Commissioning Policy (EMSCGP041V1)

Sapropterin (Kuvan®) for Phenylketonuria

Version 1

1. Definitions

Phenylketonuria (PKU) is a rare genetic condition. PKU is one of a number of disorders of the chemical breakdown of amino acids, which are building blocks of protein. In PKU the enzyme which is affected is phenylalanine hydroxylase (PAH). This enzyme is responsible for converting the amino acid phenylalanine (Phe) into another amino acid, tyrosine. When the enzyme is deficient the Phe accumulates and is converted into phenylpyruvate and other related phenylketones. These products are detected in urine giving the disease its name.

The drug sapropterin is a synthetic analogue of the molecule tetrahydrobiopterin which is the co-enzyme for the enzyme which is deficient in PKU. It is licensed for patients with PKU who respond to sapropterin over the age of 4 years.

Prior Approval refers to the EMSCG requirement for either an individual patient or a group of patients to access healthcare, including diagnostics, under a Prior Approval Scheme as set out in the current NHS Acute Services Contract.

Responsible Primary Care Trust means the Primary Care Trust which discharges the Secretary of State's functions under the National Health Service Act 2006 for an individual patient.

2. The policy

2.1 This policy applies to any patient for whom the EMSCG is the Responsible Commissioner.

2.2 Sapropterin will not routinely be commissioned.

2.3 Pregnant women with PKU who are unable to achieve satisfactory control of plasma Phe levels using standard dietary regimens will be eligible for
treatment with sapropterin. Sapropterin will only be funded during the pregnancy as per protocol (appendix 1).

2.3.1 An application should be made to the EMSCG using the approved proforma (see appendix 3) confirming that the clinical protocol in appendix 1 has and will be followed and, given that the treatment is rarely used, novel, or unknown and there is a lack of evidence of safety, confirm that the patient has given informed consent. As long as these conditions are met the drug will be funded.

2.3.2 Under normal circumstances prior approval will be required before treatment is commenced. However, in exceptional circumstances where commencing therapy is urgent e.g. patient is already pregnant and delaying treatment could have a serious effect on the foetus, treatment can commence without prior approval.

2.4 Funding will also be considered in situations where parents are not compliant with treatment and as a consequence the child is subject to Section 18 of the Safeguarding Children Act. Such funding requests will not be processed through the normal funding mechanism but the decision will be made on the recommendation of the PCT as part of the multidisciplinary team agreeing the action plan for the child at risk. (see Appendix 2).

In these instances an exit strategy should be part of the planning process, with ongoing review, and treatment will not normally go beyond 16 years of age and will not go beyond the age of 18 years.

2.5 Funding requests will only be considered from clinicians experienced in the management of PKU.

3. Cost

3.1 Sapropterin is available in packs of 30 or 120 tablets at £597 or £2,389 per pack respectively, resulting in a price per tablet of £19.91. As dose is determined by patient body weight the actual dose and cost will vary depending on the patient’s weight. Table 1 displays the cost variation with patient weight.

<table>
<thead>
<tr>
<th>Body Weight (kg)</th>
<th>Actual daily dose – mg (no of tablets)</th>
<th>Cost of treatment</th>
<th>Daily</th>
<th>Annual</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-24</td>
<td>200 (2)</td>
<td>£39.82</td>
<td>£14,534</td>
<td></td>
</tr>
<tr>
<td>25-34</td>
<td>300 (3)</td>
<td>£59.73</td>
<td>£21,801</td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>400 (4)</td>
<td>£79.64</td>
<td>£29,068</td>
<td></td>
</tr>
<tr>
<td>45-54</td>
<td>500 (5)</td>
<td>£99.55</td>
<td>£36,336</td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>600 (6)</td>
<td>£119.46</td>
<td>£43,603</td>
<td></td>
</tr>
<tr>
<td>65-74</td>
<td>700 (7)</td>
<td>£139.37</td>
<td>£50,870</td>
<td></td>
</tr>
<tr>
<td>75-84</td>
<td>800 (8)</td>
<td>£159.28</td>
<td>£58,137</td>
<td></td>
</tr>
</tbody>
</table>
4. Commissioning structure

The funding of sapropterin will fall under EMSCG commissioning.

