

E06/S(HSS)/e

**2013/14 NHS STANDARD CONTRACT  
FOR SEVERE ACUTE PORPHYRIA SERVICE (ALL AGES)**

**PARTICULARS, SCHEDULE 2 – THE SERVICES, A – Service Specification**

<b>Service Specification No.</b>	E06/S(HSS)/e
<b>Service</b>	Severe acute porphyria service (All Ages)
<b>Commissioner Lead</b>	
<b>Provider Lead</b>	
<b>Period</b>	12 months
<b>Date of Review</b>	

**1. Population Needs**

**1.1 National/local context and evidence base**

Evidence for the service need is based on clinical experience, European registry data, a British Porphyria Association patient survey and patient testimonials. The centres have an established record providing clinical services for porphyria patients for more than ten years and clinical leads have published on porphyria in textbooks and peer reviewed journals [Badminton and Elder 2008, Cox 2003, Marsden and Rees 2010].

**Therapy:**

Published evidence indicates haem arginate is effective in acute attacks, through normalising biochemistry and alleviating clinical effects and duration of attacks [Mustajoki *et al.*, 1986; Kostrzewska *et al.*, 1991; Mustajoki and Nordmann, 1993]. However it does not reverse damage to peripheral neurons and prompt treatment during an attack is essential to prevent neuropathy developing and progressing [Puy, 2010, Hift & Meissner 2005]. Clinical management in non-specialist centres is frequently sub optimal resulting both increased length of stay [Nordmann and Deybach, 1993], and inappropriate haem arginate use [Frei *et al.*, 2010].

The most severely affected patients with recurrent attacks are managed medically. However liver transplantation is now increasingly being used as a definitive treatment now that efficacy has been established [Soonawallah *et al* 2003], and guidelines for transplant indications have been proposed [Seth *et al* 2007]. This work has also improved our understanding of the pathogenesis of acute attacks [Dowman

et al 2011].

The involvement of the porphyria centres in the European Porphyria Network also allows contribution to wider aspects of development, including new approaches to treatment.

### Diagnostics

Two of the three National Acute Porphyria Centres (NAPCs - Cardiff, King's College Hospital London) have associated specialist porphyria diagnostic laboratories that are recognised by the Supraregional Assay Service ([www.sas-centre.org](http://www.sas-centre.org)). Cardiff, London and the two Regional Porphyria Centres (Salford, Leeds) are recognised by the European Porphyria Network (EPNET) ([www.porphyrria-europe.org](http://www.porphyrria-europe.org)), and operate within Clinical Pathology Accreditation (CPA) accredited laboratories. Cardiff also provides the only UK genetic testing service for Porphyria, which is recognised by the UK Genetic Testing Network (UKGTN), and has recently published on diagnostic testing and a diagnostic algorithm for acute porphyrias [Whatley et al 2009]. A limited range of DNA testing for acute porphyria is also performed at King's College Hospital but this is not part of the nationally designated service and will be funded through local arrangements. One of the innovation and research objectives of NAPS is to identify and validate novel biomarkers to aid in monitoring acute attacks, which is supported by this collaboration with diagnostic services.

### **Education and dissemination:**

Patient and healthcare professional education has a very important role in improving healthcare and preventing acute attacks. Patient information has been developed through the EPNET collaboration ([www.porphyrria-europe.org](http://www.porphyrria-europe.org)) and is available in multiple languages. The centres also work actively with the British Porphyria Association and Children Living with Metabolic disorders (CLIMB) to support knowledge and education. In addition, the British and Irish Porphyria Network (BIPNET) has focussed on improving diagnosis and patient care through two subgroups. The clinical subgroup has developed consensus guidelines on treatment of acute attacks. The laboratory subgroup is developing and implementing diagnostic quality standards. Output of both subgroups is published on a website.

