

PKU Research

Discussion Guide (HCPs)

This document serves as a guide only to the flow of discussion during the research session.

Section 1: Introduction & Warm Up (5-10 mins)

Section 2: Physical, Emotional and Social Impact of PKU (10 mins)

Section 3: Diagnosis, Management and Treatment of PKU (30-40 mins)

Section 4: Market Access and Cost (5 mins)

Section 1: Introduction & Warm Up (5-10 mins)

Objective: to introduce respondents to the study & set the scene for the discussion by understanding respondents' caseload and immediate associations with PKU

Study Introduction

- Introduce you
- Thank for agreeing to take part. Purpose of study: **To understand your feelings and thoughts about PKU itself as well as its treatment and management**
- Duration of discussion: 60 mins
- Explain market research (no selling or promotion involved). Interview conducted in accordance with MRS / EphMRA Codes of Conduct
- Tape recorded / confidentiality
- This research is being conducted on behalf of the European Society for Phenylketonuria and Allied Disorders (ESPKU), the leading PKU patient association in Europe. The ESPKU received a restricted grant from a pharmaceutical company for this research. The findings will serve as a basis to draft a PKU benchmark report, published by the ESPKU.
- Although sponsored by a pharmaceutical company, independent interviewer has no vested interest in the outcome of the study and your identity will not be revealed – comments are reported anonymously and in aggregate

MODERATOR: PLEASE LISTEN CLOSELY FOR THE RESPONDENT'S TERMINOLOGY / LANGUAGE AND USE THIS THROUGHOUT THE INTERVIEW

Respondent Introduction and case load

- To begin our discussion, could you please briefly tell me a little bit about:
 - What type of practice/setting you work in?
 - How many patients with PKU do you see in a typical year?
 - What proportion of these patients is paediatric vs. adolescent vs. adult?

MODERATOR SAY: *Thinking of PKU - the condition, patients and/or its management...*

- What makes you feel glad? Why do you say that?
- What makes you feel mad? Why do you say that?
- What makes you feel sad? Why do you say that?
- And, just out of interest, can you tell me what the prevalence of PKU in your country is?
 - And the incidence?

Section 2: Physical, Emotional and Social Impact of PKU (10 mins)

Objective: to understand HCPs' perceptions of the physical, emotional and social impact of PKU on patients

MODERATOR SAY: *Thank you for all that, that really helps us, I now would like to talk briefly about how the condition affects patients...*

- In what ways does PKU influence the daily life of a PKU patient?

MODERATOR: PROBE FULLY SPONTANEOUSLY USING THE QUESTIONS ABOVE THEN PROBE FOR THE FOLLOWING (IF NOT YET COVERED IN FULL)

- What specifically are your views on...? Reasons?
 - **Prompt:** Physical development / Neuro-cognitive development
 - **Prompt:** Eating out from home, e.g. restaurant, party
 - **Prompt:** Time management: organisation around food preparation at home / Food logistics
 - **Prompt:** Time management: going on holiday, finding a hotel
 - **Prompt:** Family life (relationship with parents / siblings)
 - **Prompt:** The ability and/or impact on patients to conceive / have a family
 - Probe: what if anything is the impact on patients before, during and after pregnancy
 - **Prompt:** School / Work
 - **Prompt:** Friendships

Section 3: Diagnosis, Management and Treatment of PKU (30-40 mins)

Objective: to understand practice standards with respect to diagnosis, management/treatment and monitoring of PKU

MODERATOR SAY: *Thank you for that insight, I now would like to move on and explore current practices with respect to diagnosis, management and treatment of PKU patients...so starting with diagnosis...*

Diagnosis of PKU

- How are patients typically diagnosed? Can you tell me more about that, please? **MODERATOR: PLEASE ENSURE THE FOLLOWING ARE DISCUSSED:**
 - What diagnostic procedures are used?
 - How, if at all, is screening organised and since when?
 - **Probe:** What, if at all, are the costs associated with screening?
 - **Prompt:** extent of use of Guthrie test; Why? Why not?
 - What does it cost to use this test? **MODERATOR: TRY AND GET AN ACTUAL ESTIMATED COST**
 - **Prompt:** extent of use of mass spectrometry test; Why? Why not?
 - What does it cost to use this test? **MODERATOR: TRY AND GET AN ACTUAL ESTIMATED COST**
 - To what extent, if at all, does BH4 responsiveness testing belong to the standard diagnosis? Why? Why not? **MODERATOR: IF NOT STANDARD DIAGNOSTIC, PLEASE EXPLORE:**
 - Used in what proportion of your PKU patients? Why?
 - Used in whom? Why?
 - Used when? Why?
- Thinking about the overall diagnostic process, to what extent, if at all, do you believe the diagnosis of PKU is currently standardised within your country? Why/ Why not? What makes you say that?
 - And across countries within the EU? Why/ Why not? What makes you say that?
- What, if any, standards and/or guidelines for diagnosis are available within your country? Why? Why not?
 - And across the EU? Why/ Why not?

