

Developed and funded by BioMarin
EU-PKU-00334 Date of Preparation: June 2022

PROTEIN, PHE AND PKU



B:OMARIN[®]

BioMarin has a

20

year track record of developing first-in-class therapies that make a big difference for small patient populations.



Phenylketonuria (PKU) is

RARE

1

in every

10,000

newborn babies
across Europe¹

A GENETIC
CONDITION

where the phenylalanine
hydroxylase (PAH)
is either missing or not
working properly,
resulting in a neurotoxic
accumulation of
phenylalanine (Phe)
in the blood²

**Phe is an amino acid
found in all protein
containing foods³**

To maintain Phe levels between
120-360 $\mu\text{mol/L}$,
management includes:⁴

1

**Reducing
natural Phe
intake with a
restricted diet**



2

**Increasing Phe
metabolism
with medical
treatment**





Phe levels and must be excluded from the diet³





Phe levels and can be included in the diet, in very small amounts³



FRUITS



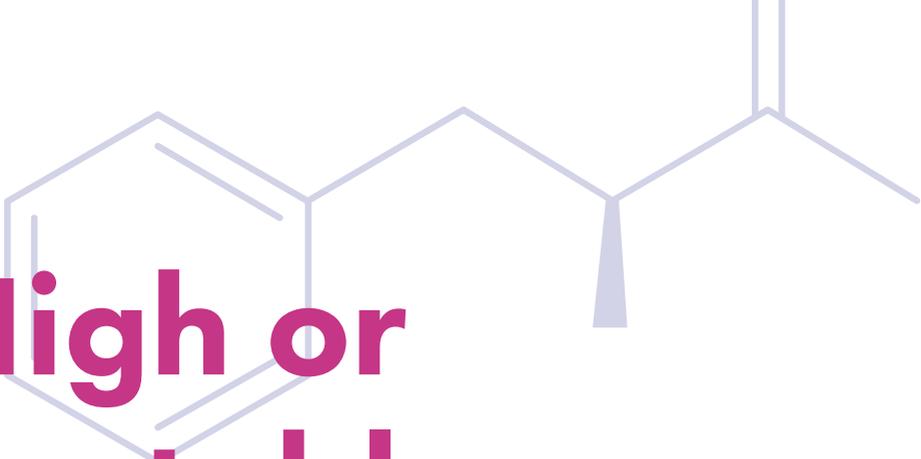
VEGETABLES



BREADS



PASTAS



**High or
unstable**

blood Phe levels
can lead to ^{3,5}



Slow processing of information

Behavioural or social problems

Intellectual disability

Problems with memory

Seizures and tremors

Inattention

Anxiety & depression

Irritability

Difficulty in decision making, problem solving & planning

PKU requires lifelong management⁵



Findings from recent online surveys* and studies^{6,7} reveal pressing unmet needs related to diet and impact on quality of life

73%

of adults & caregivers of children
find **dietary management** difficult⁶



42%

follow a **low-Phe**
nutritional plan⁷



The **top 5** issues affecting the ability to follow diet⁶

- Limited food choices
- Unpleasant protein substitutes
- Inconvenience
- Unpleasant food choices
- Diet is too time consuming to manage