One of the main modifiable risk factors for acute attacks is prescribed medication. Reliable up to date information that is available to patients and healthcare professionals is critical to risk reduction. Welsh Medicines Information Centre (WMIC) and the Cardiff Porphyria Centre publish a safe drug list annually, revise the BNF section on porphyria twice annually and provide a telephone helpline advice. Collaboration between WMIC, the Norwegian Porphyria Centre (NAPOS) and EPNET has allowed clinical validation of a searchable drug database ([www.drugs-porphyrria.org](http://www.drugs-porphyrria.org)) [Deybach et al 2010].

### **Research:**

The centres have contributed to a previous clinical trial on enzyme replacement

therapy for Acute Intermittent Porphyria (AIP) (HemBiotech, Sweden). One centre is on the external advisory board for a trial of gene therapy for AIP, which is due to start in 2011 (AIPGENE: Augmenting PBGD expression in the liver as a Novel Gene therapy for Acute Intermittent Porphyria. FP7 Project Number: 261506).

## **2. Scope**

### **2.1 Aims and objectives of service**

The National Acute Porphyria Service (NAPS) provides acute care support and clinical advice for two groups of patients with active acute porphyria suffering neurovisceral symptoms:

- patients suffering isolated acute attacks requiring haem arginate treatment;
- patients with recurrent acute attacks.

The service is delivered by three National Acute Porphyria Centres (NAPCs): Cambridge University Hospitals NHS Foundation Trust (CUH), Cardiff and Vale University Local Health Board (C&VUHB) and King's College Hospital NHS Foundation Trust (KCH). In addition, outreach services are provided in two Regional Porphyria Centres; Salford Royal NHS Foundation Trust (Salford) and Leeds Teaching Hospitals NHS Trust (Leeds) that work in partnership and under the guidance of the NAPCs.

The aim of the service is to provide immediate clinical support and advice to acute care physicians in the patient's local hospital on management and treatment of all acute attacks of porphyria. Outpatient follow-up to manage ongoing treatment and complications will then be arranged at one of the NAPCs. Wherever possible NAPS will put shared care agreements in place with an appropriate local clinician, and will support these arrangements with outreach support where necessary.

The service is targeted at patients who have acute neurovisceral symptoms that cause significant morbidity and mortality. The patients are young adults, mainly females, in whom active porphyria has a major impact on wellbeing and quality of life for them and their families.

Through early involvement in the clinical management of the patients the service will:

- reduce progression to severe neurological deficit requiring intensive care;
- reduce complications of treatment through advice on administration of haem arginate;
- reduce unnecessary administration of haem arginate;
- reduce the overall number and frequency of attacks through introducing preventative treatments;
- reduce the overall number of attacks through patient education including the provision of a safe drugs advisory service for patients and their healthcare providers.

If inpatient care is required, then this is paid for through normal arrangements under the Payment by Results (PbR) tariff system, and is outside the scope of the national service.

Services for patients with presymptomatic/latent acute porphyria or acute porphyria presenting with skin symptoms alone will continue to be cared for through existing Adult Metabolic Services and Dermatology services and are beyond the scope of the national service.

### **Objectives:**

The overall objective of the service is to improve the clinical management and care of patients with acute porphyria who suffer an attack or attacks by providing immediate two specialist clinical support and clinically appropriate follow-up after discharge, for up to two years following an acute attack.

### **Sporadic acute attacks:**

Acute attacks of porphyria are rare and most acute medicine physicians are therefore unlikely to have any experience in diagnosing and managing a patient.

**Objective 1:** Improve the overall management and treatment of sporadic acute attacks

### **Recurrent acute attacks:**

There are very few patients, probably less than 50, being treated for recurrent acute attacks at any one time in England. NAPS will provide the necessary long-term multidisciplinary specialist support to arrange specific treatments, manage side effects of treatment, manage symptoms (e.g. pain, nausea) and monitor for complications.

**Objective 2:** Improve the overall management and treatment of patients suffering recurrent attacks including symptom control and specific treatments.