5. GP prescribing

There will be no GP prescribing of sapropterin.

6. Documents which have informed this policy

- West Midlands Strategic Group Commissioning Policy 1: Ethical Framework to support priority setting and resource allocation within collaborative commissioning arrangements


- West Midlands Specialised Commissioning Team, Background paper to the West Midlands Specialised Commissioning Group, Sapropterin in PKU, August 2010

### Version Control Sheet

<table>
<thead>
<tr>
<th>Draft</th>
<th>Section/Para/Appendix</th>
<th>Version/Description of Amendments</th>
<th>Date</th>
<th>Author/Amended by</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>Para 2.3.1 rewritten to clarify how a request for funding is made</td>
<td>October 2010</td>
<td>Ami Faulkner</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Para 2.3.2 added regarding funding in pregnancy</td>
<td>10.7.2011</td>
<td>Malcolm Qualie</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>New section added regarding cost of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>Additional wording added following SCG Board meeting</td>
<td>28.7.2011</td>
<td>Malcolm Qualie</td>
</tr>
</tbody>
</table>

**Regional leads for this policy**

<table>
<thead>
<tr>
<th>Mr Malcolm Qualie</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head of Health Policy</td>
</tr>
<tr>
<td>East Midlands Specialised Commissioning Team</td>
</tr>
<tr>
<td><a href="mailto:malcolm.qualie@emscg.nhs.uk">malcolm.qualie@emscg.nhs.uk</a></td>
</tr>
</tbody>
</table>

**Version**  First

**Policy effective from**  July 2011

**Date of next review**  When new evidence is available

**Acknowledgements**  Dr Daphne Austin WMSCG

North East Treatment Advisory Group
Appendix 1

Protocol for the use of sapropterin in pregnant women with PKU whose Phe levels remain high despite dietary treatment

Preconception management

- Patients will be offered the opportunity to attend the dietetic kitchen for dietary education.
- Most women who are on normal, unrestricted diets will be expected to attend for at least two sessions, but those who have recently been on preconception or pregnancy diets, and those who habitually follow a low protein diet may not need additional dietary education.
- Patients will be established on a low protein diet and amino acid supplements. They will be asked to send blood spots for monitoring of Phe levels twice a week. With the help of the metabolic dieticians, women will adjust their protein intake to obtain plasma Phe levels of between 100 and 300 mcmol/l.
- Once levels have been stable within this range for at least three weeks, subjects will be advised that it is safe to start to try to conceive.

Pregnant women

- Once the patient is pregnant dried blood spots will be used to monitor Phe levels in PKU.
- During pregnancy, women will be asked to collect blood spots three times a week and send them in to the pathology lab at the hospital for analysis. (Often women who find it difficult to establish metabolic control on a low protein diet also find it difficult to send in blood spots regularly, and in these cases the frequency of monitoring can be much lower.)
- Failure of dietary control will be defined as an average blood spot Phe level of greater than or equal to 450 mcmol/l for one week or for two consecutive blood spots, whichever is longer at any time during pregnancy.
- For patients who present once they are already pregnant, similar dietary measures should be instituted. If after two weeks of intensive dietary intervention they do not obtain metabolic control (as defined above) then they will also be considered for treatment with sapropterin.

Treatment with sapropterin:

- All pregnant women who fail to establish metabolic control will be tested for sapropterin responsiveness.
- Sapropterin responsiveness testing will be done by administering sapropterin at a dose of 20 mg/kg per day for two weeks. During this time, patients will commit to continue to follow dietary advice as before and to collect blood spots three times a week.
• Response to sapropterin will be assessed by comparing Phe levels at baseline and during treatment, as before. If a response (which in this case would be any significant reduction in Phe levels as judged by the clinical team) is seen at any time during the two week testing period, the patient will continue on sapropterin.

• For the remainder of the pregnancy, a combination of sapropterin and low protein diet will be used to try to keep plasma Phe levels within, or as close as possible to, the target range of 100-300 mcmol/l. The dose of sapropterin used can range from 5-20 mg/kg/day.

