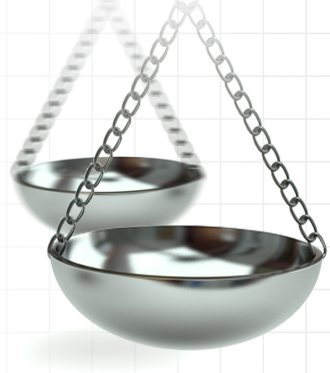
Plain Language Summary of Publication

Efficacy and safety of sepiapterin versus sapropterin in people living with phenylketonuria: a plain language summary of the AMPLIPHY trial



Journal of Comparative Effectiveness Research

Maria Giżewska[1], Laura Guilder[2], Sarah Gallagher[3] and Anita Inwood[4]

[1]Department of Pediatrics, Rare Diseases and Metabolic Medicine, Pomeranian Medical University in Szczecin, Szczecin, Poland; [2]Division of Clinical and Metabolic Genetics, Department of Paediatrics, University of Toronto and The Hospital for Sick Children, Toronto, ON, Canada; [3]National PKU Alliance, Roanoke, VA, USA, and patient caregiver; [4]Department of Metabolic Medicine, Queensland Lifespan Metabolic Medicine Service, Queensland Children's Hospital, Brisbane, QLD, Australia

First draft submitted: 16 June 2026; Accepted for publication: 13 October 2026; Published online: 11 November 2026

Summary

What is this summary about?
This summary is about a clinical trial called AMPLIPHY. AMPLIPHY was a trial that compared two treatments, sepiapterin and sapropterin, to see how well they worked in children and adults living with phenylketonuria (PKU).

PKU is a rare genetic condition where the body cannot properly break down phenylalanine (Phe), which is an amino acid found in many foods. If people living with PKU are not treated, Phe levels build up in the body, which can affect brain development, thinking skills and behaviour. If left untreated for a long time, this may cause symptoms such as seizures, rashes and problems with movement. A key goal of PKU treatment is to keep blood Phe levels within a target range to avoid these effects.

What happened in the AMPLIPHY trial?
In the AMPLIPHY trial, the researchers wanted to see how well sepiapterin worked in people living with PKU when compared with sapropterin, an alternative treatment for PKU, and to compare the safety of the treatments.

The AMPLIPHY trial had two parts:

- During Part 1, the participants took sepiapterin for 2 weeks to find out whether it decreased their Phe levels.
  - Participants whose blood Phe levels decreased by at least 20% were classed as responsive to sepiapterin and could continue to Part 2.
  - Participants whose blood Phe levels decreased by less than 20% did not continue to Part 2.
- During Part 2:
  - The participants took either sepiapterin or sapropterin for the first 4 weeks followed by 4 weeks of the other treatment.

What were the results?
During Part 1, the researchers found that most people benefited from sepiapterin. Specifically, 82% of participants (67 out of 82) had a reduction in blood Phe levels of at least 20%, and 76% of participants (62 out of 82) had a reduction of at least 30%.

During Part 2, the researchers found that sepiapterin lowered blood Phe levels by 70% more than sapropterin did.

There were no adverse events that were considered serious or that stopped anyone from taking treatment or participating in the trial.

What do the results of the trial mean?
How well did the treatments work: these results showed that sepiapterin lowered blood Phe levels more than sapropterin in children and adults with PKU.

What were the safety findings: sepiapterin was well tolerated, with no unexpected side effects or safety concerns identified.

Becaris PUBLISHING

Who is this article for?

This plain language summary of publication (PLSP) is intended for people living with PKU, the caregivers and families of people living with PKU, and non-specialist audiences.

What is phenylketonuria?

Phenylketonuria (PKU) is a **rare disorder** and **genetic condition** that is passed down from parents to their children. It is usually diagnosed through **newborn screening**. PKU is caused by changes in a **gene** that provides instructions for making an **enzyme** called **phenylalanine hydroxylase** (PAH). **Classic PKU** is the most severe form. It is associated with extremely high blood levels of Phe and is very difficult to treat.

How to say (double click on the sound icon to play the sound)

AMPLIPHY: AM-plih-fie
Pegvaliase: pehg-VAL-ee-ays
Phenylalanine hydroxylase: fee-nile-AL-uh-neen high-DROK-suh-lays
Phenylketonuria: fee-nile-kee-toh-NYOO-ree-uh
Placebo: pluh-SEE-boh
Sapropterin dihydrochloride: sahp-pro-tare-rin dai-hai-druh-klaw-ride
Sepiapterin: see-pee-ah-tare-rin
Tetrahydrobiopterin: tet-ruh-HY-droh-BY-op-tare-in
Tyrosine: TAI-roh-seen

?

Efficacy: How well a drug can do what it is expected to do to help treat a disease

Phenylketonuria (PKU): A rare, genetic condition that causes high levels of the **amino acid phenylalanine** to build up in the body. High levels of phenylalanine in the body over long periods of time can affect brain development, thinking skills, memory and behaviour, and can cause seizures and problems with movement. It is sometimes abbreviated to PKU.

Amino acids: The building blocks of **proteins**.

Phenylalanine: An amino acid that the body needs to make proteins and other important molecules. Phenylalanine levels are high in people living with phenylketonuria, and this can be harmful to the brain. It is sometimes abbreviated to Phe.

Rare disorder: A medical condition that affects a very small number of people.

Genetic condition: A health problem caused by a change in your DNA. Your DNA is like an instruction manual that tells your body how to grow and work.

Newborn screening: A set of tests done on babies shortly after birth to check for certain serious diseases, usually by collecting a few drops of blood from the baby. This allows for earlier medical treatment before symptoms happen, if needed.

Genes: Parts of DNA that contain instructions for making proteins. Genes are passed down from parents to their children, and they affect how the body works.

Phenylalanine hydroxylase: An **enzyme** that breaks down phenylalanine into another amino acid called **tyrosine**. It is sometimes abbreviated to PAH.

Enzymes: Proteins that help chemical reactions happen in the body. This includes breaking down substances, for example during the digestion of food.