### **Education:**

The most important modifiable risk factor associated with acute attacks is prescribed medication. Metabolism of some drugs by the liver directly or indirectly activates the haem synthesis pathway which can lead to an acute attack. The service will provide evidence based advice on what medication can be prescribed to acute porphyria patients in order to treat coexisting medical conditions safely.

**Objective 3:** Provide sustainable access to medicines information for acute porphyria patients and their healthcare providers.

## 2.2 Service description/care pathway

### Overview of NAPS

The National Acute Porphyria Service (NAPS) is provided by three National Acute Porphyria Centres (NAPCs), Cambridge, Cardiff and King's College Hospital London, with additional out-reach services in Salford and Leeds for patients from northern England. These outreach clinics are delivered jointly by NAPC staff and clinicians in each of these centres.

The core components of the service are:

- immediate 24-hour clinical advisory service for isolated acute attacks including outreach support, and outpatient follow-up for two years;
- multidisciplinary outpatient follow-up for patients with recurrent attacks;
- haem arginate provision, including homecare delivery in patients requiring regular infusions;
- drug information service (Welsh Medicines Information Centre, Cardiff) during office hours.

Each NAPC has a lead clinician, supported by a Porphyria Centre Specialist Nurse (PCSN) and named Consultant colleagues. The Cardiff NAPC provides Consultant support to the information pharmacists in the Drugs Information Service and Cambridge provides additional consultant support for the provision of haem arginate administered via homecare arrangements.

Patients presenting before the age of 16 will be seen in conjunction with a named Consultant Paediatrician, preferably a Metabolic Paediatrician, supported by paediatric nursing and dietetic input. However clinical presentation in this age group is extremely unusual and is likely to form less than 5% of caseload.

### Specific components of NAPS

#### Isolated acute attacks

##### Immediate care:

Clinicians wishing to prescribe haem arginate to treat an acute attack will contact the on-call National Acute Porphyria Centre via a 24-hour emergency telephone service which is publicised in the British National Formulary (BNF) and on the BIPNET website. Before authorising the use of haem arginate the consultant will discuss the case and establish that the diagnosis is correct i.e.:

- the symptoms and signs are consistent with an acute attack;
- for new patients evidence of increased urine porphobilinogen excretion will need to be demonstrated.

The local clinical team will be offered guidance on management of the attack, advised on how to access consensus guidelines and detailed advice on how to

administer haem arginate.

Emergency haem arginate stock is held in the pharmacy at each NAPC.

The local clinical team are offered regular outreach support from the Porphyrin Centre via telephone and, if required, on-site support during the acute admission. Severely ill patients can be transferred to one of the NAPCs for expert management through arrangement with local clinicians. This is paid for on a Payment by Results (PbR) basis and is outside the scope of the national service. Reasons for this could include:

- unremitting acute porphyria symptoms;
- progressive acute porphyria symptoms;
- lack of acute medical services locally (e.g. high dependency unit (HDU), intensive care);
- need for in-patient specialist review and management at a NAPC.

#### **Follow-up care:**

The patient is referred to one of the NAPCs after discharge for follow-up and to arrange shared care with the local hospital. The patient may receive their follow-up care in one of the two Regional Porphyrin Centres (RPC) after they have been referred to and reviewed by a NAPC.

Patients must be seen at 6 weeks, and at 6, 12 18 and 24 months after the initial attack. Follow-up can be shared with the local hospital.

The aim of the regular follow-up is:

- to ensure appropriate and adequate rehabilitation for any residual neurological disability;
- reduce the risk of further attacks through education and safe treatment of any associated medical conditions;
- ensure clinical genetics referral for family counselling and screening with information about the patient support group (British Porphyrin Association).

The NAPCs and/or Regional Porphyrin Centres will also ensure any further attacks are promptly and appropriately treated.

The PCSN will maintain a detailed record of all patients, treatments and monitoring for audit and review of outcomes.

