Developed and funded by BioMarin
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PROTEIN, PHE AND **PKU**

BioMarin has a

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 Europe[1]

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 blood**[2]

Phe is an amino acid found in all protein containing foods[3]

To maintain Phe levels between **120-360 umol/L**, management includes:[4]

1

Reducing natural Phe intake with a restricted diet

2

Increasing Phe metabolism with medical treatment

HIGH

Phe levels and must be excluded from the diet[3]

MILK & DAIRY PRODUCTS

MEAT

FISH

CHICKEN

BEANS

NUTS

Phe levels and can be included in the diet, in very small amounts [3]


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 management[5]

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** difficult[6]

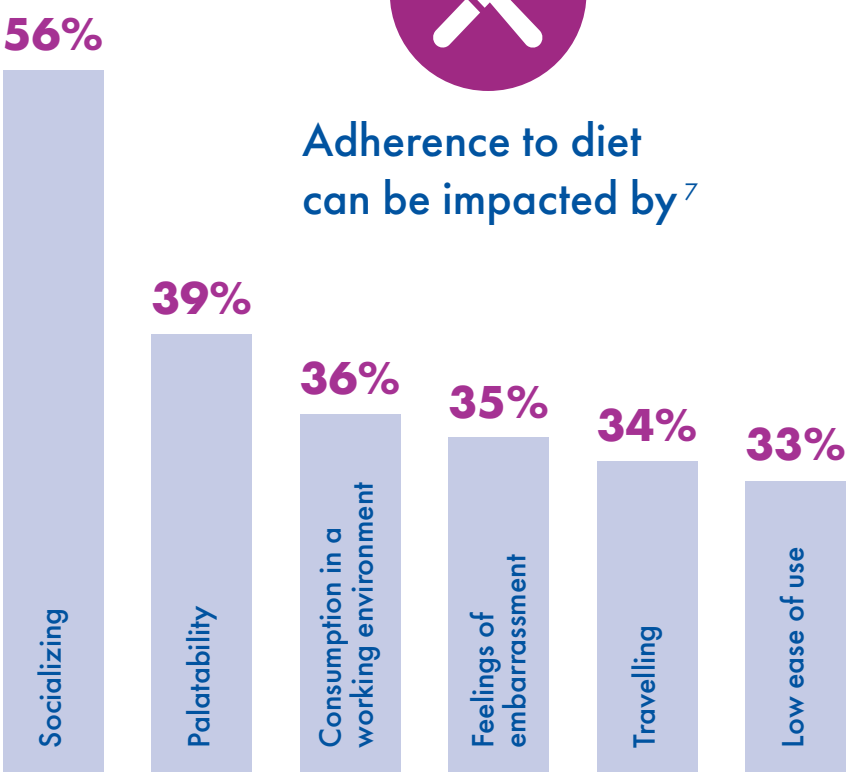
42%

follow a **low-Phe nutritional plan**[7]

The **top 5** issues affecting the ability to follow diet[6]

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

Adherence to diet can be impacted by[7]



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 survey [6]

Patients regularly report...[6,7]

(twice per week and even daily)

DIFFICULTY CONCENTRATING	FATIGUE	DEPRESSION & ANXIETY	DIGESTIVE PROBLEMS
54%	53%	52%	34%

HEADACHES	IRRITABILITY	EATING DISORDER	MOOD SWINGS
32%	14%	14%	13%

feel guilt and self-blame [6]

have relationship difficulties with friends, family or partners [6]

Many expressed frustration that their symptoms were not always taken seriously by health professionals [6]

[...] 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 survey [6]

PKU is diagnosed **through a heel prick test**[8]

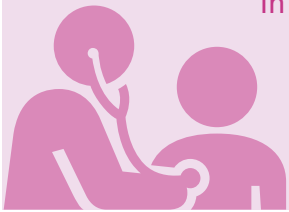
PKU was the prototype disorder for newborn screening (NBS) in the

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

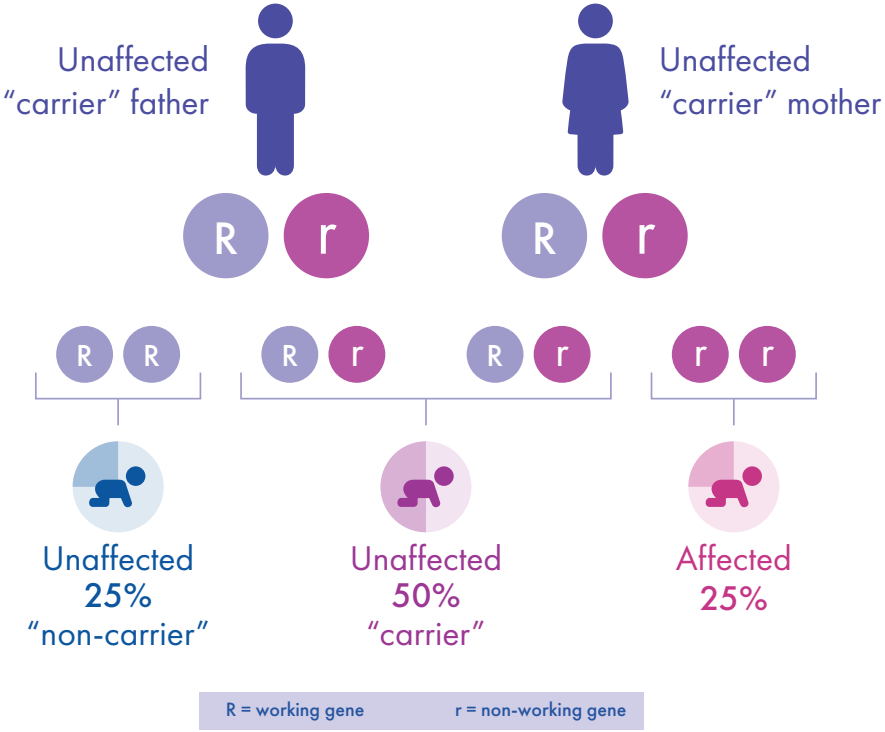
399 children with PKU

admitted during the preceding 5 years[9]

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

10-60 x above normal[10]

PKU is an inherited autosomal recessive disease, where two copies of an abnormal gene are inherited from the two carrier parents[10]



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* 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.

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