COMPLETING A PATIENT ORGANISATION SUBMISSION OF EVIDENCE TEMPLATE: GUIDELINES FOR PATIENT ORGANISATIONS

FOR HEALTH TECHNOLOGY ASSESSMENT AND APPRAISAL OF MEDICINES

Version	Date	Description of changes
1.0	August 2018	

Please Note: This document may be updated periodically, therefore please refer to the NCPE website to obtain the most recent version.

Acknowledgements:

Some of the information in this guideline is adapted from guidance produced by the HTAi Patient and Citizen Involvement in HTA Interest group and by the Scottish Medicines Consortium.

Health Technology Assessment international
An International Society for the Promotion of Health Technology Assessment

Table of Contents

1.0 Introduction

1.1 Purpose of this guideline

The National Centre for Pharmacoeconomics (NCPE) is committed to facilitating the inclusion of the patient voice in the Health Technology Assessment (HTA) process. We believe that patients have perspectives and experiences that can uniquely contribute to the decision making process. With this in mind, the NCPE provide the Patient Organisation Submission Process, to enable patient organisations to communicate their experiences directly to the decision maker, the Health Services Executive (HSE).

This guideline is designed to help Irish patient organisations like yours complete the NCPE Patient Organisations Submission of Evidence Template to provide input to an assessment of a new medicine. You will find guidance on what information to include within the template and how to collect and report that input. While this guideline provides guidance on collecting and reporting information from surveys and interviews, patient organisations should not feel that they must undertake a survey or conduct interviews to successfully complete the submission template. Patient organisations may already possess the information required to complete the template, for example through existing helpline or chatroom logs, blogs, focus groups or other interactions with your membership. If not, this guide provides you with an overview and step-by-step approach to collecting and presenting patients' and carers' experiences, needs and expectations.

If you have any more questions after reading this guide, the NCPE can support you throughout the submission process. You can get in touch by emailing info@ncpe.ie or by phoning 01 4103427.

2.0 NCPE

2.1 About the NCPE

The NCPE are a team of clinicians, pharmacists, pharmacologists, health economists and statisticians who evaluate the benefit and costs of medical technologies. Our aim is to provide impartial advice to help the HSE provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services. The NCPE provides education courses in pharmacoeconomics at undergraduate and post-graduate level and for patient organisations. We support original research in the field of HTA through doctoral programs and our links with Trinity College Dublin.

2.2 The NCPE assessment process

The Corporate Pharmaceutical Unit (CPU) of the Health Services Executive commission the NCPE to appraise new medicines following receipt of an application for reimbursement. Since September 2009, we now consider the cost effectiveness of all new medicines following receipt of an application for reimbursement. The NCPE employ a two-step process to make our recommendations in the most efficient manner and minimise time to access for new treatments. All medicines are subjected to a preliminary Rapid Review. Companies can enter the process at any point following receipt of a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA).

Products with a high cost relative to potential comparators and/or those with a net impact on the drugs budget will be subjected to a formal health technology assessment (HTA). Similarly, products where there is a query in relation to the comparative clinical efficacy and/or value for money will also be selected for formal HTA. The Rapid Review process takes approximately 4 weeks and the formal pharmacoeconomic assessment (HTA) takes 90 days.

The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified. This is done through assessment of evidence submitted by manufacturers and independent systematic review. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. In addition, information from patient organisations is gathered about how people are affected by the condition and the impact of the new medicine on patients and their carers.

Following formal pharmacoeconomic assessment, a full appraisal report outlining NCPE conclusions and recommendations is sent to the HSE-CPU to support evidence-based decision-making on reimbursement. Information on cost-effectiveness of the technology over a threshold-range up to €45,000/QALY is provided.

In addition to the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE, having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013. In the case of cancer drugs, the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

Further information on the assessment process is available on our website.

3.0 The HTA Process and Patient Organisation Submission of Evidence Template

3.1 What is an HTA?

HTA stands for Health Technology Assessment. This is a systematic process that seeks to determine the value of a health technology (such as a new medicine) compared to health technologies that are currently used. Experts review evidence from clinical trials and may also consider other scientific evidence, economic evidence, information on the way services are currently organised, and social and ethical impacts of the health technology on the health care system and the lives of patients. Its main purpose is to inform decision making by health care policy makers, for example about whether a medicine is reimbursed or recommended for use for certain patients in the health service.

3.2 What is a Patient Organisation Submission of Evidence Template?

The Patient Organisation Submission of Evidence Template is a document that enables patient organisations to provide suitable patient and carer input to the assessment of a particular medicine. Strong submissions provide clear facts, information and summaries of experiences to give a concise, accurate and balanced overview of a range of patients' and carers' perspectives. The purpose of the submission is to identify important aspects of the medicine that are:

- not identified or well presented in the published literature, or
- not well captured in quality of life measures or other outcome measures that have been used in clinical trials and other research studies, or
- not well known and/or understood by experts in HTA and decision makers

The submission is also an opportunity to identify the priorities and preferences of patients and what the added value of a particular medicine may be to them.

3.3 How is your submission used within the HTA review process?

Understanding the experiences and perspectives of patients and their carers is key in making recommendations for medicines under review. Patients can provide unique knowledge about what it is like to live with a condition and can explain advantages and disadvantages of therapies that may not be available in the published literature or captured by quality of life or other known measures.

Your efforts in collecting these experiences will provide valuable information for the HSE Drugs Committee. It is important that the HSE understands what matters most to patients (and their carers) when they make recommendations about the reimbursement of medicines.

3.4 What is involved in contributing to the HTA review process?

3.4.1 Process Overview

The NCPE have identified three key steps in the Patient Submission Process; Identification and Notification of the Patient Organisations, Submission of Patient Organisation Submission of Evidence Template (POSET), and Notification of outcome by NCPE.

Identification of Patient Organisations

- The NCPE will maintain a database of Patient Organisations who have expressed an interest in participating in the HTA process, and will inform these organisations when a relevant HTA has been commissioned. If no appropriate organisation is registered, the NCPE will work with IPPOSI and MRCG to identify a suitable organisation, and will advertise for patient submissions through social media.

Patient Organisations Submission of Evidence

- Detailed guidance on the submission process is provided on the NCPE website, including a step by step guide to completing the Submission of Evidence Template. The NCPE include the POSET in its entirety in an Appendix of our final report to the HSE, and also include extracts of the template within the main body of the report. Patient Organisations must complete and return the template to the NCPE within 90 days of the HTA commencing, as recorded on the NCPE website. We recommend that patient organisations do not start completing the template until the full HTA has been received by the NCPE, as recorded on our website. It is worth noting that despite the conclusion of the NCPE Rapid Review that a full HTA is required, not all companies choose to submit a full HTA to the NCPE. The NCPE will notify Patient Organisations to confirm that a full HTA submission has been received from the company.

Notification of HTA outcome by NCPE

- The NCPE will notify the submitting Patient Organisation of the outcome of the HTA report 48 hours prior to the publication of the summary report on the NCPE website.

3.4.2 Register as a Patient Organisation

To be part of the HTA review process, patient organisations may join our NCPE Patient Organisations Database, and consent to being contacted by the NCPE if HTAs in their therapeutic area of interest are commissioned by the HSE. This is very straightforward to do. You complete a registration form, providing details about your patient organisation. It is your responsibility to ensure registration details are up to date each time you provide a submission. You can either register at the same time as you send your first submission, or in advance. The form can be found on the “For Patients” page of our website.

We accept submissions from patient organisations which are constituted from small local support groups to large national voluntary organisations. **We are unable to accept submissions from individual patients.**

3.4.3 Complete a Patient Organisation Submission of Evidence Template

When a HTA is commissioned by the HSE, the NCPE will email the relevant patient organisation(s) in the database, inviting them to complete the Patient Organisations Submission of Evidence Template that is available to download from our website. If a suitable patient organisation is not registered on our database, we will contact IPPOSI (Irish Platform for Patient Organisations, Science and Industry) and MRCG (Medical Research Charities Group) who may invite relevant members to make a submission to the NCPE. The

NCPE website and social media platforms (e.g. Twitter) will simultaneously invite relevant patient organisations to submit on the topic.