#### **Specialist investigations:**

- 6 monthly urine porphobilinogen quantitation,
- 6 monthly plasma urea, electrolytes, creatinine and estimated glomerular filtration rate and urine albumin to creatinine ratio
- annual liver ultrasound/MRI and serum alpha-fetoprotein for patients over 50 years.

**Recurrent acute attacks:**

Patients who have had four or more acute attacks requiring haem arginate in one year are followed up on a long-term basis and a care plan is devised to prevent, or as a minimum, reduce the frequency of severe attacks.

**Follow-up care:**

Patients are seen at 3-6 monthly intervals and care is shared wherever possible with their local clinicians, or one of the Regional Porphyria Centres. The Cardiff NAPS may also review patients in the Birmingham Liver Unit where an outreach clinic is held. The activity at this clinic is held by Cardiff and University Hospitals Birmingham NHS Foundation Trust is not a Regional Porphyria Centre.

Inpatient admission to a specialist centre can be arranged when required, for example when changing treatment regimes. However this is paid for on a PbR basis and is outside the scope of the national service.

NAPCs will also ensure clinically appropriate access to and provision of associated clinical services in order to monitor and treat complications. Patients with recurrent attacks will be reviewed annually at NAPCs by pain, vascular access, gynaecology (where appropriate) and psychology services. Other support, including nephrology, rehabilitation and obstetric services, will be arranged with local providers if possible, or at NAPCs through PbR. The care plan for each patient details the appropriate follow-up and PCSN ensures that each patient receives the out-patient care specified, either at the Porphyria Centre or the local trust.

**Specialist treatment options:**

Gonadotropin-releasing hormone (GnRH) agonist therapy to suppress the menstrual cycle is offered to all females as the initial treatment approach. Although no Randomised Control Trials have been undertaken this has been shown to work in single case reports [Anderson KE et al 1984]. Follow-up for these patients specifically includes gynaecology, bone mineral densitometry.

Preventative haem arginate therapy is offered to all males and females for whom GnRH treatment is not effective. There is no randomised control trial (RCT) evidence for this treatment, although it is now widely used worldwide and recommended in several reviews [Anderson et al 2005; Elder & Hift 2001; Puy et al 2010]. Typically this involves weekly administration of a single dose of haem arginate (3 mg/kg) intravenously through a central venous catheter. This is provided either through administration at the patients local hospital, or through home care. Follow-up for these patients specifically includes venous access review and monitoring for iron overload. Iron overload is treated by venesection in the first instance and by iron chelation where this is not suitable.

### **Specialist investigations and monitoring:**

- 6 monthly urine porphobilinogen quantitation and urine albumin to creatinine ratio;
- 6 monthly plasma urea, electrolytes, creatinine, liver profile, bone profile, estimated **glomerular filtration rate** (GFR) and C-Reactive Protein (CRP);
- 6 monthly FBC;
- annual transferrin saturation, ferritin, vitamin D, vitamin B12 and folate;
- annual liver ultrasound/ Magnetic Resonance Imaging (MRI) and serum alphafetoprotein for patients over 50 years.

### **Specialist outpatient review (as appropriate):**

Annual pain review focuses on management of chronic pain and opiate dependence.

Annual venous access review for patients with central lines to ensure optimum line care and reduce the risk of blockage and infection. Monitoring includes occasional lineograms and chest X-rays to check patency and position.

Annual gynaecology review focuses on safe contraception avoiding hormonal methods, therapeutic suppression of ovulation and unwanted side effects. Monitoring includes bone densitometry every two years.

Pregnancy support includes early obstetric referral, advice about medication and close monitoring of blood pressure, renal function and foetal growth.

Annual nephrology review for patients with impaired renal function (Chronic Kidney Disease (CKD) Stage 2) and/or hypertension to ensure appropriate management and monitoring.

Annual rehabilitation review will be arranged for patients with chronic neuropathy to assess for rehabilitation requirements. Ongoing rehabilitation will be arranged through local services and is not commissioned as part of this service.

Annual psychology review is provided to support patients living with chronic illness. Ongoing psychology support will be arranged with local services and is not commissioned as part of this service.