Tyrosine: An amino acid that the body makes from the amino acid phenylalanine. It is sometimes abbreviated to Tyr.

Classic PKU: The most severe type of phenylketonuria. People who have this type have very high levels of the amino acid phenylalanine because the enzyme responsible for breaking down phenylalanine (called 'phenylalanine hydroxylase') works very poorly or does not work at all.

Proteins: Large, biological molecules with many important roles in the body. Proteins are vital for life and are essential for the structure, function and regulation of all tissues and organs throughout the body.

What happens to Phe in the body?

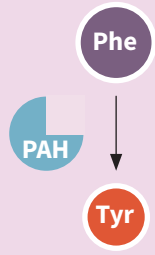


Individual eats Phe-containing foods such as milk, eggs, cereals, bread, pasta, vegetables, legumes, meat and fish

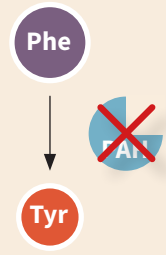


What happens normally?

PAH breaks down the amino acid phenylalanine (Phe) into another amino acid called tyrosine (Tyr)



What happens in PKU?



PAH does not work properly, so Phe builds up in the body and Tyr levels may be lower than normal

High Phe levels affect:

- brain development
- thinking skills
- memory
- behaviour
- mood
- movement

Living with PKU

There is currently no cure for PKU, so people living with PKU need to eat:



Foods with very low levels of natural proteins



Specially formulated medical foods as a source of protein

Treatment options for people living with PKU

Low-Phe diet

- A low-Phe diet can be difficult to follow for long, and it can affect the **health-related quality of life** of people living with PKU
  - For some people, it's difficult to keep blood Phe levels within the recommended range, even if they follow a special diet
- Overall, PKU can place a lifelong burden on individuals, families and carers
- PKU requires constant planning around a very strict diet, regular blood tests and specialist foods

Medicine

Sapropterin dihydrochloride

- May not work for everyone

Sepiapterin

- ✓ **Approved** for use to help control blood Phe levels in people living with PKU
- ✓ Approved in the USA and Canada (in individuals aged 1 month and older)
- ✓ Approved in Australia, Brazil, the European Union, Japan and Switzerland (in all ages)

Pegvaliase

- Limited to certain age groups (since the **AMPLIPHY trial** took place, the age group in which pegvaliase is approved for use in the USA has changed from 18 years and above to 12 years and above)
- May have serious side effects, such as allergic reactions in some people who take pegvaliase injections

10.57264/cer-2025-0115

Health-related quality of life: Refers to how any health issues that a person has can affect their daily life and activities.

Approved treatment: A medicine that health authorities have allowed doctors to prescribe after reviewing evidence that it works and that its benefits outweigh its risks.

AMPLIPHY: The name of the phase 3 clinical trial that compared sepiapterin with sapropterin for treating people living with phenylketonuria.

Sepiapterin: An approved treatment for people living with phenylketonuria of all ages (or from 1 month of age, depending on the country). The treatment helps to control blood phenylalanine levels. It was approved in the USA and in Europe in 2025.

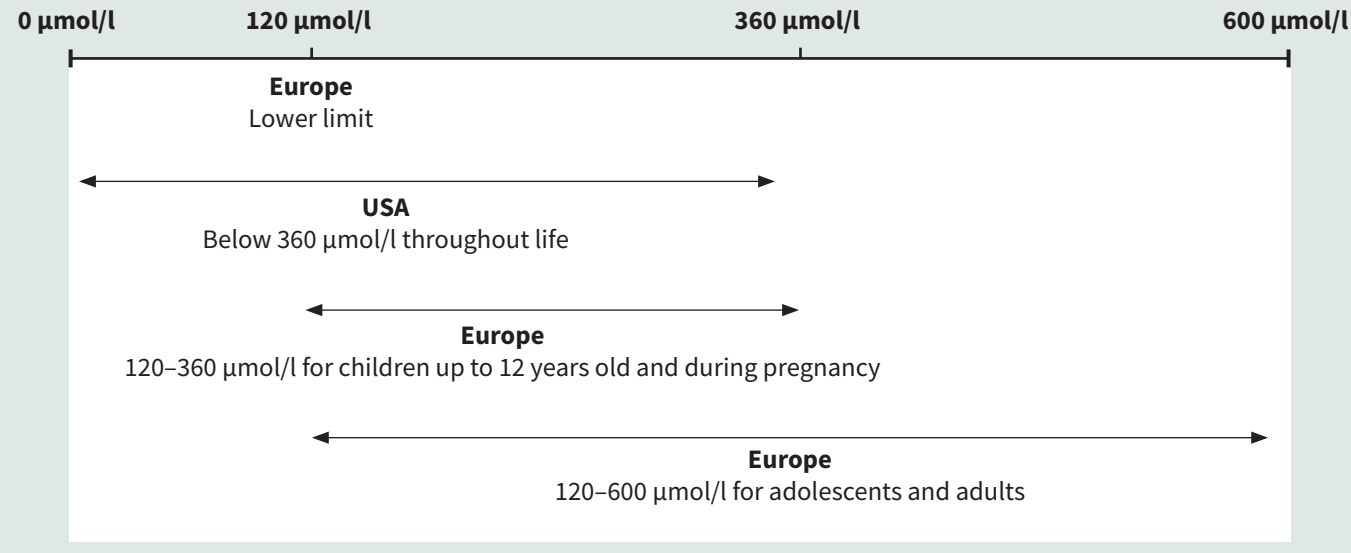
Pegvaliase: An approved treatment for people living with phenylketonuria aged 12 years or older, depending on the country. The treatment was approved in the USA in 2018 and in Europe in 2019. This treatment contains an enzyme called phenylalanine ammonia lyase, which can reduce levels of phenylalanine in the body.

Sapropterin dihydrochloride: An approved treatment for people living with phenylketonuria of all ages (or from 1 month of age, depending on the country). The treatment helps to control blood phenylalanine levels. It was approved in the USA in 2007 and in Europe in 2008.

