

Cystic fibrosis: diagnosis and management

NICE guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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This guideline replaces ESUOM37.

This guideline is the basis of QS168.

Overview

This guideline covers diagnosing and managing cystic fibrosis. It specifies how to monitor the condition and manage the symptoms to improve quality of life. There are also detailed recommendations on treating the most common infections in people with cystic fibrosis.

Who is it for

- Healthcare professionals
- Social care practitioners working with people with cystic fibrosis
- People with cystic fibrosis and their families and carers

Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in [making decisions about your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

This guideline incorporates recommendations from 2 NICE technology appraisals:

- [Mannitol dry powder for inhalation for treating cystic fibrosis](#) (NICE technology appraisal guidance 266)
- [Colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis](#) (NICE technology appraisal guidance 276).

These technology appraisals still apply, and have not been replaced by the guideline.

1.1 Diagnosis of cystic fibrosis

1.1.1 Be aware that cystic fibrosis can be diagnosed based on:

- positive test results in people with no symptoms, for example infant screening (blood spot immunoreactive trypsin test) followed by sweat and gene tests for confirmation **or**
- clinical manifestations, supported by sweat or gene test results for confirmation **or**
- clinical manifestations alone, in the rare case of people with symptoms who have normal sweat or gene test results.

1.1.2 Assess for cystic fibrosis and, when clinically appropriate, perform a sweat test (for children and young people) or a cystic fibrosis gene test (for adults) in people with any of the following:

- family history
- congenital intestinal atresia
- meconium ileus
- symptoms and signs that suggest distal intestinal obstruction syndrome
- faltering growth (in infants and young children)
- undernutrition
- recurrent and chronic pulmonary disease, such as:
 - recurrent lower respiratory tract infections
 - clinical or radiological evidence of lung disease (in particular bronchiectasis)
 - persistent chest X-ray changes
 - chronic wet or productive cough
- chronic sinus disease
- obstructive azoospermia (in young people and adults)
- acute or chronic pancreatitis
- malabsorption
- rectal prolapse (in children)
- pseudo-Bartter syndrome.

1.1.3 Refer people with suspected cystic fibrosis to a specialist cystic fibrosis centre if:

- they have a positive or equivocal sweat test result
- their assessment suggests they have cystic fibrosis but their test results are

normal

- gene testing reveals 1 or more cystic fibrosis mutations.

1.2 Information and support

- 1.2.1 Provide people who are newly diagnosed with cystic fibrosis and their family members or carers (as appropriate) with opportunities to discuss their concerns.
- 1.2.2 Information and support should be provided by healthcare professionals with expertise in cystic fibrosis.
- 1.2.3 Provide people with suspected or diagnosed cystic fibrosis and their family members or carers (as appropriate) with relevant information that they can understand, and opportunities for discussion on topics such as:
- their diagnosis
 - monitoring of their condition
 - management choices for their condition
 - possible or existing complications or comorbidities
 - implications for living independently.
- 1.2.4 Provide people with cystic fibrosis and their family members or carers (as appropriate) with information about their care pathway.
- 1.2.5 Give information to people with cystic fibrosis and to family members or carers in ways that are individually appropriate. Avoid jargon and use formats that they prefer, for example:
- face-to-face discussions
 - copies of correspondence
 - written information (such as leaflets)

- any digital media and reliable internet sources that are available.
- 1.2.6 When appropriate, provide people with cystic fibrosis and their family members or carers with opportunities for discussion with relevant expert professionals on:
- available resources and support, such as local support and advocacy services
 - managing the risks of cross-infection
 - implications of the condition for school and education
 - career planning
 - transition to adult care
 - foreign travel
 - fertility and contraception
 - pregnancy and parenting
 - organ transplantation
 - end of life care.
- 1.2.7 Provide people with cystic fibrosis with information about how to contact other people with cystic fibrosis without risking cross-infection (see [preventing cross-infection](#)), for example by directing them to online support groups.
- 1.2.8 For more information on communication, providing information and shared decision making in adult NHS services, see [NICE guidelines on patient experience in adult NHS services](#) and [shared decision making](#).
- 1.2.9 Be aware that people with cystic fibrosis and their family members or carers will need emotional support and some may need specialist psychological support (see [psychological assessment](#)), in particular:
- at diagnosis
 - at times of transition (for example, when starting or changing school, moving

from education to work, or changing to living independently for the first time)

- in relation to fertility, including family planning, pregnancy and infertility
- to cope with complications of cystic fibrosis
- when waiting for or having organ transplantation
- when approaching the end of life.