Patients with intractable symptomatic porphyria that does not respond to medical therapy and has a significant impact on quality of life are offered referral to a liver transplant unit for assessment and review



## **Associated services**

### **Medicines information service:**

Advice on appropriate choice of safe medication is provided by information pharmacists working for the Welsh Medicines Information Centre. Clinical support to this service is provided by the Cardiff NAPC. The Cardiff NAPC and WMIC also publish an updated safe drug list every year, which is mailed out to users and is available on the website ([www.wmic.wales.nhs.uk](http://www.wmic.wales.nhs.uk)).

### **Haem arginate provision:**

Patients and healthcare professionals using and administering haem arginate are supported by NAPC staff in order to minimise use and complications. Protocols for administration are provided to users and training is available from the PCSN, including on-site training if required.

Homecare delivery is offered to all patients treated with regular haem arginate infusion and is co-ordinated on a national basis by the Cambridge NAPC.

### **Risk management:**

Care delivered by the NAPS providers must be of a nature and quality to meet the care standards, specification and agreement for the service. It is the trust's responsibility to notify the commissioner on an exceptional basis should there be any breaches of the care standards. Where there are breaches any consequences will be deemed as being the trust's responsibility.

Patients must be managed in line with the specification and care standards. Any deviation from these that has not been approved by NHS England is at the trust's risk both clinically and financially. It is the trust's responsibility to inform the commissioners of any such non-approved deviations on an exceptional basis.

Where a patient's presentation challenges the assumptions that underpin the specification, service standards and contractual arrangements it is the trust's responsibility to inform the commissioners on an exceptional basis, prior to any treatment (except for emergency treatment) so that the implications of the patient's requirements can be considered. This does not affect situations where the Individual Funding Application process applies.

Patients are managed according to consensus-based protocols. Where local services lack confidence and experience in managing acute attacks, support will be provided if necessary on site. In exceptional circumstances in-patient care is provided, but commissioned through PbR arrangements.

### **Multidisciplinary NAPS meetings:**

Staff from the NAPCs and Regional Porphyria centres will meet every six months

with representation from the patient support group to discuss the management of complex patients, to review the service operation, plan development and to facilitate research and innovation. This group also plans the dissemination strategy to improve knowledge about porphyrias through peer-reviewed publications, websites and teaching of medical professionals.

