# An open-label, explorative, post launch, multicenter, multi-country intervention study of PKU Synergy (an amino-acid mixture) to evaluate change in nutrient intake in PKU subjects with an increased Phe-tolerance/intake.

Published: 26-02-2020
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The study*s main objectives are to investigate change in nutrient intake after a 24-week intervention with PKU Synergy in PKU subjects with an increased Phe-tolerance/intake and to evaluate product acceptability.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Inborn errors of metabolism |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON48912

**Source**
ToetsingOnline

**Brief title**
ESSENTIAL

### Condition

- Inborn errors of metabolism

**Synonym**
Phenylketonuria / PKU

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Nutricia Research
**Source(s) of monetary or material Support:** Nutricia Research BV en Nutricia Nederland

## Intervention

**Keyword:** Amino-acid mixture, Phenylketonuria, PKU Synergy

## Outcome measures

### Primary outcome

Main outcome parameters:

*Nutrient intake (three-day diet diary)

*Product acceptability (questionnaire)

### Secondary outcome

Other parameters:

*Compliance (weekly)

*Blood chemistry: Full fatty acid profile, full amino acid profile, Vitamins

B1, B6, B12 & D; Folic acid; Selenium; Iodine; Calcium; Zinc; Iron; Copper;

Manganese

*Biweekly dried bloodspot Phe-levels

# Study description

### Background summary

Phenylketonuria (PKU) is an inherited metabolic disorder, where subjects are born with a genetic deficiency in the phenylalanine hydroxylase enzyme (PAH). Due to the genetic deficit, Phe accumulates in the blood. Left untreated, PKU leads to severe mental retardation and neurological disabilities.
The principal goal of dietary management in PKU is to prevent an excessive Phe

accumulation in the blood and brain through means of a low Phe diet.
This classical treatment is well established for PKU patients and known to be effective and safe. Since 2008 a subgroup of patients has been treated with sapropterin dihydrochloride (BH4 treatment) with the goal to enhance the residual PAH activity.
PKU patients who are on a relaxed diet due to BH4 treatment, increase their daily tolerance and intake of phenylalanine (Phe). This means they can consume a higher amount of protein-containing natural foods. Recent research showed that patients do not easily change eating habits. Even though they can move more towards a normal diet, their food choice still differs significantly compared to controls without PKU. Consequently, this group of PKU patients does not meet the recommended intake of micronutrients and amino acids.
There are other PKU patients (mild) who also relax their diet by increasing their Phe intake >1000mg/day. The food choice and eating habits of this patient group, continue to differ significantly from the healthy, age-matched population, even after relaxation of their diet. In general, basic eating habits develop during early childhood and remain stable throughout life. Therefore, PKU patients under a relaxed diet are at risk of an insufficient nutrient supply.
The amino acid mixtures that are currently available do not provide the required amount of the necessary micronutrients and amino acids this group needs. Therefore the sponsor of this study designed a new product PKU Synergy, adjusted to the group*s specific needs

## Study objective

The study*s main objectives are to investigate change in nutrient intake after a 24-week intervention with PKU Synergy in PKU subjects with an increased Phe-tolerance/intake and to evaluate product acceptability.

## Study design

A 24-week open label, explorative, post launch, multicenter, multi-country intervention study

## Intervention

PKU Synergy is intended for oral use only. The daily indicated dosage is one 33g stick pack of test product, taken once per day at a fixed time for 24 weeks, e.g. at breakfast or supper.

## Study burden and risks

For patients, questionnaires will be administered online on five time points and they will be asked to complete a paper 3-day dietary intake diary twice. They will be asked to visit the hospital twice. In addition, a blood spot will

be collected biweekly and 22 ml blood via venapunction will be drawn twice during the hospital visits. Subjects will need to be fasted (8 hours) at the time of blood drawing, and will be asked not to take any vigorous exercise in the 24 hours prior to a visit. Subjects will take the study product once daily for 24 weeks.

## 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)
Elderly (65 years and older)

### Inclusion criteria

Inclusion criteria:
1. PKU subjects identified by newborn screening and started low-Phe diet before 3 months of age.

2. PKU subjects with an increased Phe-tolerance/intake due to: mild PKU phenotype or BH4 treatment.
3. If treated with BH4, PKU subjects should be on a stable BH4 treatment for at least 26 consecutive weeks up to start test product intake.
4. Age*12 years.
5. If subjects (irrespective whether BH4 users or mild PKU) use amino-acid mixture(s; AAM), then a maximum of 25 Protein Equivalents (PE) derived from the AAM per day applies and usage on a daily basis for at least 26 consecutive weeks up to Visit 1
6. If subjects (irrespective whether BH4 users or mild PKU) use AAMs they should be capable and willing to substitute their current AAM(s; maximum of 25 PE per day) with one portion of the test product per day
7. If subjects (irrespective whether BH4 users or mild PKU) use omega-3, antioxidant, and/or vitamin supplements, to stop usage of the supplements and be able and willing to substitute with the test product
8. Willing and able to comply with study procedures, 9. Willing and able to provide informed consent (and assent in case of minors if required by local law/regulations).
10. For women of childbearing potential: not to have the intention to become pregnant during the study.

### Exclusion criteria

Exclusion criteria:
1. For women: Currently pregnant or lactating.
2. Current or prior use of the test product within six weeks prior to entry into the study.
3. Concurrent conditions (including renal failure and severe hepatic failure) and medication that could interfere with participation, outcome parameters or safety (as determined by Investigator).
4. Psychotropic medication (i.e. medication affecting the nervous system) and inotropic medication.
5. Any condition creating high risk of poor compliance with study.
6. Participation in any other studies involving investigational or marketed products concomitantly or within six weeks prior to entry into the study. Except for studies related to Kuvan® (synthetic tetrahydrobiopterin (BH4)) without diagnostic, therapeutic or experimental intervention.

## Study design

### Design

**Study type:** Interventional

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

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 24-09-2020 |
| Enrollment: | 10 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 26-02-2020 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 16-04-2020 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

## 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 |
|---|---|
| CCMO | NL63473.042.19 |

# Study results

Date completed: 27-05-2021

Actual enrolment: 2

**Summary results**
Trial is onging in other countries