1.3 Service delivery

Service configuration

1.3.1 Care for people with cystic fibrosis should be provided by a specialist cystic fibrosis multidisciplinary team based at a specialist cystic fibrosis centre (see [multidisciplinary team](#)).

1.3.2 Specialist cystic fibrosis centres should:

- plan patient care (including outpatient and inpatient care), taking into account the risk of cross-infection (see [preventing cross-infection](#))
- maintain local and national registers of patients that include information about their clinical condition, treatment and outcomes
- audit practice and outcomes.

1.3.3 When a [shared-care model](#) is used for children and [young people](#), it should include:

- formal arrangements between the local paediatric team at the shared-care centre and the multidisciplinary team at the specialist cystic fibrosis centre
- direct involvement of specialist cystic fibrosis multidisciplinary team members
- an annual assessment and at least one other review per year by the specialist

cystic fibrosis multidisciplinary team, in addition to reviews by the local paediatric team (see [annual and routine reviews](#)).

- 1.3.4 If available and when clinically appropriate, [outreach care](#) for adults with cystic fibrosis may be provided by the specialist cystic fibrosis multidisciplinary team at a local hospital.
- 1.3.5 The specialist cystic fibrosis centre should have a point of contact available at all times (day or night) for urgent enquiries from people with cystic fibrosis and their family members or carers (as appropriate).
- 1.3.6 Consider [telemedicine](#) or home visits for routine monitoring when they are more appropriate than outpatient visits and if the person with cystic fibrosis prefers it.
- 1.3.7 Make arrangements (including providing equipment and expert support) for people to have intravenous antibiotic therapy at home, when this is appropriate.

Multidisciplinary team

- 1.3.8 The specialist cystic fibrosis multidisciplinary team should include at least one of each (depending on the size of the clinic) of the following professionals, who should have specialist expertise in the condition:
- specialist paediatricians or adult physicians
 - specialist nurses
 - specialist physiotherapists
 - specialist dietitians
 - specialist pharmacists
 - specialist clinical psychologists.
- 1.3.9 The specialist cystic fibrosis multidisciplinary team should be led by a specialist paediatrician or adult physician.

- 1.3.10 The specialist cystic fibrosis multidisciplinary team should either include or have access to social workers.
- 1.3.11 Social workers should provide advice and support to people with cystic fibrosis and their family members or carers (as appropriate), for example on:
- help with adjusting to long-term treatment (such as taking regular medicines)
 - education
 - employment
 - government benefits
 - respite care.
- 1.3.12 Specialist nurses (working with specialist paediatricians or physicians) should coordinate care and facilitate communication between other members of the cystic fibrosis team, and act as advocates for people with cystic fibrosis and their family members or carers (as appropriate). Key clinical roles could include:
- support during and after diagnosis and when starting treatment
 - triage
 - advanced clinical assessment
 - coordinating home intravenous antibiotic services, including intravenous access.
- 1.3.13 Specialist physiotherapists should assess and advise people with cystic fibrosis at clinic, at inpatient admissions, during pulmonary exacerbations and at their annual review. Assessment and advice could cover airway clearance, nebuliser use, musculoskeletal disorders, exercise, physical activity and urinary incontinence.
- 1.3.14 Specialist dietitians should assess and advise people with cystic fibrosis about all aspects of nutrition at outpatient clinic visits, during inpatient admissions and at their annual review (see nutritional interventions).