The input you provide is included in the final HTA report to provide a patient/carer perspective in the assessment process. Your input will provide valuable information for the HSE Drugs Committee in understanding what matters most to patients/carers when they make recommendations about the reimbursement of medicines.

Please send us your submission in the format of a Word document as this makes it easier for us to include in the final HTA report.

3.5 How to access the Patient Organisation Submission of Evidence Template and timeframe for completion

You can find the *Patient Organisations Submission of Evidence Template* on the "For Patients" page of our website. If you have any problems accessing the electronic version of the form, you can contact the NCPE to either email or post a copy to you. The submission must be completed and returned to the NCPE within 90 days of the HTA commencing, as recorded on the NCPE website. This is to allow the NCPE to adhere to the timelines specified in the drug reimbursement process. We recommend that patient organisations do not start completing the template until the full HTA has been received by the NCPE, as recorded on our website. It is worth noting that despite the conclusion of the NCPE Rapid Review that a full HTA is required, not all companies choose to submit a full HTA to the NCPE. The NCPE will notify Patient Organisations to confirm that a full HTA submission has been received from the company.

The NCPE can support you throughout the submission process, and can be contacted by email (info@ncpe.ie) or phone (01 4103427) if you have any further questions.

3.6 Planning and completing your submission

Completing a submission takes some time and effort, but it is an opportunity for you to provide valuable information about patient and carer experiences. Putting in time to plan your submission can help you be more efficient in collecting the information needed and completing the template. During the planning phase, you should decide whether you need to gather new information from patients and carers (e.g. via surveys or interviews), or whether you already have the necessary information to complete the submission form.

3.6.1 What information should you include in your submission?

You want to convey the experiences of those living with or caring for people with the health condition for which the medicine being assessed is used. To help you provide the most useful information, Table 1 offers suggestions on what to include in your submission and things to consider when presenting your information.

It is helpful to look at the Patient Organisation Submission of Evidence Template (Appendix 1) which also contains prompts while considering the information in this table. The template is divided into three sections, seeking to gather your experience with the condition, your views on the medicine and a summary section. Appendix 4 includes an example of a patient submission of evidence template previously submitted to the NCPE.

It is important to report on the experiences of many of the individuals living with this condition, rather than exceptional cases. Because of the small numbers of patients affected by a rare disease, we understand that it may be very difficult to report on the experiences of lots of individuals, and in this instance it is sufficient to capture the experiences of a small number of patients or individual patients. Focus on the quality of life impact on patients and carers, and the social, emotional and financial impact.

Please remember to be clear and concise. It is very important that the submission is balanced and acknowledges any shortcomings with the new medicine, as well as the advantages.

Table 1: What to include in your submission

Section of the input template	Considerations
Section 1 – Experience of patients, carers and their families	
Information gathering Question 1 and 5	• Mention how information was obtained (e.g. online surveys, interviews, focus groups, patient registries etc.). • Include the number of participants who contributed information to your submission, and if possible some of their characteristics (e.g. disease severity, sex, age). • Were there sections of the patient community that you could not reach? • Please provide information on patient and carer experiences and not references to literature or printed sources (e.g. statistics), since this type of information is already reviewed in other parts of the HTA report.

Impact of the condition on patients, carers and their families **Question 2**	• Report on the experiences of **many** of the individuals living with this condition, rather than exceptional cases. If a patient has a rare disease then it may only be possible to report on the experiences of a very small number of patients. • Describe the range of experiences, including what is going well and what is not, and if experiences might vary by different subgroups of patients. • Include information about symptoms, problems experienced with carrying out every day activities or tasks where patients require assistance and support, effects on the ability to work and on social life. • Financial impact such as loss of earnings or costs associated with treatments/travelling to appointments. • Report on how the patients' condition and treatment have affected relationships with carers/families and how it has affected carers/families and their daily activities. • Report on how the way current treatments are given impact on carers/families (e.g. driving patients to hospitals or special facilities to receive treatments or tests, etc.)
Patients' experience with their current therapies **Question 3**	• Report on the range of experiences with **current** therapies (e.g. medicines, surgery and other procedures, medical devices, radiation, physical therapy, rehabilitation, palliation) to understand whether all aspects of the patients' condition are being managed. We acknowledge that in some instances, no comparative treatments may exist, (as is frequently the case with therapies that are used to treat rare diseases or advanced cancers). In this case discuss the supportive care available. • Extent to which current treatments control or reduce the most challenging aspects of the condition. • The most important benefits of current treatments. • Side effects from treatments which are difficult to tolerate. • Concerns about long-term use of current therapy. • Be specific about what is going well and what is not, and if experiences might vary by different subgroups of patients. • Challenges in taking it as prescribed (e.g. swallowing the pill, self-injecting, use of a device to deliver the medicine, taking after food) • Ways in which the dosing is modified compared to what is prescribed (e.g. dividing the dose to avoid unwanted side effects, missing doses to fit into daily life).
What aspects of living with their condition do patients need most help?	• Identify specific unmet needs with current treatments • Identify major areas of change you would like addressed

Question 4	
Section 2 – Views of the patients, carers and their families on the difference the new medicine may make	
What are the expectations for the new medicine? **Question 6**	• This section is designed to be answered by patients who have **never used** the medicine being assessed. • Consider information about the new medicine. This information can be obtained from patient information leaflets (PILs) which are freely accessible via www.medicines.ie or www.hpra.ie. • Comment on the **anticipated** impact of the medicine being assessed and the desired outcomes of using this medicine as compared to their current therapy. Be as specific as possible, e.g. what symptom is anticipated to improve or what aspect of quality of life could be improved. Try to describe what "better than current therapy" might look like. We acknowledge that in some instances, no comparative treatments may exist, (as is frequently the case with therapies that are used to treat rare diseases or advanced cancers). In this case comparisons with supportive care can be made. • It is important that the submission is balanced and mentions any expected disadvantages or negatives about the medicine compared to current medicines. Explore whether patients are willing to live with some side effects now or in the future in return for some benefits of the new medicine and, if so, which side effects. Are there disadvantages with regards to how the medicine is administered and by whom etc.? • Include information on quality of life, daily functioning, side effects, etc. • Comment how this may address the unmet needs described in question 4
What experiences have patients had to date with the new medicine? **Question 7**	• This section is only to be completed by patients who **have** used the medicine being assessed (in the past or are currently on the medicine). • Some patients may currently be on the medicine being assessed. If this is the case, please describe their experiences in this section (not in 'What are the expectations for the new medicine?' of the input template). • Include information about how patients with experience are accessing the drug under review • The purpose of this section is to get a better understanding of the specific **advantages and disadvantages** of the medicine,

	and to learn how it has affected patients' quality of life/everyday life. Be as specific as possible, e.g. what specific symptoms have improved, what specific side effects have occurred and what aspects of quality of life have been impacted? Include side effects that are most debilitating to quality of life, AND side effects that are tolerable. • What concerns are unaddressed by the new medicine? • Are there any accessibility and financial implications?
How will the new medicine address unmet needs? **Question 8**	• This question relates to unmet needs or gaps in current treatment choices that are available to patients or people affected by the condition, identified in question 4. • Will the new medicine fill any of these gaps? • How does it fill those gaps? • Will it make a real difference to patients' lives? • How strongly do you support this medicine?
Section 3 – Summary Information	
Summary of the submission **Question 9**	• Provide a 5 point summary of the KEY points of the submission • Consider including quality of life impact, limitations of current treatments, benefits of new treatment • These 5 points are included within the HTA report provided by the NCPE to the HSE-this section requires special consideration to ensure that you are getting across your key messages
Additional information for the decision maker **Question 10**	• Provide any additional data which you believe may be helpful to the decision maker • Include ethical or social issues • Any data you have collected on societal costs of the condition, costs of not treating the condition etc.
Section 4 – Declarations	
Funding from pharmaceutical companies **Question 11**	Full details of all funding received for EACH project within the last two years should be highlighted.
Individuals who have had a significant role in drawing up your submission and have interests to declare **Question 12**	• This question relates to individuals that are a shareholder, director or employee of the applicant company, or are in receipt of payments direct or indirect from the applicant company. • Mention cash/kind received by person or organisation from the applicant company, including expenses. • Whether the interest relates to the specific medicine under consideration • Whether it relates to clinical trial work for the medicine under consideration

3.6.2 What information is not necessary?

We are aware that your time is valuable and there is limited space in the template, therefore, we want to help you focus on what is most useful to the medicine assessment process. Table 2 lists information that you do not need to provide.