Micromoles per litre (µmol/l): Units that doctors use to measure phenylalanine levels in the blood. You can think of them as the 'scale' used to report blood phenylalanine results.

Phe levels in the blood of 120 **µmol/l** or more are usually considered 'elevated', but people living with classic PKU may have levels above 1200 µmol/l if not treated.

Recommended blood Phe targets



How do sapropterin and sepiapterin work?

Sapropterin

Sapropterin is a form of **tetrahydrobiopterin** (BH_4), a molecule that helps the PAH enzyme work. Sapropterin can lower blood Phe levels in some individuals, mainly those with a milder form of PKU (only 25–50% of people living with PKU).

Sapropterin comes in the form of tablets or a powder, which can be dissolved in water or apple juice. It is approved in several countries to treat children and adults with high levels of Phe and who have the type of PKU that is responsive to BH_4.

Tetrahydrobiopterin: A substance in the body that helps certain enzymes, such as phenylalanine hydroxylase, to work properly. It is sometimes abbreviated to BH_4.

Sepiapterin

Sepiapterin works by helping the PAH enzyme to break down Phe, which lowers Phe levels in the blood. Sepiapterin works in two ways:

1. It can quickly turn into BH_4 and help the PAH enzyme to work properly.
2. It can also help the PAH enzyme to work properly directly, without being turned into BH_4.

Sepiapterin is a powdered drug that is taken once a day by mouth. The powder is mixed with water, apple juice or soft foods like apple sauce or strawberry jam. The amount of sepiapterin that is taken is based on the person's age and weight.

Sepiapterin helps people living with PKU to keep their blood Phe levels within the recommended range. It could also help to reduce symptoms of PKU and allow people living with PKU to eat more protein. This would enable people to have a diet that is less strict than they could have if they were not taking sepiapterin.

Overall comparison between sapropterin and sepiapterin

Feature	Sapropterin	Sepiapterin
Purpose	Helps lower blood Phe levels in some people living with a milder form of PKU	• Helps lower blood Phe levels and keep blood Phe within the recommended range • May be effective for people living with mild, moderate or severe PKU, including those who do not respond to BH_4 treatment
How it works	A form of BH_4 that helps the PAH enzyme work	Helps the PAH enzyme work in two ways: • by turning into BH_4 • by directly helping the PAH enzyme without turning into BH_4

Author's note

The section on "**What is phenylketonuria?**" provides background information about PKU

The section on "**What are sepiapterin and sapropterin?**" provides background information on these treatments for PKU

This information helps readers understand the results of the AMPLIPHY trial

The sources used to develop these sections are listed in the "**Further reading**" section

10.57264/cer-2025-0115

The AMPLIPHY clinical trial

Why was the AMPLIPHY trial carried out?

The AMPLIPHY trial was designed to compare how sepiapterin and sapropterin affect blood Phe levels and the drugs' **safety**. It is standard procedure to carry out such trials when new drugs are being developed.

Clinical trial: A normal and mandatory part of developing a new medicine. These are studies that test a treatment to check whether there are any safety concerns and how well it works in the condition being studied.

Safety: How a treatment affects a person's health, including any side effects or medical problems that occur while taking it.

Washout period: A period in a clinical trial when participants stop taking a treatment so it can fully leave their body. This helps to ensure that the effects of a previous treatment do not influence the results of the treatment being studied.

Who took part in the AMPLIPHY trial?

People aged 2 years and older with PKU were able to join this trial if:

- their blood Phe levels were above 360 µmol/l on their current treatment
- they had a steady dietary intake of Phe in the 4 weeks before the trial
- they were willing to stop using other PKU medications before starting the trial.

The participants stopped taking other medications for PKU for 7 days before starting treatment with sepiapterin. This was to make sure that the other medications had left the participants' bodies and would not affect the results of the trial. This is known as a **washout period**.

Individuals with PKU were allowed to take part in the trial regardless of whether they previously responded to treatment with sapropterin.

Key information about the participants in the AMPLIPHY study

Average age:
15 years



Average blood Phe level at the start of the trial: 578.6 µmol/l

18% of participants had **classic PKU**
This was 15 out of 82 or almost **2 in 10** participants

87% had previously been **treated with sapropterin**
This was 71 out of 82 or almost **9 in 10** participants

46% were being **treated with sapropterin when joining the study**
This was 38 out of 82 or almost **5 in 10** participants

When and where was this trial carried out?

The AMPLIPHY trial was a **phase 3 clinical trial** that began in January 2024 and finished in March 2025. It was carried out at 18 hospitals in 12 countries.

Australia



21 participants

Poland



10 participants

Canada



9 participants

Czechia



8 participants

Denmark



8 participants

United Kingdom



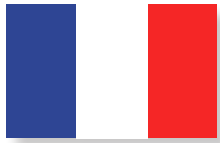
8 participants

The Netherlands



5 participants

France



3 participants

Italy



3 participants

Spain



3 participants

Germany



2 participants

Slovenia



2 participants

Phase 3 clinical trial: A late-stage clinical trial that is done in a larger group of people than earlier trials. These trials tend to compare a new treatment with either a dummy treatment (placebo) or current, standard treatments to see how well the new treatment works and whether there are any safety concerns.

How was the trial carried out?

The AMPLIPHY trial had two parts, both **open-label**. The participants stayed on their usual diet during both parts of the trial.

In **Part 1** of the trial, the researchers wanted to identify participants who benefited from sepiapterin so that they could decide who would go on to enter Part 2 of the trial.

In **Part 2** of the trial, the researchers wanted to learn more about the effects of sepiapterin on the participants' blood Phe levels compared with those of sapropterin. They also wanted to learn more about the safety of sepiapterin.

Open-label trial: A type of trial where the participants, researchers, trial doctors and other trial staff know what treatment the participants are taking.

10.57264/cer-2025-0115

Part 1

Who participated in Part 1 of the trial?

82 participants joined Part 1 of the trial.

How was Part 1 of the trial done?