- 1.3.15 Specialist pharmacists should advise people with cystic fibrosis on medicines optimisation at outpatient clinic visits, during inpatient admissions, on discharge from hospital and at annual review. They should advise healthcare professionals on all aspects of medicines use and prescribing, and support GPs, community pharmacists and homecare providers to ensure that people with cystic fibrosis get the medicines they need without interruption.
- 1.3.16 Specialist clinical psychologists should assess and advise people with cystic fibrosis and their family members or carers (as appropriate) at outpatient clinic visits and (if needed) at other outpatient appointments, during inpatient admissions, and at their annual review (see [psychological assessment](#)).
- 1.3.17 The specialist cystic fibrosis multidisciplinary team should either include or have access to specialist expertise relevant to cystic fibrosis in the following areas:
- microbiology
 - pulmonary physiology
 - diabetes
 - gastroenterology
 - hepatology
 - rheumatology
 - psychiatry
 - interventional radiology
 - surgery (gastrointestinal, thoracic, and ear, nose and throat)
 - obstetrics
 - palliative care.
- 1.3.18 The specialist cystic fibrosis multidisciplinary team should work with GPs, and provide timely information so that GPs can support people with cystic fibrosis by:
- prescribing cystic fibrosis medicines:

- in batches of at least 1 month at a time for routine medicines
 - for longer periods if advised by the specialist team
 - following guidance on arrangements for prescriptions of unlicensed medicines
- providing routine annual immunisation, including any alterations for people with cystic fibrosis and flu vaccinations for family members and carers
 - managing health problems not related to cystic fibrosis
 - certification of illnesses
 - working in partnership with cystic fibrosis homecare teams, particularly for end of life care
 - providing care for the person's family members or carers.

Transition to adult services

- 1.3.19 Begin discussing the transition process to adult services with young people with cystic fibrosis when they are 12 years old, and with their family members or carers (as appropriate).
- 1.3.20 All cystic fibrosis services should have a coordinated and documented pathway for transition from children's to adults' services that includes plans for managing all cystic-fibrosis-related aspects of care.
- 1.3.21 Ask people with cystic fibrosis and their family members or carers (as appropriate) for feedback on the quality of the transition service, taking account of the section on [planning and developing transition services in the NICE guideline on transition for young people using health or social care services](#).
- 1.3.22 For more guidance on managing transition from children's to adults' services, see [the NICE guideline on transition for young people using health or social care services](#). In particular, see the sections on:

- [transition planning](#), for guidance on when transition should happen
- [named workers](#)
- [overarching principles](#), for guidance on joint responsibility and working together with other organisations.

1.4 Complications of cystic fibrosis

1.4.1 Be aware that people with cystic fibrosis are at risk of the following common complications:

- being underweight
- meconium ileus (affects 1 in 7 newborn babies)
- fat-soluble vitamin deficiencies (including vitamins A, D, E and K)
- distal intestinal obstruction syndrome
- muscle pains and arthralgia
- male infertility caused by obstructive azoospermia (almost all males with cystic fibrosis are infertile)
- reduced female fertility
- upper airway complications, including nasal polyps and sinusitis (prevalence increases with age)
- chronic liver disease (the prevalence increases with age until early adulthood)
- urinary stress incontinence
- cystic-fibrosis-related diabetes (uncommon in children under 10 years, but the prevalence increases with age and it affects up to 1 in 2 adults)
- reduced bone mineral density (including osteoporosis).

1.4.2 Be aware that people with cystic fibrosis are at risk of the following less common complications:

- cystic-fibrosis-related arthritis
- delayed puberty (associated with severe cystic fibrosis)
- renal calculi (incidence increases with age and 1 in 20 adults are affected).

1.5 Annual and routine reviews

1.5.1 Be aware that:

- the aim of cystic fibrosis care is to prevent or limit symptoms and complications of the condition
- routine monitoring and annual assessments are crucial in providing effective care.

1.5.2 Offer people with cystic fibrosis a comprehensive annual review that includes the following:

- a pulmonary assessment (see [pulmonary monitoring](#))
- an assessment of nutrition and intestinal absorption (see [nutritional interventions and exocrine pancreatic insufficiency](#))
- an assessment for liver disease (see [liver disease](#))
- testing for cystic-fibrosis-related diabetes, from 10 years of age (see [cystic-fibrosis-related diabetes](#))
- an assessment for other potential or existing cystic fibrosis complications (see [complications of cystic fibrosis](#))
- a psychological assessment (see [psychological assessment](#))
- assessments by a specialist nurse, physiotherapist, pharmacist and social worker (see [service delivery](#))

- a review of their exercise programme (see [exercise](#)).