DO NOT identify patients or carers by their full names. Information about individuals must be kept confidential by you to protect privacy.

Table 2: What you do not need to include in your submission

Not necessary	Reason
Clinical or Scientific evidence	As part of the process for assessing the medicine, the assessment team conducts a thorough and systematic search for the available scientific evidence about the medicine; therefore, you do not need to provide this information. However, if you have views about the interpretation of a paper or a particular clinical trial, we would be happy to hear them.
Summarised or reworded information from sources other than patients or carers (e.g. clinicians or other healthcare providers, manufacturers)	The purpose of the patient group submissions is to collect input from both patients and their carers. Input and feedback from clinicians and pharmaceutical manufacturers is received separately.
The same messages repeated under different template headings	Sometimes it may be difficult to assign information to only one section of the input template. Please ensure that you are answering the specific question under each section and not repeating information to 'fill up the space'. We want to ensure that only the most relevant input is obtained in order to guarantee the best recommendations possible for the medicine being assessed.

4.0 How to collect the required information for the submission template

The type of information you collect will depend on the questions you want to answer. Information can be grouped into two categories: **quantitative** (numerical information) and **qualitative** (descriptive information).

Quantitative information

Quantitative information is input that is either counted or measured, such as:

• How much time do you spend getting to your appointments?

• How long does the treatment work for?

• How many treatments have you been on?

One common way to collect this type of information is by using closed questions within surveys, where answers are selected from a predetermined set of responses, for example using ratings on a numbered scale or multiple choice. You can then report the average response or how many times a particular response is chosen.

Qualitative information

It is also important to collect the thoughts, opinions, stories, and feelings of patients and carers. This input is described as qualitative information (descriptive information) and answers questions, such as:

• What challenges have you encountered while managing the side effects of the person you are caring for? For example, it is difficult to get to a hospital, or if special equipment or specialists are required that are only available in particular centres.

• Why is it difficult to access your current treatment?

• Can you describe how the treatment would improve your quality of life?

There are many ways to collect qualitative information. Some are very simple and quick to do, for example posting a question on a social networking website, such as Twitter or Facebook, or online discussion forums. Electronic questionnaires can also be an easy and convenient way to collect key information. You can also use group discussions, interviews or open-ended questions in surveys. These allow participants to explain their experiences in their own voice. Whichever methods you choose, it is important to track and record how you generate your information for inclusion in the submission.

An example of a survey template used by a patient organisation to gather information is included in Appendix 5.

5.0 How to summarise the information for the submission template

The way you present this information will depend on the types of questions that you asked. Remember that the HSE Drugs Committee is looking for an overview of experiences or themes. The way you present quantitative information (closed-ended questions in surveys) is different from how you should present qualitative information (descriptive, open-ended questions in surveys, and interviews).

5.1 How do you summarise the information that can be presented in numbers (quantitative information)?

The quantitative information you collect will mostly come from closed questions used in your survey. To summarise data, it is helpful to combine responses as averages, frequencies

or counts (i.e. number of people) or proportions (i.e. percentages). It is best to keep the statistics simple.

Quantitative information can be presented in sentences or as a table. Depending on how much data you have, it may be easier to use a table which allows you to present a large amount of content in a small amount of space. These examples present both methods.

Example 1: Summarising quantitative information in text

Those who completed the survey ranked 'infections' as the most important, with 71.8% (total number participants = 22) rating it as 10, a 'very important' aspect of controlling xxx cancer. 'Infections' were followed by 'kidney problems', 'pain', 'mobility', 'neuropathy', 'shortness of breath', and 'fatigue'. In all cases, more than 50% of respondents rate these aspects as a 10, 'very important' to control. In all cases the rating average was greater than 8, which meant that all listed symptoms were considered important.

Example 2: Using tables to report quantitative information

Symptom or problem related to xxx cancer	% of respondents who rated a '10'	Number of respondents	Rating average (rounded)
Infections	71.8%	22	9
Kidney problems	68.2%	21	9
Pain	64.3%	22	9
Mobility	59.7%	22	9
Neuropathy	56.7%	22	9
Shortness of breath	51.0%	20	8
Fatigue	50.9%	22	9

5.2 How do you summarise the descriptive (qualitative) information?

Regardless of how you collected input, patient and carer experiences need to be summarised. A great way to present descriptive information is to include quotes from participants to highlight or illustrate key points. Before you choose quotes, it is important to analyse all of your qualitative information as a whole. If you begin by selecting random quotes you may not realise that there are specific themes that a majority of participants collectively discussed.

Qualitative information can come either from:

- Responses collected through interviews; or
- Open-ended questions asked in your surveys.
-

TIP: Use the voice of the participant

Remember that findings should be in the voice of the participant e.g. what participants expressed, reported, said, described, etc. It should be made apparent that they were taken directly from the participants' experiences and are not the opinion of the interviewer.

Example 3: Using quotes to support themes

For an overall theme called 'accessibility', with labels 'distance to place of treatment' and 'financial burden', a response may look like this:

Patients reported difficulties with respect to access to treatments. The most widely discussed factor that affected access to treatment was financial burden, given that the treatment was not covered by some private health plans. Some patients reported that the particular treatment was difficult to access because it was only available at a centre far from their home, which made distance an important factor that limited accessibility. As described by one patient:

> "*It's frustrating that my therapy isn't easier to access because I find that it is working well. I just get so tired having to drive so far to be able to receive my IV medicines at the hospital. This is costing me a lot of time and money, especially as we have to pay for some of my medications out of pocket."*

5.3 Summary of the qualitative or quantitative analysis process

1. Do an initial read through of all documents (e.g. notes) to become familiar with the information.
2. During the second reading, highlight sections of text with a label that you think is relevant and representative of what is being said. Try to focus on those aspects of the information that relates to the purpose for collecting patient input (e.g. describes patient and carer experiences with the condition, current therapy or a new medicine).
3. Once you have labelled your documents, look for common themes.
4. Review your themes. If some themes do not seem to fit on a second review, consider either reassigning the response or creating a new theme. Alternatively, it may become clear that several themes can be combined into a single idea (i.e. if they are ultimately getting to the same topic or point).

6.0 Reporting your findings in the submission template

To increase the amount of space you have to report responses, remove any instructions and examples provided in the *Patient Organisations Submission of Evidence Template.*

You are now ready to present the patient and carer experiences in the template. Remember there is no right or wrong way to report your responses. Just remember to highlight important experiences from a group of participants, rather than exceptional cases. A good way to do this is to describe general trends and then present a quote to support the finding. This section provides examples of helpful responses on:

- Information gathering
- Impact of the health condition on patients' lives
- Impact on carers and families
- Patients' experience with current therapies
- What aspects of living with their condition do patients need most help?
- What are the expectations for the new medicine?
- What experiences have patients had to date with the new treatment?

TIP: Be concise yet descriptive

It may feel like there is limited space to report responses, but this reporting structure ensures that you are being clear and concise when providing meaningful and descriptive information so that your submission has maximum impact

TIP: Use plain English and avoid technical language whenever possible

DO NOT identify patients or carers by their full names. Information about individuals must be kept confidential by you to protect privacy.

6.1 Examples of Helpful Responses

6.1.1 Describing information gathering (Question 1 and Question 5)

Below is an example of a useful way to describe how you collected the information.

[Patient Organisation] conducted a participant [anonymous] online survey, which was sent by e-mail to xxx patients and carers across xxx who were on the [Patient Organisation] database. Respondents of the survey were from across xxx [xxx respondents were from outside of xxx.].

There were a total of xxx respondents; of this total, xxx were individuals living with the condition, and xxx were carers. A total of xxx respondents indicated that either they, or the person they provide care for, used the medicine under review for their condition.