**Days/hours of operation:**

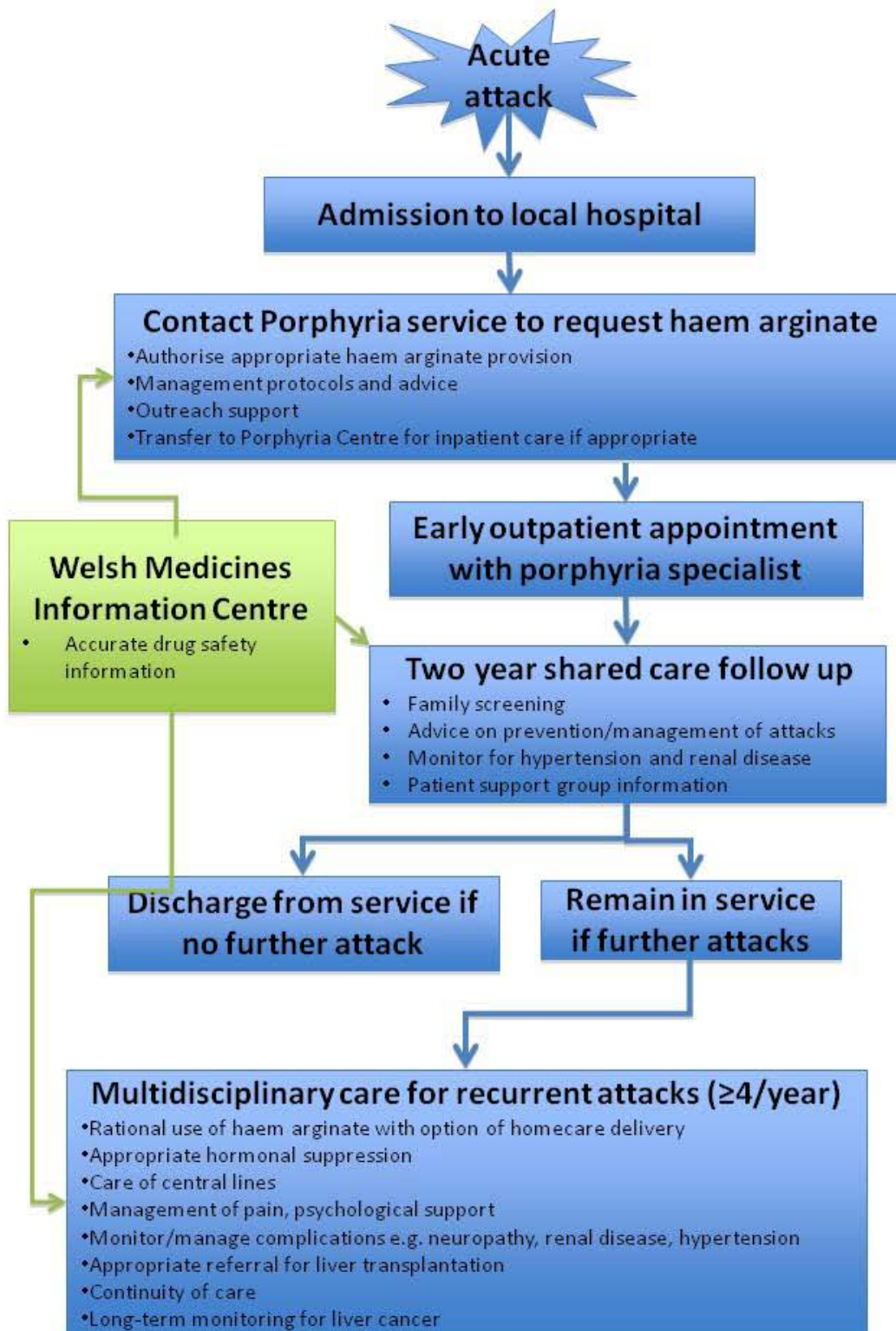
Consultant and or specialist nurse advice for patients known to a Porphyria Centre is provided every weekday.

Outpatient clinics are weekly or twice monthly depending on centre.

NAPS provide a consultant clinical advisory service for newly presenting patients (isolated attacks) at all times based on a 1:3 on-call service (each National Acute Porphyria Centre covers the service for 1 week at a time).

Adopted

## Care Pathway



**Discharge planning:****Sporadic acute attacks:**

Patients are discharged back to the local clinician providing shared care in local secondary hospital after two years without porphyria symptoms; they may continue under review in a National Porphyria Centre through PbR, but are not included in this commissioned service. If the clinical service is no longer appropriate (e.g. adolescence into adult care) the NAPC will advise on referral to an appropriate local/regional Adult Metabolic Clinic through informal networking (e.g. British Inherited Metabolic Diseases Group).

**Recurrent acute attacks:**

These patients will not be discharged unless they undergo a definitive treatment such as liver transplantation. Lifelong follow-up to screen for chronic hypertension, impaired renal function or hepatocellular carcinoma will be provided.

**2.3 Population covered**

This service covers patients registered with an English General Practitioner, resident in the European Union and eligible for treatment in NHS under reciprocal arrangements.

Patients from Scotland, Wales and Northern Ireland are not part of this commissioned service. Patients may be accepted by the Porphyria Centres but the trusts must have separate contractual arrangements in place in relation to these patients.

**2.4 Any acceptance and exclusion criteria****Target Patients:**

The service is for porphyria patients suffering isolated acute attacks requiring haem arginate treatment and patients with recurrent acute attacks.

