1. Population Needs

1.1 National/local context and evidence base

The incidence and prevalence of cases of chronic pulmonary aspergillosis (CPA) in England has not been determined. To do so would require a large cross-sectional study using aspergillus antibody testing; this has never been systematically done. It is estimated that there are 400-750 cases of CPA in England. Those at risk of infection include people with the following precursors:

- **Tuberculosis (TB)**
  Cavities of 2cm or larger after tuberculosis subsequently develop aspergillomas in 15-20% of patients\(^1\). 49 cases of aspergilloma were seen over a period of 6 years among 36,340 hospital admissions in India\(^2\). In the UK, there will be approximately 370 cases of CPA related to tuberculosis, given the incidence of pulmonary TB.

- **Atypical tuberculosis**
  Pulmonary atypical mycobacteriosis is associated with CPA, but the actual frequency of atypical infections is not known. Estimated at <100 patients.

- **Sarcoidosis**
  The prevalence of sarcoidosis in the UK is 22/100,000, of which ~60-75% involves the lung parenchyma. ~5% develop fibrocystic disease and 50% of these aspergillomas. This equates to ~200 cases nationally.

- **Recurrent pneumothorax**
  The rate of admission for pneumothorax\(^3\) is 17/100,000 for men and 6/100,000 for women, and 50 % of patients get recurrences\(^4\). This estimate suggests a population at risk of aspergillosis of ~5,870, of whom possibly 5% develop CPA (estimate), or ~300 patients.
• **Other patient groups**
  Occasional patients with other chronic pulmonary disease, allergic bronchopulmonary aspergillosis, resected lung cancer and other rare conditions such as histoplasmosis develop CPA, all estimated to be <100 cases annually.

The clinical pathways for the nationally commissioned service have been developed in light of the best available evidence on drug use in CPA. These pathways will be subject to review as new clinical evidence and associated economic analysis is produced.

2. **Scope**

2.1 **Aims and objectives of service**

CPA is a chronic, incurable progressive infection of the lung with the fungus *aspergillus fumigatus* that follows a lung insult (typically sarcoidosis, atypical TB or recurrent pneumothoraces) and occurs in those with one or more innate genetic defects.

The service is an assessment and long-term clinical management service for CPA as defined in this specification. It will diagnose patients referred by appropriate hospital consultants with probable chronic aspergillus infection and classify the specific nature of any detected aspergillus infection. Those patients confirmed to have CPA within the parameters of this specification will be offered clinically appropriate treatment options that include:

- anti-fungal drug therapy (itraconazole and voriconazole)
- embolisation
- surgery
- physiotherapy advice.

The understanding of aspergillus infection is poorly developed within the NHS. This service aims to provide patients with expert assessment and management of their condition to maximise their quality of life throughout the progression of the disease.

Where supportive and/or end of life care is deemed necessary, or patients are not obtaining any benefit from the commissioned treatment pathways included in the contract, then the patient must be discharged from the nationally commissioned service to their referring clinician with appropriate advice.

The **overall strategic objectives** for the service are to:

- provide an exemplary diagnostic and management service for all patients with CPA in England, Scotland and eligible European Union residents
- develop and evolve the evidence base for the assessment and treatment of CPA to improve efficacy and efficiency within the specified service
• develop the skills and experience of healthcare professionals in the management of patients with CPA as necessary to meet the demands of the specified service
• provide high quality, patient-guided, online, written and verbal information for patients with CPA and their families
• to act as a resource for healthcare professionals outside the nationally designated service with regard to patients with possible and confirmed CPA
• to maximise the quality of life of patients in relation to their CPA and to demonstrate this through the use of agreed quality of life tools applied during the first year of treatment
• to monitor the IgG ImmunoCAP® levels at appropriate intervals for all patients under the care of the service.