MODERATOR: ASK ALL:

- How beneficial, if at all, would (further) standardisation / additional guidelines with respect to diagnosis within your country be? Why? Why not?
 - And across the EU? Why/ Why not?

MODERATOR: EXPLORE FOR BOTH WITHIN COUNTRY AND ACROSS EU WITH:

- How, if at all, feasible is it? Why? Why not?
- What would need to happen?
- Would you be willing to play a role in it? Why? Why not?

Management & treatment of PKU

MODERATOR SAY: *Now thinking about the management of this condition...*

- Which professionals are involved in care? Who else? **MODERATOR: INVITE RESPONDENT TO EXPLAIN TO YOU IN DETAIL WHO IS INVOLVED AT WHAT AGE AND IN WHAT CAPACITY/ROLE USING THE FOLLOWING PROBES:**
 - What involvement do they have / what role do they play in the management of PKU?
 - To what extent, if at all, does it vary for different patient ages? Why?
 - **Prompt:** children
 - **Prompt:** young adults
 - **Prompt:** adults

MODERATOR: IF NOT SPONTANEOUSLY MENTIONED PROMPT FOR ROLE OF THE FOLLOWING HCPS:

- **Prompt:** Endocrinologist
- **Prompt:** Paediatrician
- **Prompt:** Paediatrician with metabolic disease experience
- **Prompt:** Physician being trained in metabolic disease
- **Prompt:** Psychiatrist
- **Prompt:** Psychologist
- **Prompt:** Dietician
- **Prompt:** Primary Care Physician
- **Prompt:** Nurse(s)
- **Prompt:** Social Worker

- To what extent, if at all, are there specific 'PKU Centres' in your country? **IF SO:**
 - How are they organised? Can you tell me more about that?
 - **Prompt:** PKU team, e.g. physician, dietician, psychologist
 - What services are patients being offered?
 - **Prompt:** Access to low phe food
 - **Prompt:** Community support
 - **Prompt:** Home cooking support
 - **Prompt:** Access to Kuvan/BH4
 - **Prompt:** Home blood testing
 - Are adults being treated at this centre? Why? Why not?
- What are your key goals when it comes to managing and treating PKU? What are you looking to achieve in these patients? Why? **EXPLORE SPONTANEOUSLY FIRST, EXPLORING EXACTLY WHAT HCPS ARE LOOKING TO ACHIEVE, THEN IF NOT ALREADY DISCUSSED PROBE FOR THE FOLLOWING:**
 - **Prompt:** Avoiding severe mental retardation/ lack of neuro-cognitive damage; Why? Why not?
 - **Prompt:** Optimal Neuro-cognitive development/ Enabling patients to reach their full potential; Why? Why not?
 - **Prompt:** Management of Phe levels; Why? Why not?
 - What, if any, are the typical Phe targets that you aim for?
 - How, if at all, does this vary by age or patient type?
- What is your current typical approach to managing and treating PKU? Why?

MODERATOR: EXPLORE FULLY USING ALL QUESTIONS AREAS BELOW; AND IF NOT MENTIONED SPONTANEOUSLY, PROMPT FOR THE FOLLOWING APPROACHES:

- **Prompt:** Low Phe food
- **Prompt:** Amino acid supplements/ Protein substitutes
- **Prompt:** Medication (BH4/Kuvan)
- How, if at all, does it vary by age or patient type?
- What clinical and non-clinical parameters, if any, other than the goals we already discussed, do you take into consideration when you make treatment and patient management decisions within PKU? Why?