This section can be short and concise. The most important information to get across is:

- The method used to collect patient and carer experiences; and
- The number of participants (divided into patients and carers) who were recruited (e.g. who were sent the survey), who participated, and who are on the treatment under review.

6.1.2 Impact of the health condition on patients' lives (Question 2)

Below is an example of how you can use the information you have gathered from a survey to provide the assessment with an understanding of some specific impacts of the condition on patients' lives.

According to the survey, xx% of patients are negatively impacted by their [condition] in their day-to-day life. Only xx% indicated no major change. The respondents indicated that the biggest impact has been on their ability to work or volunteer (xx %). In many cases, individuals retired early or went on extended leave due to the increased fatigue and pain experienced living with the disease.

> *"Symptoms and problems at this time impact my day-to-day life and quality of life to a great extent. In the past xxx months I have found that I needed to build up stamina to cook and many times I overexert myself with any day-to-day housekeeping activities. I still need to rest for a minimum of 1-2 hours each afternoon and go to bed between 8 and 9 each evening. The limitations of this disease are frustrating and can bring about fits of depression."*

As a patient organisation, you know how important it is to understand how patients are dealing with their condition on a daily basis. Your goal is to highlight how the diagnosis of the [condition] impacts patients' lives by emphasising general trends and providing quotes, like in the example above. The focus is not to present information you would find in a textbook or scientific article. You are being asked to provide patient and carer experiences on a personal level.

6.1.3 Impact on carers and families (Question 2)

Carers' experiences are an essential component to understanding the impact of the therapies for the condition on the daily routines, quality of life, relationship with family/friends, and stress and mental health of those dealing with the condition and themselves. Being able to discuss these challenges is the key goal of this section. Usually carers put on a strong face in front of patients, in order to ensure that they are a stable form of support, so patients may not have an accurate description of their true feelings. It is best to ask these questions directly to carers rather than through the patient survey.

Below is an example of how you can use the information you have gathered from carers to describe and provide an understanding of some specific impacts that caring for a patient with the condition has on carers' lives.

Carers were asked to rate the impact of providing assistance and care on various activities, using a scale of 1 to 7 with 7 being most impacted. xx% (N= aa/bb) of responding carers rated impact on the ability to travel as 7 and xx% rated impact on ability to work as 7. Carers rated all activities in the list as 5 or higher on average. Other impacted abilities included the abilities to spend time with family and friends, to fulfil family obligations, to exercise, to volunteer and to do household tasks. In addition, xx% (N=cc/dd) of carer respondents ranked emotional/physical challenges related to fear, anxiety, depression, insomnia, fatigue, personal isolation and negative health effects as the main challenge. They also reported other challenges: helping the patient cope (xx %) and balancing daily routine (xx %).

> *"I was 21 years old at the time and the primary carer for my mother. I was faced with the following challenges: depression, inability to care for myself (healthy eating, etc.), a lack of resources caused me to feel lost and uninformed. The biggest challenge was financial. My mother was no longer able to work and so I had to work to support the household while caring for her."*

The above example reports responses given by carers, including how they rated the impact of providing assistance and care on their various activities and how they ranked various challenges to them. It also includes a quotation from a carer that illustrates the impact of caregiving.

6.1.4 Patients' experience with current therapies (Question 3)

xx% (xxx respondents) of individuals living with [condition] and their carers indicated that they did experience some hardship in accessing treatment for [condition]. Hardships included:

- *the need to pay out-of-pocket for treatments*
- *the need to travel long distances to receive treatment*
- *the need to meet significant criteria to qualify for the treatment*
- *discontinuation of the treatment when the funding ran out*
- *lack of access through the hospital or private health plan to necessary treatment.*

Patients may be on one of many treatments, yet they may describe similar experiences across treatments.

6.1.5 What aspects of living with their condition do patients need most help? (Question 4)

Identify specific unmet needs with current treatments and major areas of change you would like addressed.

In this example the patient organisation highlights the unmet needs from current treatments in combination with numerical information (e.g. percentages) to help the reader understand the response:

Current treatment for condition X requires a fortnightly home intravenous (IV) infusion. Xx% of respondents (n=xxx) indicated that the treatment has a "very significant" impact on social lives of patients. Patients cannot go on extended holidays or work placements abroad. All social activities revolve around being at home on the day an infusion is due and this typically requires missing time from work, school, meetings or appointments.

Another example from a submission provided by the PKU Association of Ireland highlights a number of unmet needs in the area of PKU:

Patients/caregivers were surveyed and asked: "What are the main issues that affect adherence to the diet?" (n=118). Difficulty in planning meals = 55.08% (n=65). Too time-consuming = 48.31% (n=57). Unpalatable/Unpleasant food = 75.42% (n=89), Too expensive/financial burden = 29.66% (n=35). Too complicated = 23.73% (n=28). Do not see value in diet 0.85% (n=1). Inconvenience = 54.24% (n=64).

Other issues affecting adherence to the dietary management of PKU identified by patients/caregivers included social awkwardness, lack of variety in available dietary (low protein) products and concerns that synthetic formula/prepared low protein foods are not healthy.

Issues flagged by patients and caregivers, especially the lack of variety in available products as well as the 'bad' palatability and pleasantness of the products that are available, often lead to poor adherence in PKU patients, often resulting in cognitive deficits as well as nutritional deficiencies, osteoporosis, depression and anxiety.

6.1.6 What are the expectations for the new medicine (Question 6)?

If patients have no experience using the new medicine, you should report what their expectations are for it.

- *In considering new treatments, xx% of the respondents (n=xxx) indicated that it is 'extremely important' to see an improvement in their condition (symptoms and signs).*
- *xx% of the respondents (n = xxx) indicated that it was 'extremely important' to realise an improved quality of life when considering a new treatment.*
- *When asked about whether it was important to evaluate the average period of the expected benefit, again, the respondents (xx %) (n = xxx) indicated an extremely high degree of importance to this decision.*
- *In considering a new treatment, xx% of the respondents (n = xxx) indicated that they were willing to tolerate a moderate to high severity of side effects (xxx respondents in the range of 5 to 10, where 10 = significant side effects).*

Bullet points are a quick and easy way to discuss a number of topics in a small amount of space. In the example, the patient group was able to describe the key expectations of the treatment under review, in combination with numerical information (e.g. percentages). It is helpful to include rating scales when reporting numerical information to help the reader understand the response.

6.1.7 What experiences have patients had to date with the new medicine (Question 7)?

It is important to always provide the specified response under the correct section. Many patient organisations tend to combine the *expectations* of the treatment under review with the *experiences* of those currently on the treatment.

A total of xxx respondents had direct experience with the medicine under review in which xx% were accessing it in a late line of treatment. Xxx respondents were receiving it in the second line. When asked about the side effects experienced with the treatment, respondents mentioned fatigue, nausea, diarrhoea, and high blood pressure. In rating the side effects of the treatment, xx% of xxx respondents assigned a score of low to moderate (respondents in the range of: 1, no side effects at all, to 4) and xx% indicated that the side effects were debilitating (respondents in the range of 8 to 10, with one of these respondents (xx%) rating the side effects at 10, debilitating side effects that impact daily life). Of the side effects experienced, respondents indicated xx% were willing to accept them, xx% felt some were acceptable and others were not, one person (x%) had an adverse event and discontinued usage; xxx respondents did not answer directly.

The above example incorporates a number of points into a small paragraph. This response highlights:

- The number of respondents who had direct experience with the treatment under review
- The key side effects experienced by patients
- The percentage of respondents who were in each section of the rating scale

6.1.8 How will the new medicine address unmet needs? (Question 8)

This question relates to unmet needs or gaps in current treatment choices that are available to patients or people affected by the condition, identified in question 4. You should highlight:

- Will the new medicine fill any of these gaps?
- How does it fill those gaps?
- Will it make a real difference to patients' lives?
- How strongly do you support this medicine?