Participants took sepiapterin once a day by mouth for 2 weeks. The daily dose was 60 milligrams per kilogram (mg/kg) of body weight.

After 2 weeks, the researchers looked at how well the participants had responded to sepiapterin.

- Participants whose blood Phe levels decreased by at least 20% were classed as 'responsive' to sepiapterin, and they could **continue to Part 2**.
- Participants whose blood Phe levels decreased by less than 20% **did not** continue to Part 2.

To test the effects of sepiapterin on blood Phe levels, the researchers measured Phe levels in dried blood samples from the participants. The researchers worked out how blood Phe levels changed by comparing results from before and after 2 weeks of sepiapterin treatment.

What were the results of Part 1 of the trial?

The researchers found that most of the people who took part in the study benefited from taking sepiapterin.

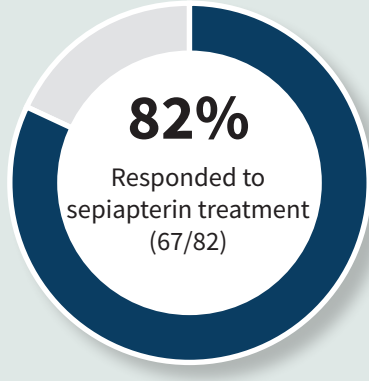
Specifically:

- **82%** of participants (67 out of 82) had a reduction in blood Phe levels of **at least 20%**
- **76%** of participants (62 out of 82) had a reduction in blood Phe levels of **at least 30%**.

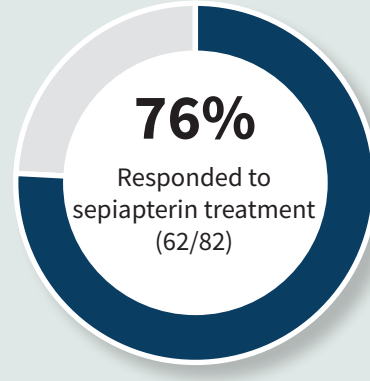
Part 1 results: Sepiapterin response rates



13 participants could not join the trial (their dietary intake was not steady enough during the 4 weeks before their planned entry into the trial)



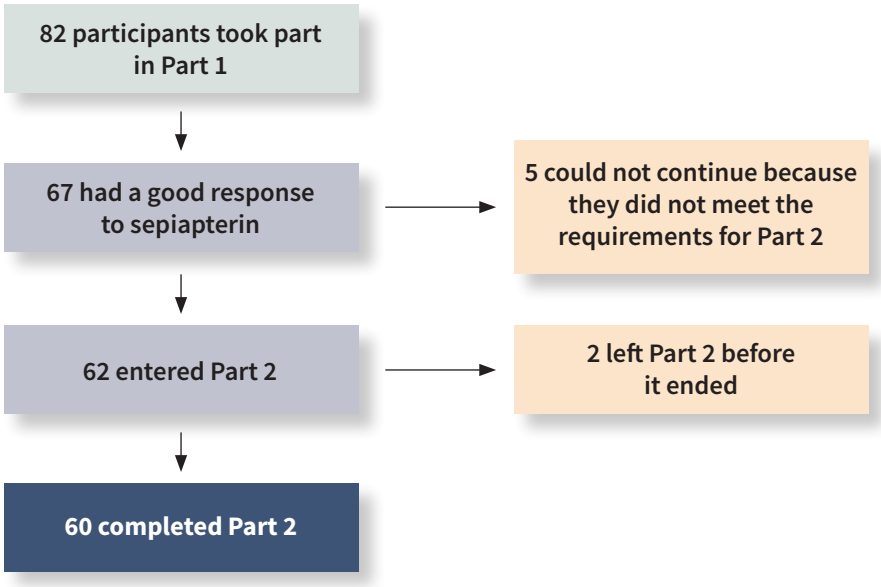
had a reduction in blood Phe levels of at least 20%



had a reduction in blood Phe levels of at least 30%

Part 2

Who participated in Part 2 of the trial?



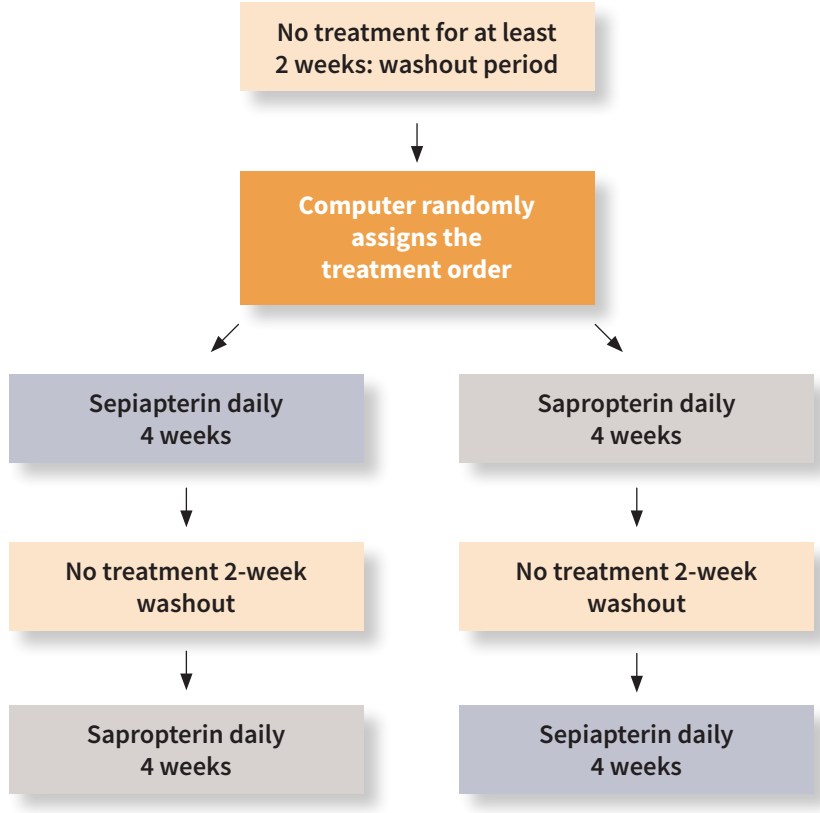
How was Part 2 of the trial done?