• In women who are not responsive to sapropterin, failure of metabolic control will be managed in the usual way. Patients are offered intensive dietary support. The dose and frequency of amino acid supplements can be increased. If necessary, patients can be admitted to hospital for direct supervision of their diet. These measures will also be available, if needed, for sapropterin responsive patients who continue to have poor metabolic control once established on sapropterin.

• For patients who are taking sapropterin, the drug will be stopped immediately after delivery. All patients will return to standard management after delivery. They will be given the option to continue on a dietary treatment if they choose.

• As the effects on the foetus are currently unknown the patient should be fully informed of the status and experience of this drug.

• All foetal anomalies occurring in patients treated with sapropterin (regardless of the potential cause) must be reported on the Yellow Card System.

• Detailed foetal anomaly scans in women who are failing to obtain adequate metabolic control will be undertaken.

Based on guidance produced by Dr Robin Lachmann PhD MRCP, Consultant in Metabolic Medicine, Charles Dent Metabolic Unit, National Hospital for Neurology and Neurosurgery, Queen Square, London WC1N 3BG
Appendix 2

Under the Children’s Act 2004 all Local Authorities should have a Local Safeguarding Board. Each Board will have developed policies and procedures for safeguarding children.

Once the child is subject to a child protection plan (Section 18) those professional organisations responsible for the child’s care need to develop an action plan. It is within this context that sapropterin may be considered as an option for treatment (in line with any other Section 18 where a parent’s failure to comply with the requirements of a medical condition puts the child’s health at risk.

Here is an example of part of a Council’s procedures (Blackburn and Darwen Borough Council)

Action following an initial conference

Role of the key worker

When a conference decides that a child should be the subject of a child protection plan the social care department should carry future child care responsibility for the case and designate a member of its social work staff to be the key worker.

The key worker is responsible for making sure that the outline child protection plan is developed into a more detailed interagency plan. S/he should complete the core assessment of the child and family, securing contributions from Core Group members and others as necessary. The core assessment should be completed within a maximum of 35 working days and should focus particularly on those areas highlighted by the conference as requiring further exploration and understanding. The key worker is responsible for acting as lead worker for the inter-agency work with the child and family and should analyse the findings of the assessment to inform planning, case objectives and the nature of service provision S/he should coordinate the contribution of family members and other agencies to planning the actions which need to be taken, putting the child protection plan into effect, and reviewing progress against the objectives set out in the child protection plan.

The core group

The core group is responsible for developing the child protection plan into a detailed working tool, and implementing it based on the outline plan agreed at the initial child protection conference. It should be refined as necessary and the progress of the child and family members should be monitored against the objectives specified in the plan.

The core group membership should include the key-worker who leads the core group, the child if appropriate, family members and professionals or carers who have direct contact with the family. Although the key worker has the lead role, all members of the core group are jointly responsible for the formulation and implementation of the child protection plan, refining the plan as needed and monitoring progress against specified objectives in the plan.

Core groups are an important forum for working with parents, wider family members and children of sufficient age and understanding. It can often be difficult for parents to agree to a child protection plan within the confines of a formal conference. Their agreement may be forged later when details of the plan are worked out in the core group. Sometimes there may be conflict of interest between family members who have a relevant interest in the work of the core group. The child’s best interest should always have precedence over the interest of other family members.
The first meeting of the core group should take place within 10 working days of the initial child protection case conference. The purpose of this first meeting is to flesh out the child protection plan and to decide what steps need to be taken by whom to complete the core assessment on time. Thereafter, the core group should meet monthly to facilitate working together, monitor actions and outcomes against the child protection plan and make any necessary changes as circumstances change.

The core group should ensure that a written record is made of actions agreed and decisions taken at core-group meetings updating the child protection plan as necessary. All those who attended and were invited to the core group should receive a copy of the record for their agency files—this record should include the names and designation of those who attended.

The core group is responsible for completion of the core assessment within 35 days.

The analysis of the findings of the core assessment will inform the plan on how best to safeguard and promote the welfare of the child and support parents in achieving this aim.

The core group should be the only forum for decisions to de-commission services. Any agency withdrawing services to a child/family, which have previously been agreed at a case conference should attend the next review conference or at least prepare a report following the core group decision.