**Accessibility/acceptability:**

The service is accessible to all patients in England either registered with an English GP or normally resident in England regardless of sex, race, or gender.

Staff within the NAPCs are required to attend the Health Board/trust's mandatory training on equality and diversity and the facilities provided offer appropriate disabled

access for patients, family and carers.

When required the porphyria services will use translators and printed information is available in multiple languages (see: [www.porphyrria-europe.org](http://www.porphyrria-europe.org)).

The providers have a duty to co-operate with the commissioner in undertaking

Equality Impact Assessments as a requirement of race, gender, sexual orientation, religion and disability equality legislation.

## **2.5 Interdependencies with other services**

The service is specifically aimed at providing clinical support for the care of patients with active acute porphyria, wherever possible through shared care within their secondary and primary care services. The NAPCs therefore communicate with local clinicians by telephone, email or letter as the situation requires. We also encourage direct contact with the service from the patients and their immediate family in order to facilitate and support their inpatient and outpatient requirements. This allows a more immediate response where treatment is sub optimal and treatment strategy needs to be revised.

We are also available for advice to patients contacting us directly or via the British Porphyria Association. The national centres have hosted patient information days, annual general meetings and/or a patient group conference (see: [www.porphyrria.org.uk](http://www.porphyrria.org.uk)).

## **3. Applicable Service Standards**

### **3.1 Applicable national standards e.g. NICE, Royal College**

The nationally designated NAPCs must be fully integrated into their trust's corporate and clinical governance arrangements.

Please see separate service standards.

## **4. Key Service Outcomes**

### **Outcomes 1:**

Improve the overall management and treatment of sporadic acute attacks:

- length of hospital stay during attack;

- mortality 12 months after attack onset;
- absolute number of new sporadic patients;
- number of clinical telephone enquiries to service;
- number of patients followed up appropriately by NAPCs following an acute attack.

### **Outcomes 2:**

Improve the overall management and treatment of patients suffering recurrent attacks including symptom control and specific treatments:

- number of patients with 4 or more attacks in the last 12 months;
- number of days per year as hospital in patient (related to porphyria);
- number of haem arginate infusions per year for each patient;
- number of patients receiving haem arginate through Homecare.

### **Outcomes 3:**

Provide sustainable access to medicines information for acute porphyria patients and their healthcare providers:

- annual review, publication and distribution of safe drug list;
- annual contribution of clinical evidence to Nordic drug safety project;
- number of drug safety enquiries to Welsh Medicines Information Centre.

These will be assessed through audit and compared with historical information.

### **Quality Outcomes:**

- mortality during or following an acute attack as a consequence of disease and/or management after referral to NAPS - <1%;
- number of patients on preventative treatment for recurrent attacks requiring hospital admission to treat an acute attack- <10%;
- number of patients on treatment for recurrent attacks referred for liver transplantation- <10%;
- percentage of patients with acute attack requiring admission to intensive care unit - <10%;
- percentage of acute porphyria patients who have genetic counselling and family studies - All patients offered appropriate genetic counselling within six months of presentation;
- percentage of patients with recurrent attacks offered appropriate prophylactic treatment - All patients offered appropriate prophylactic treatment within three months of referral;
- satisfaction of patients with recurrent and acute porphyria with services offered by Specialist Porphyria Service - All issues concerning NAPS or individual centres responded to within three months.

## 5. Location of Provider Premises

### Location of service:

- Cambridge University Hospitals NHS Foundation, Cambridge
- University Hospital of Wales, Heath Park, Cardiff
- Kings College Hospital NHS Foundation Trust, London
- Leeds General Infirmary, Great George Street, Leeds, LS1 3EX
- Hope Hospital, Eccles Old Road, Salford, M6 8HD

### Sub-contractors:

- Salford Royal NHS Foundation Trust, Stott Lane, Salford, M6 8HD
- Leeds Teaching Hospitals NHS Trust, James University Hospital, Beckett Street, Leeds, West Yorkshire, LS9 7TF

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Adopted