Before starting Part 2, the participants did not take any treatment for at least 2 weeks. This break of at least 2 weeks between each 4-week treatment period is known as a washout period. This gave the previous treatment time to leave the body before the next treatment started, helping the researchers to compare the treatments fairly.

After this washout period:

1. The participants took sapropterin or sepiapterin once a day by mouth for 4 weeks.
2. Then the participants took no treatment for 2 weeks.
3. Then the participants took the other treatment for another 4 weeks. So, if a participant took sepiapterin during the first 4 weeks of Part 2, they would then take sapropterin for the last 4 weeks.

The order in which the participants took the two treatments was randomly assigned by a computer.



10.57264/cer-2025-0115

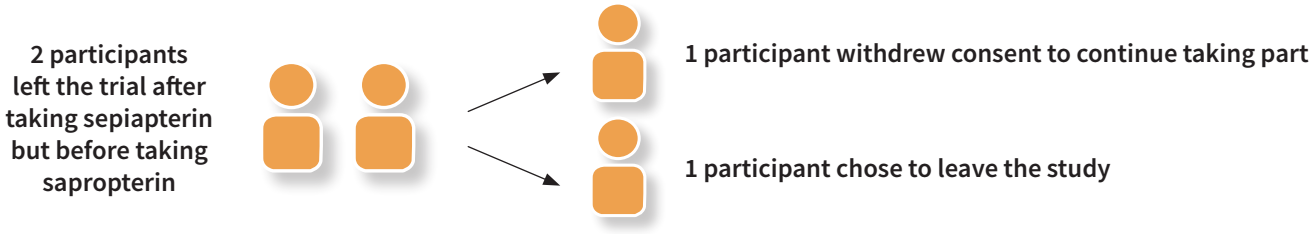
All the participants took the same doses of sepiapterin (60 mg/kg) or sapropterin (20 mg/kg) by mouth.

To test the effects of sepiapterin and sapropterin on blood Phe levels, the researchers measured Phe levels in dried blood samples from the participants. Blood samples were collected before treatment started, on the first day of treatment, and then on Days 7, 10 and 14 of each treatment. This allowed the researchers to track changes in blood Phe levels over time. Dried blood samples are used because only a small amount of blood is needed. People can collect the sample at home using a finger prick, and the dried sample can be easily transported to a laboratory for testing.

The researchers worked out how blood Phe levels changed by comparing results from before and after each treatment. The researchers then compared the changes seen with sepiapterin and sapropterin treatment to each other to see which treatment had the bigger effect.

The researchers looked at the changes in blood Phe levels for the participants in Part 2 who had at least a 30% reduction during Part 1. Out of the 62 participants who joined Part 2, 58 had a reduction in Phe levels of at least 30%.

During Part 2:

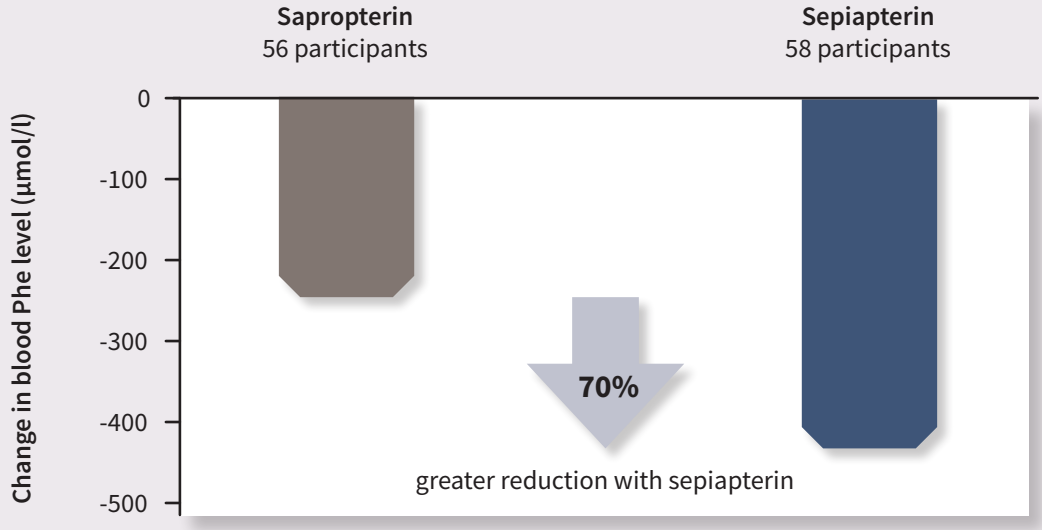


So, the results below are reported for 58 participants who took sepiapterin but only for 56 participants who took sapropterin.

What were the results of Part 2 of the trial?

After 4 weeks of treatment, participants taking sepiapterin had a larger decrease in blood Phe levels than those taking sapropterin. The decrease was about 70% greater (around 180 µmol/l more).

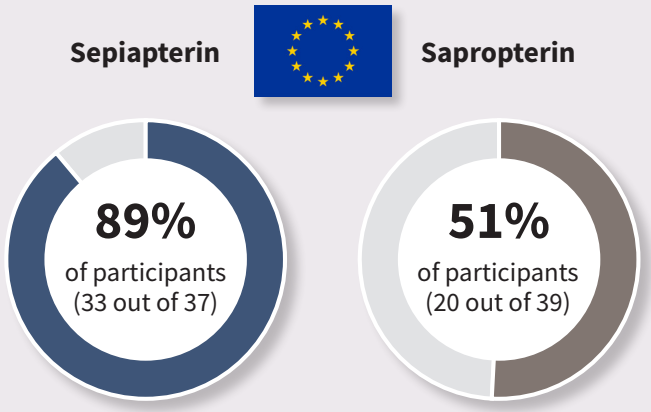
Change in blood Phe levels after 4 weeks of treatment with sepiapterin