- **Prompt:** Nutritional deficiencies; Why? Why not?
- **Prompt:** Neuropsychological symptoms (e.g. Information processing, attention, motor control); Why? Why not?
- **Prompt:** Psychosocial issues (e.g. depression, anxiety and social withdrawal); Why? Why not?
- **Prompt:** Quality of Life (QoL)
- **Prompt:** Level of compliance with diet

MODERATOR: FOR EACH APPROACH MENTIONED EXPLORE:

- Extent of use - In what proportion of patients is this approach taken; Why?
- Reasons for use – What drives you to use this approach in these patients? **MODERATOR: PROBE FULLY UNTIL NOTHING ELSE**
 - **Prompt:** Cost considerations
 - **Prompt:** Budget restrictions
 - **Prompt:** Market availability
- Typical situations / patient types – In what situations / patient types do you typically use this approach? Why?
- How does this approach interlink with your standard / typical treatment approach?
- What do you perceive to be the benefits and shortcomings of this approach in the management of PKU patients? Why? Can you say a bit more about that?

MODERATOR: WHEN DISCUSSING DIET PLEASE EXPLORE:

- In your every day practice how, if at all, do you evaluate the diet's success?
 - What would be the indicators that diet is working well? Why?
 - What would be the indicators that diet is failing? Why?
- How do your patients feel about their diet? Why?
 - What does this mean for the treatment of PKU?
 - What are the implications of this for treatment outcomes?

MODERATOR: WHEN DISCUSSING MEDICATION PLEASE ENSURE YOU EXPLORE THE FOLLOWING ONLY IN COUNTRIES WHERE BH4 IS NOT YET APPROVED:

- What medical treatment do you currently typically use?
 - Reasons for use – What drives you to use this treatment in these patients?

Education and Monitoring of patients with PKU

MODERATOR SAY: *To conclude this section I would briefly like to explore the typical approach with respect to on-going follow up / monitoring...*

MODERATOR: USING THE FOLLOWING QUESTIONS ENSURE YOU GAIN CLARITY ON WHO SEES PATIENTS UNTIL WHAT AGE AND WITH WHAT FREQUENCY (WEEKLY, MONTHLY, ANNUALLY ETC.) AND WHAT TYPICALLY IS MONITORED/MEASURED

- How, if at all, are PKU patients typically monitored? Why? Why not?
 - Which HCPs, if any, are typically involved in conducting follow up / on-going management?
 - How often do they typically see PKU patients?
 - What, if anything, is typically discussed/measured/monitored?
 - How, if at all, does it vary by age or patient type?
- Would you think that a home blood testing device could facilitate your PKU management? If **yes**, where do you see the benefits?
 - **Prompt:** Better compliance to treatment
 - **Prompt:** More regular monitoring
- What do you think should be done with PKU patients in case of a short illness or needing emergency surgery?
 - What would be the difference in treatment when a patient is treated by BH4 alone, BH4 and diet or diet alone?
- What, if any, additional care / support do patients get? Why? In which cases? From whom?
 - **Prompt:** Social Support; What does it look like? Who provides this?
- What, if anything, might trigger a referral to any other specialist? Why? To whom?
- How, if at all, is the transition from child to adult medical support/ care managed? Can you tell me more about that?
 - **Probe:** What, if anything, typically happens?
 - **Probe:** What, if anything, doesn't typically happen?
 - **Probe:** How, if at all, do you think this transition could be improved and/or should ideally be managed? Can you tell me more about that? Can you give me an example?
 - **Probe:** What, if anything, in your view needs to be done to ensure lifelong management/treatment for all PKU patients? Can you tell me more about that? What else?

MODERATOR SAY: *Finally to finish off our discussion on the current management of this condition...*

- To what extent, if at all, do you believe the management of PKU is currently standardised within your country? Why/ Why not? What makes you say that?
 - And across countries within the EU? Why/ Why not? What makes you say that?
- What, if any, standards and/or guidelines for management / treatment are available within your country? Why? Why not?
 - And across the EU? Why/ Why not?

MODERATOR: ASK ALL:

- How beneficial, if at all, would (further) standardisation / additional guidelines with respect to the management within your country be? Why? Why not?
 - And across the EU? Why/ Why not?

MODERATOR: EXPLORE FOR BOTH WITHIN COUNTRY AND ACROSS EU WITH:

- How, if at all, feasible is it? Why? Why not?
- What would need to happen?
- Would you be willing to play a role in it? Why? Why not?