Adherence to diet can be impacted by⁷

56%

Socializing

39%

Palatability

36%

Consumption in a
working environment

35%

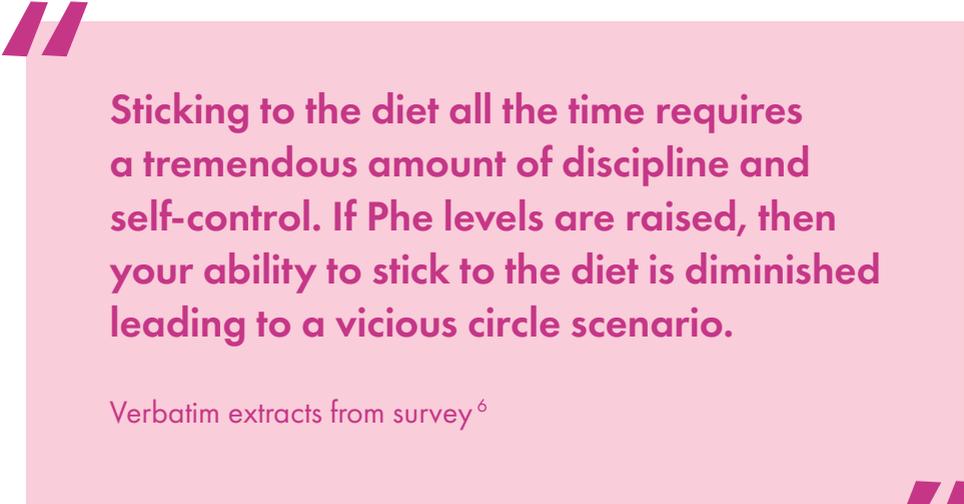
Feelings of
embarrassment

34%

Travelling

33%

Low ease of use



Sticking to the diet all the time requires a tremendous amount of discipline and self-control. If Phe levels are raised, then your ability to stick to the diet is diminished leading to a vicious circle scenario.

Verbatim extracts from survey⁶





**Patients
regularly
report...^{6,7}**

**(twice per week
and even daily)**



**DIFFICULTY
CONCENTRATING**



54%

FATIGUE



53%

**DEPRESSION
& ANXIETY**



52%

**DIGESTIVE
PROBLEMS**



34%

HEADACHES



32%

IRRITABILITY



14%

EATING DISORDER



14%

MOOD SWINGS



13%



feel guilt and self-blame⁶



have relationship difficulties
with friends, family or partners⁶



Many expressed frustration that their
symptoms were not always taken
seriously by health professionals⁶



[...] I have blank moments where I can't think or get my words out that I am trying to say. I experience anxiety and I get paranoid. All this impacts my work life as my job is very fast paced. I get "brain fog" tend to become irritable and uneasy in social settings.

