study burden and risks

Results of this study will provide insight into the acceptability and tolerance of PDE Max as part of the dietary treatment to improve the metabolic health of people with PDE.

The risks of the measurements are low and little physical or mental discomfort is expected. Expected side effects could include gastrointestinal disturbance from consuming PDE MAX. Patients are already using other lysine-free protein supplements, although these are not well adapted to the PDE disease. PDE Max has a more adequate protein composition for this group of patients. This may lead to better outcomes for the patients and makes it possible to prescribe

patients a more appropriate diet for PDE.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)
Babies and toddlers (28 days-23 months)

Inclusion criteria

i) Diagnosis of Pyridoxine Dependent Epilepsy (PDE), biochemically and/or genetically confirmed.
ii) Males or females aged one (1) year and above. Any participant aged 16 years and over at screening must have the capacity to consent for themselves.
iii) Currently following a lysine-restricted diet for a minimum of four (4)

weeks prior to screening.
iv) Willing to take the study product and follow advice given by the dietitian.
v) Willingly given, written, informed consent from patient or parent/guardian.
vi) Willingly given, written assent (if appropriate).

Exclusion criteria

i) Inability to comply with the study protocol, in the opinion of the investigator.
ii) Use of additional macro/micronutrient supplements during the study period, unless clinically indicated and prescribed by the investigator, such as but not limited to arginine and pyridoxine. In which case, supplementation must have started four (4) weeks prior to screening with no anticipated changes to intakes during the study duration.
iii) Participants who are pregnant / breastfeeding at the start of the study or planning to become pregnant during the study period. Participants of child-bearing potential will be required to undergo pregnancy test prior to enrolment.
N.B.: Participants who become pregnant unexpectedly during this study may, in consultation with their doctor, continue on the study*s dietary product if they wish but will not have any investigations that would not normally be carried out during pregnancy.
iv) Allergy to any ingredient present in the study product.
v) Other concurrent medical or psychiatric conditions, which, in the opinion of the Investigator, would place the subject at increased risk, preclude obtaining voluntary consent/assent or compliance with required study procedures, or would confound the objectives of the study.
vi) Is participating in any other interventional study and has received any other investigational drug, product or device within 30 days prior to screening or are taking part in a non-medication study which, in the opinion of the investigator, would interfere with study compliance or outcome assessments.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-06-2021
Enrollment:	7
Type:	Actual

Ethics review

Approved WMO Date:	17-02-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-11-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	NCT04672226
CCMO	NL75819.091.20

Study results

Date completed:	30-11-2022
Actual enrolment:	5