1.5.3 Provide regular routine reviews for people with cystic fibrosis, and do these more frequently immediately after diagnosis and in early life. For example:

- weekly in their first month of life
- every 4 weeks when they are between 1 and 12 months old
- every 6 to 8 weeks when they are between 1 and 5 years old
- every 8 to 12 weeks when they are over 5 years old
- every 3 to 6 months as adults.

1.6 Pulmonary monitoring, assessment and management

Pulmonary monitoring

1.6.1 For people with cystic fibrosis who have clinical evidence of lung disease, base the frequency of routine reviews on their clinical condition but review children and [young people](#) at least every 8 weeks and adults at least every 3 months. If appropriate, think about using the review schedules in recommendation 1.5.3.

1.6.2 Include the following at each routine review, in relation to pulmonary assessment, for people with cystic fibrosis:

- a clinical assessment, including a review of clinical history and medicines adherence, and a physical examination with measurement of weight and length or height
- measurement of oxygen saturation
- taking respiratory secretion samples for microbiological investigations, using sputum samples if possible, or a cough swab or nasal pharyngeal aspirate (NPA)

- lung function testing with spirometry (including forced expiratory volume in 1 second [FEV₁], forced vital capacity [FVC], and forced expiratory flow [FEF] 25–75%) in adults, and in children and young people who can do this.
- 1.6.3 If spirometry is normal at a routine review, consider measuring lung clearance index.
- 1.6.4 Include the following at each annual review in relation to pulmonary assessment for people with cystic fibrosis:
- a clinical assessment, including a review of the clinical history and medicines adherence, and a physical examination, with measurement of weight and length or height
 - a physiotherapy assessment
 - measurement of oxygen saturation
 - a chest X-ray
 - blood tests, including white cell count, aspergillus serology and serum IgE
 - taking respiratory secretion samples for microbiological investigations (including non-tuberculous mycobacteria)
 - lung function testing (for example with spirometry, including FEV₁, FVC, and FEF 25–75%) in adults, and in children and young people who can do this.
- 1.6.5 Consider measuring lung clearance index at each annual review if spirometry is normal.
- 1.6.6 For people with cystic fibrosis with lung disease who have symptoms that are concerning them or their family members or carers (as appropriate), consider which of the following may be useful:
- review of clinical history
 - physical examination, including measurement of weight and length or height
 - measurement of oxygen saturation

- taking respiratory secretion samples for microbiological investigations, using sputum samples if possible, or a cough swab or NPA if not
- for adults, blood tests to measure white cell count and inflammatory markers such as C-reactive protein
- lung function testing, for example with spirometry (including FEV₁, FVC, and FEF 25–75%) in adults, and in children and young people who can do this
- lung clearance index for people with normal spirometry results.

Depending on the assessments that are needed, decide whether to provide a remote [telemedicine](#) or face-to-face assessment.

1.6.7 Think about doing a low-dose chest CT scan for children with cystic fibrosis who have not had a chest CT scan before, to detect features that other tests (such as a plain chest X-ray) would miss (for example early bronchiectasis).

1.6.8 Think about doing a chest X-ray for people with cystic fibrosis during or after treatment for an exacerbation of lung disease (taking account of severity), if:

- the exacerbation does not respond to treatment **or**
- a chest X-ray before treatment showed new radiological abnormalities.

1.6.9 Monitor the treatment response during and after an exacerbation of lung disease by assessing whether the symptoms and signs have resolved, and as appropriate:

- take respiratory secretion samples for microbiological investigations, using sputum samples if possible, or a cough swab or NPA if not
- test lung function, for example with spirometry (including FEV₁, FVC and FEF 25–75%) in adults, and in children and young people who can do this
- measure oxygen saturation.

Be aware that some pulse oximeters can underestimate or overestimate oxygen saturation levels, especially if the saturation level is borderline.

Overestimation has been reported in people with dark skin. See also the [NHS](#)

England Patient Safety Alert on the risk of harm from inappropriate placement of pulse oximeter probes.

- 1.6.10 Think about using broncho-alveolar lavage to obtain airway samples for microbiological investigation in people with cystic fibrosis if:
- they have lung disease that has not responded adequately to treatment **and**
 - the cause of the disease cannot be found with non-invasive upper airway respiratory secretion sampling (including sputum induction if appropriate).