Verbatim extracts from survey⁶



PKU is diagnosed through a heel prick test⁸

PKU was the
prototype disorder
for newborn
screening (NBS)
in the

1960s



Leading to early
dietary treatment
and vastly

**improving
patient
outcomes**



Screening was promoted to **reduce overcrowding in psychiatric institutions**

In 1962, the Children's Bureau Census found

399 children with PKU

admitted during the preceding 5 years⁹

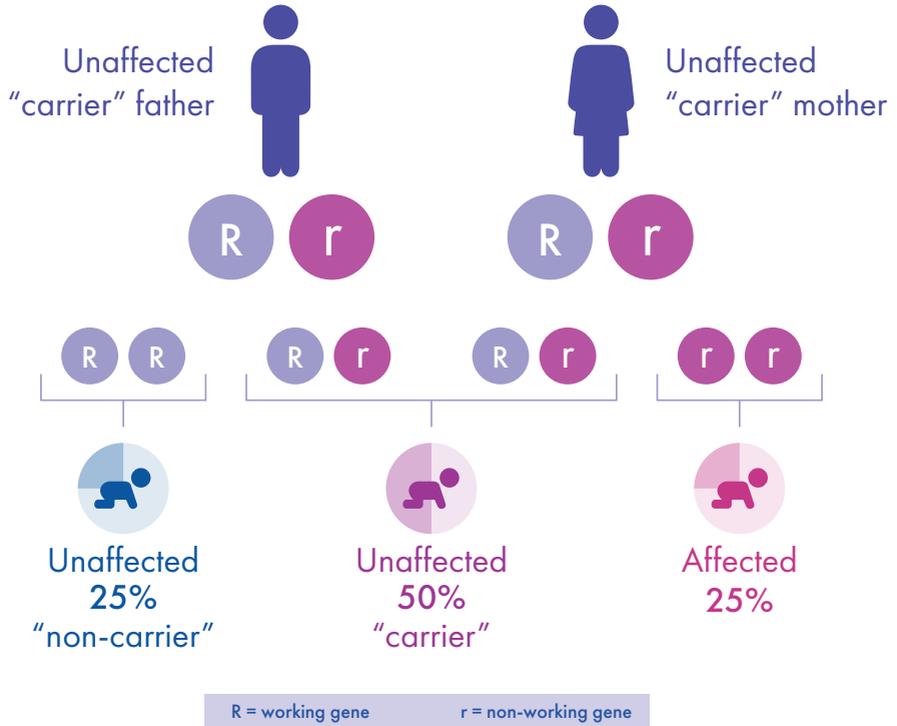


Laboratory tests in infants with PKU typically confirm plasma levels of Phe

10-60 x
above normal¹⁰



PKU is an inherited autosomal recessive disease, where two copies of an abnormal gene are inherited from the two carrier parents¹⁰



References

1. van Wegberg AMJ, MacDonald A, Ahring K, et al. The complete European guidelines on phenylketonuria: diagnosis and treatment. *Orphanet J Rare Dis.* 2017;12(1):162. Published 2017 Oct 12. <https://doi.org/10.1186/s13023-017-0685-2>. Last accessed: April 2019
2. Blau N. Genetics of Phenylketonuria: Then and Now. *Hum Mutat* 2016; 37:508. Published 2016 Feb. 26. <https://doi.org/10.1002/humu.22980>. Last accessed: April 2019
3. BioMarin Pharmaceuticals. 2019. PKU. [ONLINE] Available at: <https://www.biomarin.com/patients/diseases/pku>. Last accessed: April 2019
4. Macleod EL, Ney DM. Nutritional Management of Phenylketonuria. *Ann Nestle Eng.* 2010;68(2):58–69. Published 2010 Jun <https://doi.org/10.1159/000312813>. Last accessed: April 2019
5. BioMarin Pharmaceuticals. 2017.Phe In The Brain | PKU. Phenylketonuria (PKU) Information [ONLINE]. Available at: <http://www.pku.com/about-pku/phe-in-the-brain>. Last accessed: April 2019
6. Ford S, O'Driscoll M, MacDonald A. Living with Phenylketonuria: Lessons from the PKU community. *Mol Genet Metab Rep.* 2018;17:57-63. Published 2018 Oct 18. <https://doi.org/10.1016/j.ymgmr.2018.10.002>. Last accessed: April 2019
7. Cazzorla C, Bensi G, Biasucci G, et al. Living with phenylketonuria in adulthood: The PKU ATTITUDE study. *Mol Genet Metab Rep.* 2018;16:39-45. Published 2018 Jul 11. <https://doi:10.1016/j.ymgmr.2018.06.007>. Last accessed: April 2019
8. Pitt JJ. Newborn screening. *Clin Biochem Rev.* 2010;31:57–68. Last accessed April 2019
9. Diane B. Paul (1997) 'APPENDIX 5. THE HISTORY OF NEWBORN PHENYLKETONURIA SCREENING IN THE U.S.*', in Neil A. Holtzman, Michael S. Watson (ed.) *Promoting Safe and Effective Genetic Testing in the United States.* Available at: <https://biotech.law.lsu.edu/research/fed/iftg/appendix5.htm>. Last accessed: April 2019
10. NORD. 2019. Phenylketonuria. [ONLINE] Available at: <https://rarediseases.org/rare-diseases/phenylketonuria/>. Last accessed April 2019

* An online questionnaire was voluntarily completed and submitted by 631 adults with PKU or parents/caregivers of children or adults unable to complete the survey themselves from across the UK. The questionnaire was placed on the UK NSPKU website, Facebook and Twitter accounts between 9th November 2017 and 31st January 2018. In 2017, 116 adult PKU patients aged between 19–30 years took part in a study across 5 Italian centres.

Today and every other day for the past 17 years – BioMarin has shared an unmatched commitment to the PKU community, from patients, to scientists, to healthcare professionals. Our dedication to discovering and advancing new therapies that lessen the burden on patients' lives continues. Join us in spreading awareness and advocating for those affected by this rare, genetic condition.

B  **OMARIN**®