Exploration of satisfaction with current management and ideal management of PKU

MODERATOR SAY: *Thinking about the current management of PKU...*

- On a scale of 0-10, where 0 is not at all and 10 is very much so, how satisfied are you with the current management/treatment of PKU / care given to patients? Why do you say that?

MODERATOR: ENSURE YOU GET A SCORE FROM EACH RESPONDENT

- In what proportion of patients do you achieve the goals / Phe target levels that we discussed earlier?
 - How, if at all, does this vary by age / patient type?
 - **Prompt:** children
 - **Prompt:** young adults
 - **Prompt:** adults
- What, if any, do you consider to be the key unmet needs in the management of PKU? Why? What makes you say that? **MODERATOR: PROBE FULLY UNTIL NOTHING ELSE**
 - **Probe:** What would be required for you to give a score of 9 or 10 on the satisfaction scale we just discussed?

- What would be the one thing that would improve your management/treatment of PKU? Why? Can you tell me more about that?
- If I asked you to describe what you would consider to be the ideal management of PKU, how would you describe it?
 - How far away do you feel current management is from that ideal? What makes you say that?
 - What would need to happen to achieve that ideal? Can you tell me more about that?

MODERATOR SAY: *To complete this section I am going to read out a few statements and I would like you to give me a number on a scale of 0 to 10, where 0 is totally disagree and 10 is totally agree..*

MODERATOR: PLEASE READ OUT THE FOLLOWING STATEMENTS; ROTATING THE ORDER IN WHICH STATEMENTS ARE READ OUT BETWEEN INTERVIEWS

“All PKU patients should have access to the same treatment options to develop their full potential”

“PKU medication should be better recognised as an orphan drug”

“There should be best possible management for all PKU patients by having standardised PKU guidelines in place”

Section 4: Market Access and Cost (5 mins)

Objective: to understand the current reimbursement situation and implications for access to treatment

MODERATOR SAY: *Thanks for all that feedback. In this final section I would briefly like to explore the reimbursement situation for these products and how, if at all, this impacts patient’s access to treatment...*

- What is the current reimbursement situation for the treatment approaches we discussed (i.e. low Phe food, amino acid supplements, and medication)?
 - Which ones are currently reimbursed? Why? Up to which age?
 - How available, if at all, are these approaches to patients?
 - What, if any, barriers or restrictions are there?

MODERTOR: ENSURE YOU ESTABLISH REIMBURSEMENT STATUS FOR EACH OF THE FOLLOWING:

- Low Phe foods
- Amino acid supplements/ Protein substitutes
- Medication
 - BH4 / Kuvan

- Have you ever encountered a situation where you've felt a patient is suitable / could really benefit from Low Phe food and/or amino-acid supplements and/or medication, but the patient/parent can't afford it? **MODERATOR: IF YES, PLEASE PROBE FOR THE FOLLOWING**
 - **Probe:** How does such a situation make you feel?
 - **Probe:** How does such a situation make the patient / carer feel?
 - **Probe:** What usually happens in such a situation?
 - **Probe:** Is there anywhere patients can go to receive financial support / access to the medication?
- Do you always discuss all treatment options with all patients? Why? Why not?
 - Are there any situations in which you may not mention certain treatments to patients, if you believe they are unlikely to be able to afford them? Can you give me an example?
- What, if any, other barriers to treatment access are there? Please tell me more about that? What else?

MODERATOR SAY: *Talking about costs...*

- To what extent, if at all, might patients be entitled / receive subsidies?

MODERATOR: IF NOT MENTIONED SPONTANEOUSLY, PROBE FOR:

- Estimated annual income from medical subsidies
- Estimated annual income from unemployment benefits
- Estimated annual income from housing benefits
- Any others?
- To what extent, if at all, are you aware of the existence of / plans to put in place 'rare disease plans'? **MODERATOR: IF AWARE EXPLORE WHAT THE RESPONDENT KNOWS ABOUT THEM AND HOW (S)HE FEELS ABOUT THEM?**
- To what extent, if any, do you agree that there is a need to lobby the Government / Health Authorities in your country to put PKU in their 'rare disease' plans and put pressure on them to ensure that these plans are implemented by 2013? Why? Why not? Can you tell me more about that?

These are all my questions. Do you have any further comments or suggestions you would like to add to the discussion we've had today?

THANK AND CLOSE