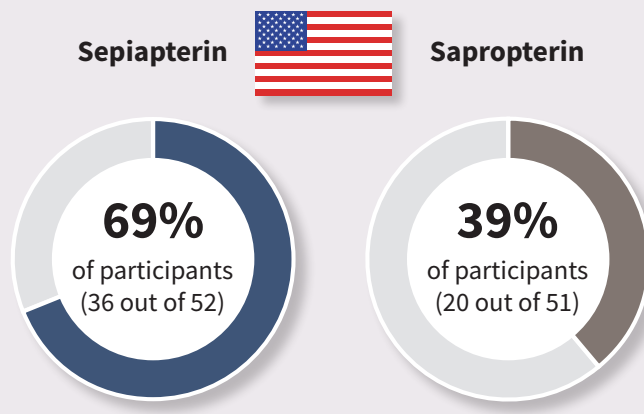
The researchers also looked at how many participants reached US and European guideline-recommended blood Phe levels. They did this in a group of the participants who had blood Phe levels above these recommended levels before treatment. Researchers were interested in this because keeping blood Phe levels within guideline-recommended ranges is an important goal of PKU management and may help reduce the risk of health problems associated with high blood Phe levels.

More people reached guideline-recommended levels with sepiapterin than with sapropterin.

Proportion of participants with blood Phe levels at or above European Guidelines for adolescents and adults (600 µmol/l) at the beginning of the trial, who had levels below 600 µmol/l in Part 2 of the trial



Proportion of participants with blood Phe levels at or above US Guidelines (360 µmol/l) at the beginning of the trial, who had levels below 360 µmol/l in Part 2 of the trial

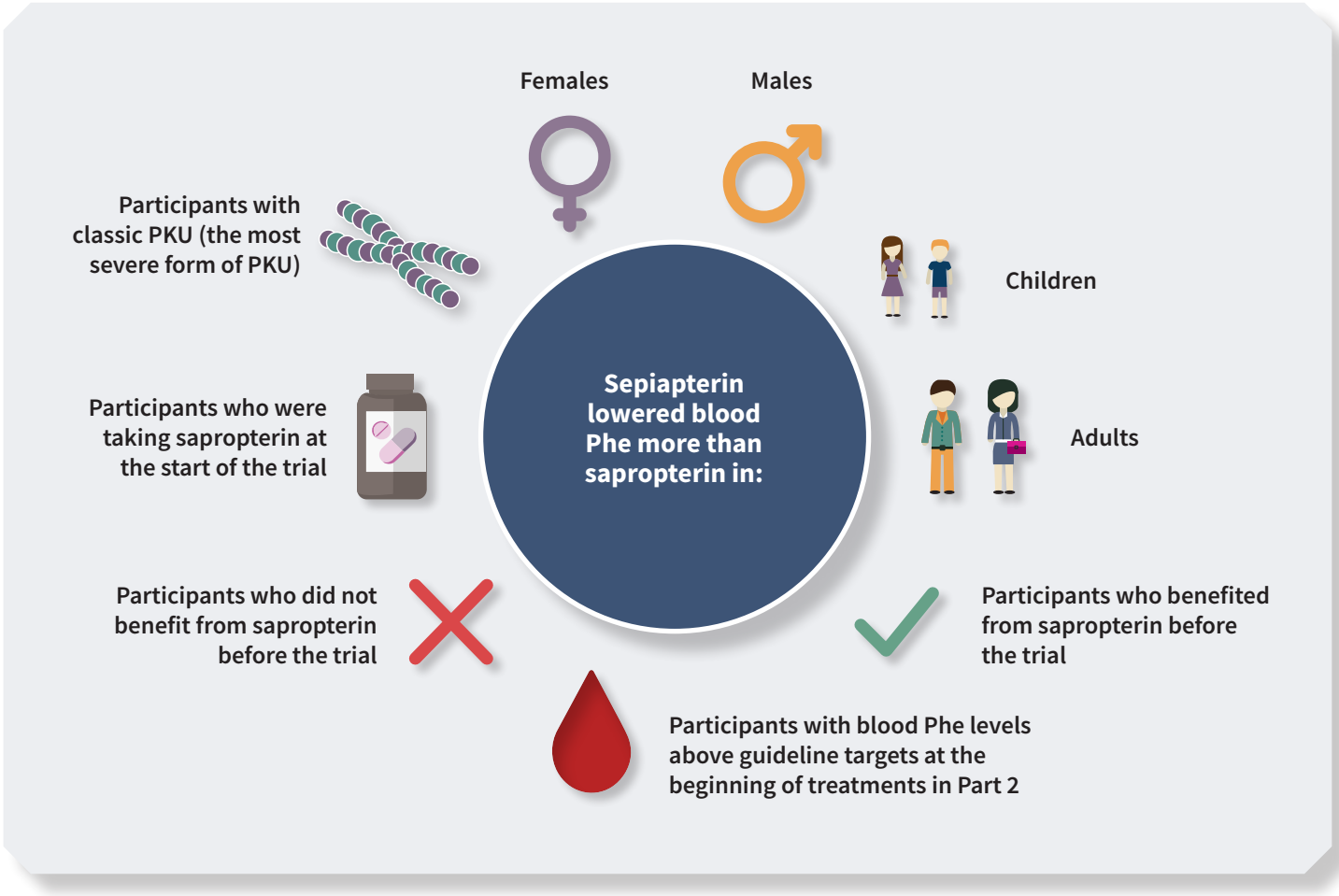


Time to reach guideline-recommended blood Phe levels of less than 360 µmol/l



10.57264/cer-2025-0115

The researchers also looked to see how sepiapterin and sapropterin worked in specific groups of participants:

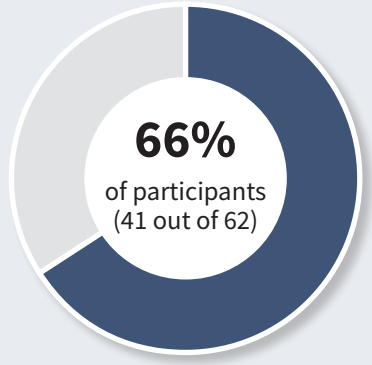
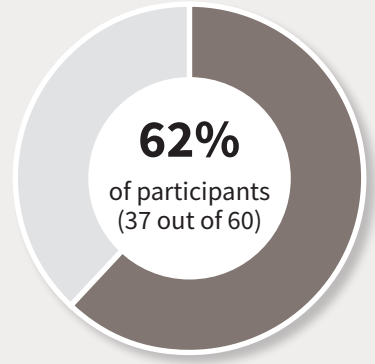
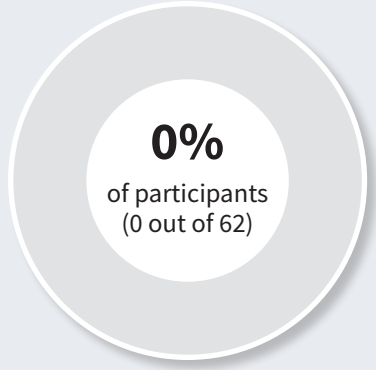
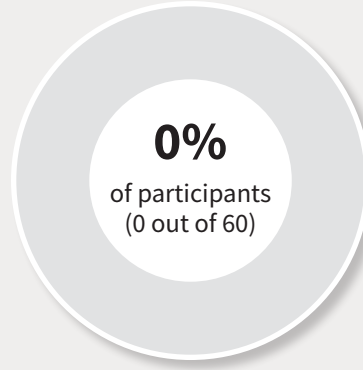
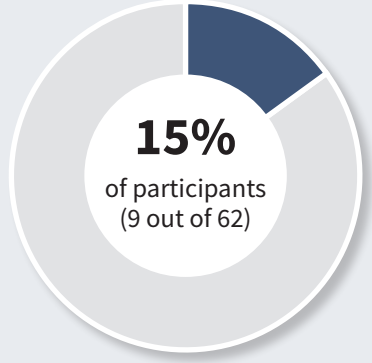
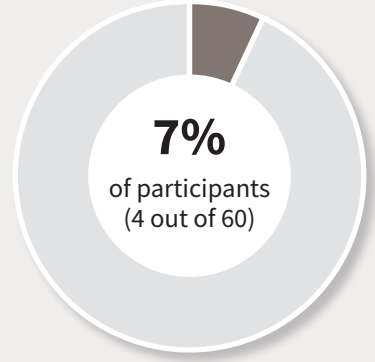
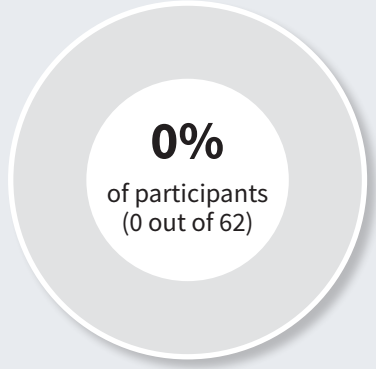
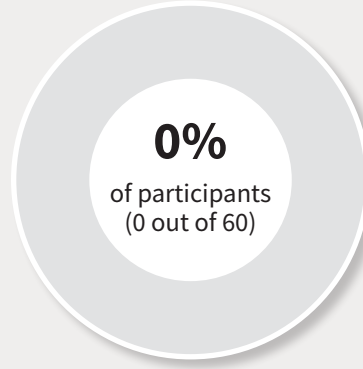


In all these groups, sepiapterin resulted in a greater decrease in blood Phe levels than did sapropterin. However, the subgroups of people with classic PKU and of people who had not benefited from sapropterin before the trial only had a small number of participants. This means the results could have been influenced more by individual participants and may not represent the experience of all people in these groups. Therefore, these findings should be interpreted with caution.

What did the researchers learn about the safety of sepiapterin?

Throughout Part 2 of this trial, the researchers also looked at the safety of sepiapterin by keeping track of all the medical problems the participants had during this trial. Researchers collect this information to help identify possible side effects and understand how safe a treatment is. Any medical problem that occurs during a clinical trial is called an **adverse event**. Adverse events may or may not be caused by the treatments in the trials. An adverse event is considered serious when it is life-threatening, causes lasting problems or requires hospital care.

Adverse event: Any medical problem that occurs during a clinical trial regardless of whether it is related to a trial treatment or not.

	Sepiapterin	Sapropterin
How many participants had an adverse event?		
How many participants had a serious adverse event?		
How many participants had an adverse event that was thought to relate to the treatment they took?		
How many participants stopped taking treatment because of an adverse event?		

10.57264/cer-2025-0115

Most common adverse events (percentage of participants)	Sepiapterin	Sapropterin
Infections in the nose, sinuses, throat or voice box	13% of participants (8 out of 62)	15% of participants (9 out of 60)
Cold	8% of participants (5 out of 62)	7% of participants (4 out of 60)
Diarrhoea	10% of participants (6 out of 62)	2% of participants (1 out of 60)
Nausea	10% of participants (6 out of 62)	3% of participants (2 out of 60)
Headache	8% of participants (5 out of 62)	13% of participants (8 out of 60)

What do the results of this trial mean?

Overall, the AMPLIPHY study showed that sepiapterin lowered blood Phe levels more than sapropterin

More participants reached recommended blood Phe levels when taking sepiapterin than when taking sapropterin

There were no new safety concerns for sepiapterin and sapropterin because the adverse events that were recorded were similar to those seen in other clinical trials investigating sepiapterin

What is the experience with sepiapterin treatment for people living with PKU and their caregivers?

This section has been answered by the caregiver author.

People living with PKU who have not been able to reduce their blood Phe levels before may be able to do so with sepiapterin. Due to the impact of blood Phe levels on physical and mental well-being, sepiapterin may help support clearer thinking, more stable mood, improved focus and better overall day-to-day functioning. For individuals living with PKU and their caregivers, that can mean more confidence and fewer worries about long-term outcomes.