The new medicine would allow for daily oral treatment instead of an IV infusion every two weeks. Xx% of respondents (n=xxx) indicated that the new medicine would have a "very significant" improvement in their quality of life by avoiding the need for IV infusions. Comments received included "less disruption" and "less intrusion" in one's daily life when compared to current treatment and "oral treatment can be taken at a time that suits the patient"

xx% of respondents (n=xxx) believe that the new treatment will make patients more employable as there will be less disruption to their working hours.

Patients and careers were asked how strongly they support the new medicine on a scale of 1-5 (5 being "very strong" support); xx% of respondents (n=xxx) very strongly support the new medicine.

Another example based on a submission from the PKU Association of Ireland for a new therapy "sapropterin dihydrochloride" (Kuvan®) uses numerical information (percentages) and rating scales to help the reader understand the response:

Patients/caregivers were asked to rate the importance of the opportunity to normalize their/the PKU patient's diet in relation to improving their/the PKU patient's Quality of Life on a likert scale of 1-5, 1 = "not important at all" and 5 = "very important", (n=118). The overall weighted average was 4.76.

When asked to rate how they feel Kuvan® has improved the management of their/the patient's PKU on a 1-5 likert scale (1 = "no improvement at all", 5 = "significant improvement"), the weighted average response of patients/caregivers (n=10) was 4.40.

They were then asked to rate how beneficial they think it would be if they/the PKU patient could increase your number of daily exchanges by 50%/100%/150%/200% on a 1-5 likert scale, 1 = "not beneficial at all" and 5 = "very beneficial", (n=118). The overall weighted average responses were 4.47/4.53/4.52 and 4.57, respectively.

We also asked patients/caregivers how important it is for them to have access to new treatments for PKU (5-point likert scale, 1 = not important at all" and 5 = "very important"; n=118). The overall weighted average was 4.86.

Patients/caregivers were asked how important they think medical advances are in terms of providing hope for patients with PKU (5-point likert scale, 1 = not important at all" and 5 = "very important"; n=118). The overall weighted average was 4.92.

Appendix 1: Patient Organisations Submission of Evidence Template

Patient Organisation

Submission of Evidence Template

Record of Updates

Version	Date	Description of changes
2.0	August 2018	

Please Note: This document may be updated periodically, therefore please refer to the NCPE website to obtain the most recent version

The National Centre for Pharmacoeconomics (NCPE) welcomes submissions from patient organisations as part of our commitment to ensuring the patient's voice is heard in the Health Technology Assessment (HTA) process. We recognise that patients have unique knowledge about what it's like to live with a specific disease or medical condition. They can describe advantages and disadvantages of therapies, which may not be reported in published literature. They can tell us what they would most value from a new treatment.

Purpose of this template:
This template has been created to help patient organisations provide information for the assessment of a particular medicine. It provides prompts to draw out the unique patient knowledge that has the greatest potential to influence the decisions made by the decision maker, the Health Services Executive.

This submission template should be completed with reference to the '*Completing a Patient Organisations Submission of Evidence Template: Guidelines for Patient Organisations'* available on the NCPE website. This document contains detailed information and advice on what type of information to include, and how to collect relevant information within your organisation. If your organisation has not previously registered, you must also complete and return the Database Registration Form.

The submission must be completed and returned to the NCPE within 90 days of the HTA commencing, as recorded on the NCPE website. This is to allow the NCPE to adhere to the timelines specified in the drug reimbursement process. Please send your submission to us as a Word document.

If you have any more questions after reading the guidelines, the NCPE can support you throughout the submission process. You can email us at: **info@ncpe.ie** or phone: **01 4103427.** Please do not hesitate to get in touch, as we are here to help you.

Name of Patient Organisation	
Name of Medicine	
Condition treated by Medicine	
Contact details for this submission	*Please provide the name(s) of one or more contact persons within your organisation, phone and email address*
Consent for further contact from the NCPE	*The NCPE wish to email the above named contacts in relation to this submission, to acknowledge receipt of the submission, to provide information on the outcome of the HTA process and next steps, and to send a feedback questionnaire on your experience with the process.* *Please tick this box if you are happy to be contacted by the NCPE for the above specified reasons.* ☐
Consent to share this document with the HSE Drugs Group	*This submission must be shared with the HSE Corporate Pharmaceutical Unit, Drugs Committee and Leadership Committee in order to be considered as part of the decision making process.* *Please tick this box if you are happy for the NCPE to share this submission in its entirety with the HSE Corporate Pharmaceutical Unit, Drugs Committee and Leadership Committee.* ☐

Experience of patients, carers and their families

Question 1: Please provide details of how you have gathered information about the experience of patients, carers and their families

e.g. helpline, focus groups, published or unpublished research, user-perspective literature (e.g. personal stories), questionnaires, one to one discussions

Question 2: Please provide information about how this condition affects the day-to-day lives of patients, carers and their families

In describing the impact of the health problem on the lives of patients, carers and their families, you should include information about:

- *symptoms,*
- *problems that patients experience carrying out every day activities or tasks where patients require assistance and support,*
- *the impact on personal /family relationships*
- *ability to work*
- *social life*
- *financial impact*
- *emotional health*

Question 3: Please describe your experience of currently available treatments

Question 4: In what aspects of living with their condition do patients need most help?

Views of the patients, carers and their families on the difference the new medicine may make

Question 5: Please provide details of how you gathered information about the new medicine
e.g. helpline, focus groups, published or unpublished research, user-perspective literature (e.g. personal stories), questionnaires, one to one discussions

Question 6:

For patients who have <u>NOT</u> used the medicine being assessed, what are the expectations of patients, carers and their families on the anticipated advantages or disadvantages of the new medicine might be compared to existing treatments.

Keep in mind that this section is designed to be answered by patients who have <u>never</u> used the medicine being assessed.

*We want to know **<u>YOUR views</u>** on the difference the new medication would make. For example-*

- *side effects,*
- *administration (liquid form easier to swallow, once a week injection better that daily injection, tablet form better than injection etc)*
- *better compliance (stick to treatment regimens and take medication as directed)*
- *less reliance on health care professionals or carers*
- *fewer visits to hospital*
- *shorter recovery times and able to return work*

Question 7: If possible, please provide any information you might have from patients who have RECEIVED the medicine?

- *How has it affected quality of life and ability to perform daily activities?*
- *What specific symptoms have improved?*
- *What side effects have occurred?*

Question 8: To what extent will this new medication help to address the unmet needs you have previously highlighted in Question 4?

Unmet needs or gaps in treatment choices available to patients or people affected by the condition.

Does the new medicine;

- *Fill any of those gaps?*
- *How does it fill those gaps?*
- *Will it make a real difference?*
- *How strongly do you support this medication?*

Summary Information

Question 9: In no more than 5 points please summarise the <u>key aspects</u> of your submission that you feel are most important

*This section is included in the main body of the NCPE report to the HSE. Summarise key messages you would like the decision maker to consider f*or example:

- *Quality of life impact: The biggest challenges of living with this condition are…*
- *Limitations of current treatments: Current therapies are inadequate because…*
- *Benefits of new treatment: This new medicine will be important for patients because…*

Question 10: Please provide any additional information which you believe would be helpful to the decision maker
For example ethical or social issues, data you have collected on societal costs of the condition, and costs of not treating the condition.

Declarations

Question 11: Please provide FULL details of any funding received from pharmaceutical companies within the last TWO years

(***Please note that hyperlinks to other documents or websites will not be acceptable***)

Pharmaceutical Company	Amount of funding provided	Purpose of funding

Question 12: Please provide details of any individuals who have had a significant role in drawing up your submission and have interests to declare

Name	Role in Submission	P	O	Description of Interest

*Please tick either **P,** to indicate a personal interest or **O** to indicate an interest related to the organisation of which they are part. The description should include details of:*

- *whether the individual is a shareholder or director of the applicant company*
- *cash/kind received by person or organisation from the applicant company*
- *whether the interest relates to the specific medicine under consideration,*
- *whether it relates to clinical trial work for the medicine under consideration.*

Thank you for your submission of evidence – we appreciate your time and effort

Appendix 2: Key ethical considerations for patient groups collecting and reporting information for HTA submissions

Purpose

To complete submissions for health technology assessments (HTAs), patient groups may gather information about patients' and carers' experiences of living with a condition, preferences and unmet needs for treatment. This may involve (but is not limited to) conducting interviews, focus groups and surveys and collecting input using social media. As a result, patient groups need to think about the ethical and legal issues involved when engaging with people and using their personal information. This document aims to help your patient group identify and respond to those issues. It is not mandatory guidance and can be adapted to meet your needs.