Specifically the purpose of the service is to:
• provide outpatient care for patients with CPA, including diagnosis, evaluation of clinical and disease status, treatment, appropriate patient information and follow up
• provide short-term inpatient care for patients with CPA, including diagnosis, evaluation of clinical and disease status, medical, surgical and interventional radiology treatment, acute exacerbation of symptoms requiring acute medical care, training in intravenous therapy and line management, appropriate patient information and follow up. Longer-term supportive and/or palliative inpatient care is beyond the scope of this service
• prescribe antifungal therapy (itraconazole and voriconazole) according to their needs in the context of the clinical pathways contained in this specification
• support provision of appropriate supportive care and or end of life care, in the location and manner best suited to each patient through appropriate arrangements with other healthcare providers and commissioners
• provide a comprehensive laboratory diagnostic and monitoring service for patients with CPA, including those receiving antifungal therapy, including evaluation of novel tests and technologies as agreed in advance with NHS England
• establish effective shared care relationships with referring units as they will retain responsibility for management of the patient’s other lung pathologies. In addition, owing to the progressive nature of the disease, establishing this relationship early will facilitate a seamless transfer of care at the point when the patient requires discharge back to their referring hospital
• undertake a program of clinically-focussed audit to be agreed with NHS England
• continuously evaluate key diagnostic tools, interventions and outcome measures for patients with CPA
• understand and respond to patients' and carers' information needs in appropriate ways including group meetings, online information and support groups, provision of written information and direct verbal explanation.
2.2 Service description/care pathway

The service provides outpatient and inpatient care for eligible patients following referral from a specialist respiratory consultant. Eligible patients should be offered assessment and treatment as soon as is possible within the context of the resources and funding of the service. It is assumed that, as a minimum standard the 18-week guidelines will apply.

Referral

All CPA referrals will be scrutinised to ensure that they are compatible with the specified service before an appointment is offered. If a referral appears to be outside the scope of the national service as specified herein, the service may seek clarification from the referrer.

All patients offered an appointment must be sent appropriate information on the service to establish reasonable expectations and the agreed quality of life questionnaire. The service must take reasonable steps to ensure that all questionnaires are completed prior to the first appointment.

Assessment

The minimum that initial assessment of eligible patients must cover is:

- full clinical history
- lung function studies
- aspergillus testing
- appropriate radiological studies (primarily X-ray and magnetic resonance imaging (MRI))
- allocation to the appropriate band (see below) as per the definitions contained in this specification.

Band 1

- ambulant and independent
- no evidence of antifungal resistance
- treatment with itraconazole capsules (or liquid as an alternative if capsules are clinically unsuitable) or no treatment.

Band 2

- significant impairment of respiratory function, sufficient to impair activities of daily living, but ambulant and/or
- failed or developed toxicity to itraconazole capsules and
- no evidence of azole antifungal resistance and/or
- evidence of mycobacterial disease.
Band 3

- antifungal azole resistance documented and/or
- long term nebulised or IV antibiotic treatment required (bronchiectasis, *Pseudomonas* colonisation) and/or
- wheelchair bound due to respiratory distress? and/or
- HIV infected and/or
- severe hepatic disease.

Treatment

Treatment of patients must be in line with the agreed clinical pathways. Any deviation from this which has not had prior approval via NHS England’s individual cases process will be at the trust’s risk both clinically and financially.

Inpatient Care

Inpatient care will be utilised when clinically appropriate to do so to manage CPA, including emergency admissions for acute exacerbations. This includes admissions for surgical resection, other agreed operative procedures and embolisation when clinically indicated. Typically, inpatient care within this specification will be short-term to deliver diagnostic and treatment modalities that are included in this specification and the clinical pathways. Additionally, patients must still be on azole therapy to be admitted within the scope of the national CPA service.

Longer-term supportive and end of life care for patients who have not responded to therapy within the clinical pathways is outside the scope of this service.

Surgery and Embolisation

Agreed surgical procedures and embolisation will be offered to CPA patients to address aspects of their CPA disease as is clinically indicated. Patients must be given sufficient information on the procedure and any alternative forms of treatment to allow them to make an informed decision and give appropriate consent.

Patients who have been discharged from the service as they are no longer responding positively to the commissioned treatments may be re-referred to the national CPA service for embolisation if their local hospital does not have the required competency to carry out the procedure.
On-going Management

Patients must receive appropriate on-going care and management as required by their presentation of CPA. This must include clinically sufficient follow-up, lung function testing, aspergillus testing, radiology and other tests. Whenever clinically appropriate and practical, testing and radiology should be done locally to maximise convenience for the patient.