Sepiapterin may also support a change in quality of life and emotional well-being by reducing burnout, anxiety and the constant mental load that often comes with managing PKU. Sepiapterin could improve the quality of life for both people living with PKU and their caregivers by allowing them to participate more fully in social, educational and family activities. This could improve their mental health and reduce feelings of isolation.

Sepiapterin provides a new treatment option for people living with PKU. For some people living with PKU, sepiapterin may be the alternative to a restrictive low-phenylalanine diet.

Although AMPLIPHY did not directly measure **health-related quality of life** or dietary changes, keeping blood Phe levels within recommended levels is an important goal of PKU management. Ongoing studies are looking at the longer-term effects of sepiapterin and how it may affect diet and daily life.

10.57264/cer-2025-0115

Where can readers find more information on this trial?

- The original article discussed in this summary is called "Efficacy and safety of sepiapterin versus sapropterin in patients with phenylketonuria: Results from the Phase 3, randomized, crossover, open-label, active-controlled AMPLIPHY trial". You can read the original article here: https://www.metabolismjournal.com/article/S0026-0495(26)00022-3/fulltext.
- You can read more about this trial on the UK's clinical study registry here: https://www.isrctn.com/ISRCTN79102999.
- You can also read more about this trial here: https://clinicaltrials.gov/study/NCT05099640.

Educational resources

You can find out more about PKU on the following websites:

- UK National Society for Phenylketonuria (NSPKU): https://nspku.org/.
- US National PKU Alliance (NPKUA): https://www.npkua.org/.
- flok: https://flok.org/.
- European Society for Phenylketonuria and Allied Disorders Treated as Phenylketonuria (E.S.PKU): https://www.espku.org/.
- Canadian PKU and Allied Disorders (CanPKU+): https://www.canpku.org/.

Further reading

1. The original publication of the phase 3 AMPLIPHY trial. Available here: https://doi.org/10.1016/j.metabol.2026.156513. Written by Giżewska M *et al.* and published in 2026 in *Metabolism*, volume 178 (issue 156513).
2. The plain language summary of publication of the phase 3 APHENITY trial. Available here: https://doi.org/10.57264/cer-2025-0116. Written by Muntau AC *et al.* and published in 2025 in *Journal of Comparative Effectiveness Research*, volume 15.
3. The original publication of the phase 3 APHENITY trial. Available here: https://doi.org/10.1016/S0140-6736(24)01556-3. Written by Muntau AC *et al.* and published in 2024 in *The Lancet*, volume 404 (issue 10460).
4. A publication of an earlier phase 2 clinical trial of sepiapterin in PKU. Available here: https://www.metabolismjournal.com/article/S0026-0495(21)00416-9/fulltext. Written by Bratkovic D *et al.* and published in 2022 in *Metabolism*, volume 128 (issue 155116).
5. A review of PKU and its current and future management. Available here: https://doi.org/10.1016/S0140-6736(10)60961-0. Written by Blau N *et al.* and published in 2010 in *The Lancet*, volume 376 (issue 9750).
6. Dietary guidelines for people living with PKU. Available here: https://doi.org/10.1186/s13023-020-01391-y. Written by MacDonald A *et al.* and published in 2020 in *Orphanet Journal of Rare Diseases*, volume 15 (issue 1).
7. European medical guidelines for diagnosing and treating PKU. Available here: https://doi.org/10.1016/j.ymgme.2025.109125. Written by van Wegberg AMJ *et al.* and published in 2025 in *Molecular Genetics and Metabolism*, volume 145 (issue 2).
8. A paper discussing the differences in the diagnosis, treatment and management of PKU between Europe and the USA. Available here: https://doi.org/10.1186/s13023-020-01541-2. Written by Lowe TB *et al.* and published in 2020 in *Orphanet Journal of Rare Diseases*, volume 15 (issue 1).
9. Medical guidelines for diagnosing and managing PAH deficiency. Available here: https://doi.org/10.1016/j.gim.2024.101289. Written by Smith WE *et al.* and published in 2025 in *Genetics in Medicine*, volume 27 (issue 1).
10. A publication of clinical trial results for sepiapterin to learn how it works in the bodies of healthy people. Available here: https://doi.org/10.1002/cpdd.1363. Written by Gao L *et al.* and published in 2023 in *Clinical Pharmacology in Drug Development*, volume 13 (issue 5).
11. A review of pegvaliase for the treatment of PKU. Available here: https://doi.org/10.1177/11773928198570 89. Written by Hydery T and Coppenrath VA, and published in 2019 in *Drug Target Insights*, volume 13 (issue 1).

Acknowledgements

The authors and PTC Therapeutics would like to thank the participants and their families for their involvement in the studies that were included in this summary, as well as the individuals who were involved in the conduct and data collection for these studies.

Writing assistance disclosure

Writing and editorial assistance was provided by Hannah Wedge, MChem, of Oxford PharmaGenesis, and funded by PTC Therapeutics.

Financial disclosure

This study and summary were sponsored by PTC Therapeutics.

Competing interests disclosure

M Giżewska: honoraria as a speaker, researcher or for travel support from BioMarin Pharmaceutical, Nutricia and PTC Therapeutics; principal investigator in clinical trials sponsored by Agios Pharmaceuticals, Otsuka Pharmaceutical Development & Commercialization and PTC Therapeutics; participation in advisory boards for Agios Pharmaceuticals, BioMarin Pharmaceutical, Nutricia, PTC Therapeutics and Otsuka Pharmaceutical Development & Commercialization. L Guilder and S Gallagher: nothing to disclose. A Inwood: participation in advisory boards and clinical trial support for PTC Therapeutics. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

Data sharing statement

The original article discussed in this summary is called “Efficacy and safety of sepiapterin versus sapropterin in patients with phenylketonuria: Results from the Phase 3, randomized, crossover, open-label, active-controlled AMPLIPHY trial”.

You can read the original article here: https://doi.org/10.1016/j.metabol.2026.156513.

Open access

This work is licensed under the Creative Commons Attribution 4.0 License. To view a copy of this license, visit http://creativecommons.org/licenses/by/4.0/.