Background

Many patient groups do not have the time, resources or training to undertake the rigorous, systematic investigations required for academic healthcare research. But most patient groups do have a network of patients and caregivers that they can collect information from to inform their HTA submissions.

Collecting information of relevance to HTAs can touch on sensitive issues and has the potential to impact on personal privacy. This means there are ethical issues that patient groups should consider when undertaking these activities.

When gathering information from patients and caregivers, it is important to protect their personal safety, dignity, rights and well-being. A balance is needed between fairness in providing the opportunity to have a voice in the HTA process and overburdening people with requests for information and feedback. This document provides some guidance on:

- The need for the activity
- Inclusivity
- Informed consent
- Ensuring anonymity and confidentiality
- Data protection and privacy

Issue	Consider
1. Need for activity	• Do you already have information that can answer the HTA submission questions? • Have you found a gap in the available information? Does this gap mean you need to collect new information? • Have you planned and tested the way you will collect the information to make sure it meets your needs?
2. Inclusivity	Have you taken steps to reach out to as broad a population (including vulnerable groups) as feasible?
3. Informed consent	Is each person who is asked to take part competent to consent? If yes, have they been told: • How the information being collected will be used and shared? • Who is collecting the information? • That they can refuse to take part, stop taking part at any time, or choose not to answer all the questions without this being held against them? • Any perceived or potential conflicts of interest of the person(s) or group collecting the information? • What is involved in taking part (how much time, what will be discussed, possible use of their actual words or stories in the submission)? • The realistic potential benefits? • The risks or potential harm of taking part (such as distressing thoughts, sense of stigma)? • That they will not be able to be identified from the submission? Have the people taking part: • Knowingly given consent for the collection and use of their information for this submission? • Been asked if they consider themselves to belong to a vulnerable population (which will be noted)? • Declared their own conflicts of interest? • Knowingly given consent for the information collected for the submission to be used again for other submissions? Does your patient group have:

	• A process in place to destroy information given by people who choose to no longer take part (if permitted by law)? • Steps in place to reduce any potential risks to the people taking part?

4. Ensuring anonymity and confidentiality	Have you put in place a process that makes sure that people taking part:
	
	• cannot be identified in the submission, such as:
	  ○ not using the real names of those taking part
	  ○ using initials, letters or numbers
	  ○ not collecting any identifying information?
	• are told the outcome of the HTA in a way that does not reveal to others that they took part?
	
	Do the people taking part understand:
	
	• the guarantees given about concealing their identity?
	• how their information will be stored and kept safe?

5. Data protection and privacy	Does your patient group have a data protection policy you need to follow?
	
	• Does your region/country have a data protection or privacy policy you need to follow?
	• Have you informed the people collecting the information that:
	  ○ responses must be stored securely
	  ○ they must not discuss or report responses in a way that would allow someone to be identified?
	• Have you locked the data you collected and reported in a drawer or password protected it?
	• Have you backed up the data you collected and reported?

This information has been taken from Health Technology Assessment international (HTAi). A longer version of this guide is also available, see: *Key Ethical considerations for patient groups collecting and reporting information for HTA submissions: Long Guide* if further details are required www.HTAi.org.

Appendix 3: Useful resources

- Health Technology Assessment International (HTAi) provides a variety of educational and learning tools for helping patient organisations capturing patient and carer experiences. Find out more at: www.htai.org/index.php?id=744

- Survey Monkey™, a free online survey tool, www.surveymonkey.com

- Plain language dictionary of health research terms, http://getitglossary.org/

Appendix 4: Example of a Patient Submission of Evidence Template

****Please note that this template reflects our OLD template version that is no longer in use****

Patient Interest Groups

Submission of Evidence Template

Version 1.1

Drug Name: Kuvan (Sapropterin dihydochloride)

Date of submission to NCPE: May2017

Version	Date	Description of changes
1.0	01.05.2014	N/A
1.1	26.07.2016	Corrected typographical errors, included treatment indication and removed option to not be listed as a contributor

Please Note: This document may be updated periodically, therefore please refer to the NCPE website to obtain the most recent version

Patient Interest Groups Submissions

1. Timelines

NCPE completes the entire HTA review process within tight targeted time frames. The total review — from the time a full HTA submission is received by NCPE to the time the reimbursement recommendation is released — is 90 days. The steps in the HTA process and targeted time frames for each new medicine under review can be found in the submission process section of the NCPE website. [http://www.ncpe.ie/submission-process/process-flochart/]. The patient interest group template is intended to be completed by patient interest groups and submitted within 3 months of the full HTA start date (the submission start dates are recorded under each individual drug on the website).

2. Submission length and format

Patient group input should be clear and concise, and kept to a maximum 6 pages of typed pages. We suggest that you delete the questions and examples under each heading for more space when completing each section of the template.

Electronic submissions should be submitted as a Word document, to facilitate incorporation into the NCPE reviewers' reports if needed. The NCPE does not accept submissions from individual patients. Information should come from patient organisations which represent patients, carers and families.

Further information may be requested by the NCPE if necessary. Please send the completed form by email to info@ncpe.ie.

3. How to use this template

This template has been developed to support the consistent and uniform submission of information by Patient Interest Groups. It suggests areas of information that Patient Interest Groups should consider when presenting evidence to the NCPE regarding the introduction of a new medicine in Ireland.

The template consists of a cover sheet and four sections:-

Section: 1	Information on the submitting organisation.
Section: 2	Information on the experience of patients, carers and their families.
Section: 3	Views of patients, carers and their families on the difference the new medicine might make to them.
Section: 3	Additional information to assist NCPE.

It is suggested that Patient Interest Groups should adopt a two-stage approach to the completion of the template.

Stage 1: Sections 1 & 2

These sections of the template can be prepared without any timescale for the consideration of a new medicine by NCPE and can be kept up to date when changes take place.

Stage 2: Sections 3 & 4

If sections 1 & 2 have been previously completed, it is only sections 3 & 4 of the template that will require attention when consideration of a new medication is notified by the NCPE.

It is compulsory to provide the information requested about the submitting organisation. Groups are asked to complete as much of the rest of the template as possible.

Patient organisations will need to have a good general knowledge of the views of patients, carers and their families on the range of medicines currently prescribed. This will assist them to identify which existing medicines will be relevant to the indication for the new medicine under consideration.

Guidance on specific questions

Guidance on specific questions is included under each question. Word limits are suggested word limits for some questions this is to encourage your organisation to focus on the richness of information provided, as this may have more impact on the reviewer.

Summary Cover

Name of Organisation	PKU Association of Ireland

Name	#####
Address	####
Telephone Number	####
Email Address	####

Product to which submission relates	Kuvan (Sapropterin dihydrochloride)
Product indication	Kuvan is indicated for the treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients of 4 years of age and over with phenylketonuria (PKU) who have been shown to be responsive to such treatment. Kuvan is also indicated for the treatment of hyperphenylalaninaemia (HPA) in adult and paediatric patients with tetrahydrobiopterin (BH4) deficiency, who have been shown to be responsive to such treatment.[1]

Please Note: This document may be updated periodically, therefore please refer to the NCPE website to obtain the most recent version

[1] http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/000943/WC500045036.pdf

DRAFT

Section 1: Submitting Patient Organisation

Question 1: Name of Organisation
PKU Association of Ireland.