Patients must be able to contact the service to discuss any changes within their condition in between formal appointments. The service must have the flexibility to respond appropriately to patients including rapid access outpatient appointments and emergency admissions.

On-going management must consider:

- evaluation of current sign and symptoms;
- evaluation of the effectiveness of any treatment;
- monitoring and management of any drug reactions/side effects;
- the need to change or withdraw treatment if there is no evidence of effectiveness or if the risk of reactions/side-effects outweighs the benefits of treatment. Any changes in treatment must be within the context of the agreed clinical pathways. Any withdrawal of treatment must be accompanied by facilitation of appropriate supportive care with the patient’s local care providers;
- liaison with clinicians who are managing the patient’s other lung pathology(ies) and/or other relevant pathologies;
- consideration of the patients banding must be a key component of on-going management.

Patient and public engagement

The provider will work with NHS England to ensure sufficient consideration is given to communications:

- the service must provide appropriate information for patients consistent with the specified scope of the service;
- where applicable self-management information should be provided in appropriate formats;
- the service must maintain appropriate structures for patients to evaluate and give feedback on the service. The service must be able to demonstrate to commissioners and patients that patient feedback has influenced service improvement;
- patient information must include contact details for the trust’s Patient Advice and Liaison Service (PALS).

Governance

The service sits within the trust governance structures as monitored by the host Clinical Commissioning Group (CCG) and regional arm of NHS England. Any
internal governance issues with the service subject to the trust’s internal processes must be shared with NHS England. Any outcomes and change as a result of such processes must be shared with NHS England.

The agreed service standards included in this agreement provide a set of minimum standards that the service must achieve. These standards should be read in conjunction with this specification and the rest of the agreement. If the service standards appear to be in conflict with the agreement then the terms and conditions of the agreement should be read as superseding the service standards.

**Risk management**

Care delivered by the CPA service 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 clinical pathways (below). Any deviation from these pathways which has not been approved via NHS England’s Individual Funding Panel, 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 clinical pathways, service standards and contractual arrangements it is the trust’s responsibility to inform the commissioners on an exceptional basis, prior to 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.

**Days/hours of operation**

The service will operate to meet the needs of the patients, including 24 hour care for in-patients, email access at all times for professional staff, patients and relatives and telephone access in working hours through the centre administrator and mobile phones of the specialist nurses.

**Discharge planning**

The national CPA service must establish effective shared care relationships with referring providers from the outset as the progressive nature of the disease and the current treatments commissioned and available dictate that the patient will be transferred back to their referring hospital for on-going supportive care at some point in their journey. Patients who have ceased to benefit positively from the commissioned treatments and any treatment approved by NHS England Individual Cases Panel (according to criteria set by the panel) should be discharged back to their local/referring provider for on-going supportive care. The service must consider
where in the commissioned pathways a patient falls at each clinical contact with the service.

The specialist nurses & medical team must regularly review in-patients to evaluate and monitor patient’s status. Criteria for discharge include:

- medical condition stabilised;
- oxygen requirements assessed and catered for at home;
- antifungal medication optimised in terms of therapeutic monitoring and any toxicities addressed;
- patient and carer(s) fully informed about expectations at home;
- any physical aids and home support packages arranged;
- treatment modalities as described in the clinical pathways have been exhausted;
- if terminally ill – hospital/community care of the dying pathway in place.

To support discharge the service must do or consider the following:

- specialist nurses’ contact details are given to the different health care professionals / members of the multi-disciplinary team (MDT);
- referrals to support services from ward staff if in-patients and via GP/district nurses;
- specialist nurses are involved in MDT meetings/case conferences;
- liaison with community teams as required from ward staff and National Amyloidosis Centre (NAC) staff;
- transport for discharge – own transport, hospital transport, paramedic crew;
- inter-hospital transfer;
- port-a-cath education, self-administration, patient/carer assessment;
- oxygen service referral as needed;
- liaison with other commissioners as required to ensure continuity of care beyond the scope of this specification.