**The detailed protection plan**

The detailed child protection plan should address:

- Action to make a child safe;
- Action to promote a child’s health and development;
- Action to help a parent/carer in safeguarding a child and promoting his/her welfare;
- Therapy for an abused child; and
- Support or therapy for a perpetrator of abuse

The plan should:

- Describe the identified developmental needs of the child, and what therapeutic services are required,
- Include specific, achievable, child focussed outcomes intended to safeguard and promote the welfare of the child,
- Include realistic strategies and specific actions to achieve the planned outcomes,
- Clearly identify roles and responsibilities of professionals and family members, including the nature and frequency of contact by professionals with children and family members,
- Lay down points at which progress will be reviewed, and the means by which progress will be judged,
- Set out clearly the roles and responsibilities of those professionals with routine contact with the child, for example, health visitors, GPs and teachers, as well as any specialist more targeted support to the child and family.

The plan will take into consideration the wishes and feelings of the child, and the views of the parents, insofar as they are consistent with the child’s welfare. Family members and core group members will be asked to sign the plan to evidence their acceptance and willingness to work to it.

All parties to the plan will receive a copy of the most recent plan following core group meetings so that they are clear about who is doing what and when and what the
planned outcomes are for the child. Records of core group meetings should be sent to the parties within 10 working days. All professionals have a responsibility for keeping their own records, this includes making notes of any actions agreed which can be used pending receipt of the official meeting record.

**Interventions**

Irrespective of where a child is living interventions should specifically address:

- The developmental needs of the child
- The child’s understanding of what has happened to him/her
- The abusing caregiver/child relationship and parental capacity to respond to the child’s needs;
- The relationship between the adult caregivers both as adults and parents;
- Family relationships; and
- Possible changes to the family’s social and environmental circumstances

Intervention may have a number of inter-related components;

- Action to make a child safe;
- Action to help promote a child’s health and development i.e. welfare;
- Action to help a parent(s)/caregiver(s) in safeguarding a child and promoting his or her welfare;
- Therapy for an abused child;
- Support or therapy for a perpetrator of abuse

A key issue when deciding upon suitable interventions will be whether the child’s developmental needs can be responded to within his/her family context, and within timescales that are appropriate for the child. These timescales may not be compatible with those of the carer/s who is/are in receipt of therapeutic help. Where the family situation is not improving or changing fast enough to respond to the child’s needs then decisions will be necessary about the long-term future of the child.

http://www.blackburn.gov.uk/server.php?show=ConWebDoc.26459&setPaginate=No #page1
Appendix 3

Application to request Sapropterin for Phenylketonuria in pregnancy

<table>
<thead>
<tr>
<th>PATIENT PERSONAL DETAILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Name:</td>
</tr>
<tr>
<td>Date of Birth:</td>
</tr>
<tr>
<td>NHS Number:</td>
</tr>
<tr>
<td>GP Name &amp; Practice Details:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DETAILS OF REQUESTER</th>
</tr>
</thead>
<tbody>
<tr>
<td>(include referring clinician contact details in the event of query or need for clarification)</td>
</tr>
<tr>
<td>Name:</td>
</tr>
<tr>
<td>Trust:</td>
</tr>
<tr>
<td>Secure email for correspondence:</td>
</tr>
<tr>
<td>Provider Trust MDT Support:</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CLINICAL DETAILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current status</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>☐ Patient is already pregnant</td>
</tr>
<tr>
<td>Estimated date of delivery:</td>
</tr>
<tr>
<td>☐ Patient is planning to become pregnant</td>
</tr>
<tr>
<td>Current plasma phe level (micromol/l)</td>
</tr>
<tr>
<td>Daily dose of Sapropterin requested (mg)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CONSENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>I confirm that this Request has been discussed in full with the patient and that the patient is aware that the Sapropterin has not been tested in pregnancy.</td>
</tr>
<tr>
<td>I confirm that the agreed clinical protocol has been followed in full and that treatment will be stopped immediately after delivery.</td>
</tr>
<tr>
<td>Signature of Requester:</td>
</tr>
</tbody>
</table>

Please return completed forms to EMSCGfundingrequests@nhs.net