Question 2: Alternative/Previous Names of Organisation
PKUAI

Question 3: Date of Change
N/A as it is alternative name

Question 4: Organisation's main or registered address
Please see the attached Constitution of the PKU Association of Ireland

DRAFT

Question 5: Type of Organisation *(please tick as appropriate)*

Type A – (see Note:1) ☐ X

Type B – (see Note:2) ☐

Type C – (see Note:3) ☐

Other ☐

Further information on organisation type is available on www.governance.ie (additional information is provided at the end of this document)

Question 6: Please provide details if you have ticked 'Other'

Question 7: Please provide a short description of the nature and purpose of your organisation

The aims of the PKU Association of Ireland are:

- To help and support those affected by PKU and other metabolic disorders that can be managed just like PKU.
- To campaign for additional foodstuffs to be made available on the GMS long term illness card.
- To campaign for additional funding of both the children's and adult metabolic clinics where PKU patients are treated.
- To ensure that all new treatments are made available in Ireland.
- To share tips, advice, stories, and recipes and generally support each other as we learn about this rare condition, helping to make it as easy to manage as possible.
- To strive continuously for the best possible care for people with PKU. This includes raising awareness of the condition and calling for more proactive and holistic care throughout

DRAFT

childhood and into adulthood.
We believe that with a more determined and scientific approach to treating PKU, people living with PKU will find it less of a burden on their lives and will be better able to reach their full potential.

Question 8: If you are a membership-based organisation, please indicate the number of members and geographical spread

400 members throughout Ireland

Question 9: Please list any pharmaceutical companies that are corporate members of your organisation

None

Question 10: Please provide FULL details of any funding received from pharmaceutical companies within the last TWO years

Please note that hyperlinks to other documents or websites will not be acceptable

Pharmaceutical Company	Amount of funding provided	Purpose of funding
####	####	####

Question 11: Please provide details of any individuals who have had a significant role in drawing up your submission and have interests to declare

DRAFT

Name	Role in Submission	P	O	Description of Interest
None				

*Please tick either **P,** to indicate a personal interest or **O** to indicate an interest related to the organisation of which they are part. The description should include details of:*

- *whether the individual is a shareholder or director of the pharmaceutical company who manufacture the medicine*
- *cash/kind received by person or organisation from the manufacturing company,*
- *whether the interest relates to the specific medicine under consideration,*
- *whether it relates to clinical trial work for the medicine under consideration.*

Section 2: Experience of patients, carers and their families

Question 12: Please can you provide details of how you have gathered information about the experience of patients, carers and their families

The PKUAI conducted an online survey amongst PKU patients and caregivers (n=118). Respondents identified as one of "patient" (n=57), "caregiver" (n=57), "partner/spouse" (n=2) or "other" (n=2). "Other" was typically a secondary adult caregiver such as a grandparent, second parent or sibling. Ages of patients were: 0-4 years (n=17), 5-12 years (n= 21), 13-17 years (n= 14), 18-24 years (n=15), 25+ years (n=51). Respondents-by-Country: Ireland (n=97), Australia (n=1), Canada (n=5), Germany (n=1), the Netherlands (n=2), New Zealand (n=1), Spain (n=1), UK (n= 5), USA (n= 1). 12 survey respondents had experience with Kuvan.

The survey contained the use of free-form commentary, scoring options and limited closed questions. A copy of the survey is attached (Appendix 1).

We have also consulted published and unpublished research, as well as user-perspective literature[2] and relevant research outcomes shared during patient conferences (Appendix 2).

Question 13: Please provide information about how this condition affects the day-to-day lives of patients, carers and their families

Phenylketonuria is a metabolic disorder in which patients are unable to sufficiently break down the amino acid phenylalanine (Phe) into tyrosine (Tyr) due to decreased activity or inactivity of the liver enzyme phenylalanine hydroxylase (PAH). When left untreated, Phe accumulates in the blood leading to increased Phe levels, decreased Tyr levels and a disturbed Phe:Tyr ratio (Blau et al. 2010). Without early detection and management of the disorder, PKU leads to severe neurological impairments and mental retardation

To protect brain function, most children and adults with PKU must follow a special diet that involves strictly limiting and controlling the intake of natural protein (restricting the intake of Phe) and drinking a synthetic Phe-free protein formula (to ensure intake of important nutrients lacking in the patients' natural diet). Patients and caregivers find the dietary management of PKU burdensome: it is expensive, laborious, time-consuming and complex. It is very unpleasant and lacks food choices. The diet has a tremendous impact on day-to-day life for patients and caregivers. For children and adolescents it is particularly onerous because it has the effect of segregating them from their peers, leading often to poor adherence. Poor adherence and non-adherence have been linked to deficits in cognitive functioning, especially executive (frontal lobe) functions such as planning, attention and inhibition.

The *European Society for Phenylketonuria and Allied Disorders Treated as Phenylketonuria*

(ESPKU) recently issued guidelines[3] for target PHE concentrations: 120–360 µmol/L for individuals aged 0–12 years and for maternal PKU, and 120–600 µmol/L for non-pregnant individuals older than 12 years.

However, there are no clear guidelines or care pathway PHE ranges defined for PKU patients in Ireland.

Ironically, living well with PKU requires exemplary executive function as diet planning is astonishingly complex, record-keeping is onerous, maintaining supplies and monitoring blood Phe levels are time-consuming and require excellent organization skills.

Patients/caregivers were asked to rate the **level of effort required to adhere to a diet restricted in Phe (as prescribed by a doctor) on a likert scale of 1 – 5, 1 = "no effort at all" and 5 = "much effort",** (n=118). The overall weighted average was 4.58, indicating that patients/caregivers

[2] Hagedorn TS, van Berkel P, Hammerschmidt G, Lhotáková M, Saludes RP. Requirements for a minimum standard of care for phenylketonuria: the patients' perspective. Orphanet journal of rare diseases. 2013 Dec 17;8(1):191.

[3] http://www.thelancet.com/pdfs/journals/landia/PIIS2213-8587(16)30320-5.pdf

recognize the extreme difficulty this diet poses.

We asked patients/caregivers: **How has PKU had an impact on your life (or on the life of the person under your care)?** 9 choices were provided, with respondents able to "please select all that apply" (n=104). *Difficulties with diet* = 65.55% (n=78). *Difficulty with focus (attention deficit)* = 36.13% (n=43), *Exclusion or difficulties in social settings* = 36.97% (n=44), *Depression or Anxiety* = 35.29% (n=42), *Problems at school/work/clubs/events related to diet compliance* = 31.93% (n=38), *Learning disabilities* = 11.76% (n=14), *Difficulty forming interpersonal relationships* = 13.45% (n=16), *Difficulties maintaining employment* = 3.36% (n=4), *Tummy aches/diarrhoea* = 28.57% (n=34).

Other PKU related issues highlighted by patients/caregivers affecting patients included feelings of guilt surrounding food, food obsession, anorexia, mood swings, bad hair quality, teeth discolouring, tiredness, self-harming, pain in head, sleep walking, discrimination, difficulty when eating out, severe acid reflux when on diet, and eczema.

We asked: **In a typical week, how much time do you spend on the following PKU-related tasks?** (n=118) A list of tasks (developed by an examination of relevant published literature) was provided, along with time measure selections. Average times as follows: *Cooking for Phe-restricted diet* = 7.5 hrs/wk. *Supervising protein intak*e = 8.5 hrs/wk. *Planning daily Phe intake* = 6 hrs/wk. *Baking bread or other low protein foods* = 3 hrs/wk. *Weighing foods* = 2 hrs/wk. *Keeping records* = 2 hrs/wk. *Food research* = 2.5 hrs/wk. *Preparing for social events* = 1.5 hrs/wk. *Researching PKU* = 2 hrs/wk. *Blood testing* = 1 hrs/wk. *Ordering low proteins* = 1 hrs/wk. *Clinic appointments* = 1 hrs/wk. *PKU events* = 1 hrs/wk. *Ordering amino acids* = 1 hrs/wk. **Total Time (average) all tasks = 40 hrs/wk**. **Nearly 6 hours a day.**

Question 14: Which aspects of living with this condition, <u>NOT MET</u> by current treatments, do patients need most help with?

We also asked patients/caregivers: **"What are the main issues that affect adherence to the diet?" (7 choices, "please select all that apply")** (n=118). Difficulty in planning meals = 55.08% (n=65). Too time-consuming = 48.31% (n=57). <u>Unpalatable/Unpleasant food = 75.42%</u> (n=89), Too expensive/financial burden = 29.66% (n=35). Too complicated = 23.73% (n=28). Do not see value in diet 0.85% (n=1). Inconvenience = 54.24% (n=64).