2.3 Population covered

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

Patients from Wales and Northern Ireland are not part of this commissioned service and the trust must have separate arrangements are in place.

2.4 Any acceptance and exclusion criteria

Referral criteria, sources and routes

Patients will only be referred by specialist respiratory consultants. All referrals will be reviewed by an appropriate senior doctor with suitable expertise in the diagnosis and management of CPA. Only those referrals which indicate the likelihood of fitting the
CPA criteria below will be accepted into the service. The service may seek additional information before accepting or rejecting a referral.

Out-patients will be offered an appointment, sent information on on-going research protocols, and a request for imaging to their referring hospital.

In-patient transfers will be seen by an appropriate senior doctor with suitable expertise in the diagnosis and management of CPA within 24 hours of transfer.

Patients will be accepted onto the service if they fulfil the criteria for chronic pulmonary aspergillosis (CPA) i.e.

- two or more pulmonary cavities on chest imaging, OR one single, unresectable cavity, with or without a fungal ball (aspergilloma)
- symptoms (usually weight loss, fatigue, cough, haemoptysis and breathlessness) for at least 3 months
- serology or cultures implicating aspergillus spp.

Exclusion criteria

Patients with single resectable cavities (usually with an aspergilloma) will not be accepted into the service.

Patients who have had a mass/cavity/potential tumour resected which is shown on pathology to be an aspergillus lung infection or aspergilloma will not be accepted if no antifungal therapy is required, and there is no evidence of residual disease.

Post-lung transplant patients will be managed by the transplant service, not the NAC service, if they have chronic pulmonary aspergillosis.

Where patients have exhausted the possibilities for active treatment under the clinical pathways, their supportive care is not included in this specification.

Response time & detail and prioritisation

The objective will be that all patients are seen within a maximum of six weeks of referral. In-patient transfers will be arranged as soon as transport is possible and a bed is available, typically in less than seven days.

Coverage

The provider has 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.

All patients who might or do have chronic pulmonary aspergillosis are eligible for the service and will be offered an out-patient appointment, or in-patient transfer, as appropriate.
2.5 Interdependencies with other services

The service is the only nationally designated provider for CPA and it must be equally available to all regions in the NHS as required by patient need for the service. The service accepts referrals from specialist respiratory consultants only but it must be available to other healthcare professionals to provide advice on the condition and access to the service.

The service is represented on the Health Protection Agency (HPA)-supported UK Clinical Mycology Network [see http://www.hpa.org.uk/HPA/Topics/InfectiousDiseases/InfectionsAZ/1201094590966/] by Professor Malcolm Richardson, the Director of the Regional Mycology Laboratory, Manchester.

3. Applicable Service Standards

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

The nationally designated CPA providers must be fully integrated into their trust’s corporate and clinical governance arrangements.

The service will provide agreed performance monitoring data on a monthly basis. Where any elements of this deviate from the agreed plan the service will provide a brief explanation accompanying the submission of the report. The commissioner may wish to follow this up and request further information to inform any necessary actions that will be agreed between the service and commissioners in the context of the terms and conditions of the Agreement.

4. Key Service Outcomes

Outcomes:
- quality of life at referral, six and twelve months;
- Medical Research Council (MRC) breathlessness score at referral, six and twelve months;
- IgG ImmunoCAP at assessment six and twelve months.

5. Location of Provider Premises

The service will be provided by
- University Hospital of South Manchester NHS Foundation Trust (UHSM) at the Wythenshawe Hospital for inpatient and outpatient treatment, and assessments.
Direct community outreach will be facilitated by the specialist nurses for the service by telephone, with the patient, their carers, GPs, local community services, local referring consultant and hospital.

Patients will attend at UHSM; it is not intended that professional staff visit patients in their homes or local hospitals. See www.nationalaspergillosiscentre.org.uk

Specialised laboratory services for Mycology will be provided by the Mycology Reference Centre, Manchester, also based at Wythenshawe Hospital. See www.mycologymanchester.org

References