Other issues affecting adherence to the dietary management of PKU identified by patients/caregivers included social awkwardness, <u>lack of variety in available dietary (low protein) products</u> and concerns that synthetic formula/prepared low protein foods are not healthy.

Issues flagged by patients and caregivers, especially the lack of variety in available products as well as the 'bad' palatability and pleasantness of the products that are available, often lead to poor adherence in PKU patients, often resulting in cognitive deficits (see Q13) as well as nutritional deficiencies, osteoporosis, depression and anxiety.

DRAFT

Section:3 Views of the patients, carers and their families on the difference the new medicine may make

Question 15: Please provide details of your sources of information about the new medicine

Several patients / caregivers (N=12) that completed the online survey indicated they have (had) experience with Kuvan (either now or in the past, by participating in a clinical trial). These respondents were asked to complete several questions (free-form commentary, scoring options and limited closed questions) with regards to their experience with the new medicine.

Question 16: Please advise us of the views of patients, carers and their families on what the advantages or disadvantages of the new medicine might be compared to existing treatment

Existing Treatment	Advantages of new medicine	Disadvantages of new medicine
Low-protein diet + Phe-free protein substitutes	Improvement in protein tolerance (due to increase in PAH activity) either leading to [1] a more relaxed diet (increased natural protein intake, less protein substitutes) or [2] no need for the low-protein diet/protein substitutes at all (normalisation of diet). Improved adherence / easier to adhere to the PKU diet Improvements in mood, wellbeing and self-confidence	Not all patients respond to (benefit from) Kuvan (in our survey N=2/12 were non-responders). 4 responsive patients (40%) reported some side effects from using Kuvan, but also reported that none of the side effects they experienced were serious enough to stop using the new medicine. Symptoms patients/caregivers reported were: stomach pain (n=1), diarrhoea* (n=2), runny/stuffy nose (n=1), cough (n=2).

	Improvements in school performance and concentration Social life and work life easier to manage ***"It has been a game changer for us. It makes managing her PKU easier."***	

Question 17: To what extent will this new medication help to address the unmet needs you have previously highlighted in Q14?

Patients/caregivers were asked to rate the **importance of the opportunity to normalize their/the PKU patient's diet in relation to improving their/the PKU patient's Quality of Life on a likert scale of 1-5, 1 = "not important at all" and 5 = "very important"**, (n=118). The overall weighted average was **4.76**.

When asked to rate how they feel Kuvan **has improved the management of their/the patient's PKU on a 1-5 likert scale (1 = "no improvement at all", 5 = "significant improvement")**, the weighted average response of patients/caregivers (n=10) was **4.40**.

They were then asked to rate how **beneficial they think it would be if they/the PKU patient could increase your number of daily exchanges by 50%/100%/150%/200% on a 1-5 likert scale, 1 = "not beneficial at all" and 5 = "very beneficial"**, (n=118). The overall weighted average responses were **4.47**/**4.53**/**4.52** and **4.57**, respectively.

We also asked patients/caregivers how **important it is for them to have access to new treatments for PKU (5-point likert scale, 1 = not important at all" and 5 = "very important"**; n=118). The overall weighted average was **4.86**.

Finally, we asked patients/caregivers how **important they think medical advances are in terms of providing hope for patients with PKU (5-point likert scale, 1 = not important at all" and 5 = "very important"**; n=118). The overall weighted average was **4.92**.

Section 4: Additional Information

Question 18: In no more than 5 points please summarise the key aspects of your submission that you feel are most important

PKU and its associated diet imposes a significant burden on patients, carers, healthcare resources and ultimately wider society through illness and reduced productivity.

There are long- term health sequelae and costs associated with the PKU diet and poor PHE control:

- Decreased quality of life due to the extremely challenging PKU diet
- Medical problems associated with the diet e.g. osteoporosis, dental decay, deficient executive function etc.

Many patients struggle to maintain normal PHE levels with diet alone.

The introduction of Kuvan for suitable patients has the potential to dramatically improve the quality of life for people with PKU and their carers. Kuvan can also reduce treatment costs by lowering the requirements for specialised medical foods, and reducing long-term healthcare system costs through improved outcomes (e.g. fewer osteoporotic fractures). Additionally people with PKU who have better control of their PHE levels as well as improved executive functioning will be able to make greater societal productivity contributions.

Question 19: Please provide any additional information which you believe would be helpful to the decision maker

A subgroup of the patients reported they had been pregnant in the past (n=13), are pregnant now (n=3), or are following a preconception diet as they are planning to get pregnant (n=3). Nearly half (**46.15%)** of the pregnancies were reported to be unplanned.

In PKU pregnancies have to be well planned and monitored: patients are put on a pre-conception diet to decrease Phe levels even more, as elevated maternal Phe levels during pregnancy are teratogenic and may result in growth retardation, microcephaly, significant developmental delays, and birth defects in the offspring of women with poorly controlled PKU during pregnancy (referred to as the ‘maternal PKU syndrome’). In unplanned pregnancies the clinical team’s primary concern is decreasing and controlling blood Phe levels as quickly as they can in an attempt to prevent the maternal PKU syndrome.

The ESPKU guidelines recommend PHE levels of 120–360 µmol/L for maternal PKU.

With respect to Kuvan (BH4), the expert working group advises:

"Patients with PKU, especially with a higher residual PAH activity, might respond to BH4 administration with a significant increase in phenylalanine tolerance, or decrease in blood phenylalanine concentrations, or both. All patients warrant testing for BH4 responsiveness either by genotyping or BH4 loading. If a female patient with PKU fails to achieve target levels with a low Phe diet pre conception and during pregnancy, BH4 should be considered."

DRAFT

Thank you for your submission of evidence

Notes: Organisation Type *(www.governance .i.e.)*

Note: 1 Checklist for Type A

This group is run by volunteers and do not employ staff. The members of the board are therefore responsible for:

1. Overseeing the work of the organisation (governance);
2. Organising the daily work (management), and;
3. Carrying out the work of the organisation (operations).

Many such groups operate on less than €10,000 a year although some may have a larger income. They may or may not have a CHY number. Type A groups are may be incorporated but some may be required to do so by funders.

Note: 2 Checklist for Type B

These organisations usually employ a small number of staff and many may have a single member of staff. While the most senior (or only) member of staff may have a title such as manager, coordinator or administrator, the people who sit on the board will still have some management and operations responsibilities as well as their governance/oversight role.
Annual income may vary considerably from one organisation to the next in this category and many organisations may receive grants from statutory bodies and/or trusts and foundations. A 'Type B' organisation may tend to be incorporated, and may have a CHY number.

Note: 3 Checklist for Type C

The main characteristics of these organisations are that the people who sit on the board focus solely on their governance/oversight role, delegating management and operational duties to the staff. There is a clear division between the governance role of the board and the management role of staff.
These organisations tend to employ more than ten members of staff and may often have hundreds of staff which in turn, may require a structure based on functional or geographic departments. It is most likely that 'Type C' organisations will be incorporated and may have a CHY number, but this is not always the case.

Appendix 5: Example of a Survey Template Used by a Patient Organisation to Gather Information

MS Ireland is planning to make a submission to the HSE regarding Sativex. If you have been affected by the lack of availability of Sativex, please take a few minutes to complete this short survey, which will help us to develop a strong submission. This survey is completely confidential and you will not be asked to provide any identifying information. We may use anonymous quotes from answers provided as part of the submission.

If you have any questions please contact ############

Questions for survey/focus group regarding Sativex:

1. Can you describe how spasticity affects you?

2. Can you describe any difficulties you experience carrying out everyday activities or tasks or instances where you require assistance and support with everyday activities as a result of spasticity?

3. Can you describe the impact on personal and family relationships?

4. Can you describe the impact on your ability to work?

5. Can you describe the impact on your social life?

6. Have you been offered or prescribed any treatments or therapies (besides Sativex) to treat spasticity and associated symptoms? If so, how effective were these?

7. What do you think would be different about Sativex, compared to other treatments?

8. What difference do you believe that Sativex would make to your daily life?

DRAFT