Airway clearance techniques

- 1.6.11 Discuss the use of airway clearance techniques with people with cystic fibrosis who do not have clinical evidence of lung disease and their parents or carers (as appropriate). Provide them with training in airway clearance techniques and explain when to use them.
- 1.6.12 Offer training in airway clearance techniques to people with cystic fibrosis who have clinical evidence of lung disease and their parents or carers (as appropriate).
- 1.6.13 When choosing an airway clearance technique for people with cystic fibrosis:
- assess their ability to clear mucus from their lungs, and offer an individualised plan to optimise this
 - take account of their preferences and (if appropriate) those of their parents and carers
 - take account of any factors that may influence adherence.
- 1.6.14 Regularly assess the effectiveness of airway clearance techniques, and modify the technique or use a different one if needed.
- 1.6.15 Do not offer high-frequency chest wall oscillation as an airway clearance technique for people with cystic fibrosis except in exceptional clinical

circumstances. The specialist cystic fibrosis team will decide whether these circumstances apply, and their decision would then be subject to the [NHS England policy on Individual Funding Requests](#). Be aware that the evidence shows high-frequency chest wall oscillation is not as effective as other airway clearance techniques.

- 1.6.16 Consider using non-invasive ventilation in people with cystic fibrosis who have moderate or severe lung disease and cannot clear their lungs using standard airway clearance techniques.

Mucoactive agents

- 1.6.17 Offer a mucoactive agent to people with cystic fibrosis who have clinical evidence of lung disease.
- 1.6.18 Offer rhDNase (dornase alfa; recombinant human deoxyribonuclease) as the first choice of mucoactive agent. October 2017: note that this was an off-label use for children under 5. See [NICE's information on prescribing medicines](#).
- 1.6.19 If clinical evaluation or lung function testing indicates an inadequate response to rhDNase, consider both rhDNase and hypertonic sodium chloride or hypertonic sodium chloride alone. October 2017: note that this was an off-label use for children under 5. See [NICE's information on prescribing medicines](#).
- 1.6.20 Consider mannitol dry powder for inhalation for children and young people who cannot use rhDNase and hypertonic sodium chloride because of ineligibility, intolerance or inadequate response. October 2017: note that this was an off-label use of mannitol dry powder for children. See [NICE's information on prescribing medicines](#).
- 1.6.21 Mannitol dry powder for inhalation is recommended as an option for treating cystic fibrosis in adults:
- who cannot use rhDNase because of ineligibility, intolerance or inadequate response to rhDNase **and**
 - whose lung function is rapidly declining (forced expiratory volume in 1 second

[FEV₁] decline greater than 2% annually) **and**

- for whom other osmotic agents are not considered appropriate.

[This recommendation is from [the NICE technology appraisal guidance on mannitol dry powder for inhalation for treating cystic fibrosis](#)]

- 1.6.22 People currently receiving mannitol whose cystic fibrosis does not meet the criteria in 1.6.21 should be able to continue treatment until they and their clinician consider it appropriate to stop.

[This recommendation is [the NICE technology appraisal guidance on mannitol dry powder for inhalation for treating cystic fibrosis](#)]

- 1.6.23 For recommendations on using lumacaftor–ivacaftor, see [the NICE technology appraisal guidance on lumacaftor–ivacaftor for treating cystic fibrosis homozygous for the F508del mutation](#).

Pulmonary infection

Staphylococcus aureus

- 1.6.24 Offer flucloxacillin as antibiotic prophylaxis against respiratory Staphylococcus aureus infection for children with cystic fibrosis from the point of diagnosis up to age 3, and consider continuing up to 6 years of age. Before starting flucloxacillin, discuss the uncertainties and possible adverse effects with their parents or carers (as appropriate). For children who are allergic to penicillins, consider an alternative oral anti-Staphylococcus aureus agent.

October 2017: note that this was an off-label use. See [NICE's information on prescribing medicines](#).

- 1.6.25 For children who are taking antibiotic prophylaxis and have a respiratory sample culture that is positive for Staphylococcus aureus:
- review prophylaxis adherence and help the child's parents or carers (as

appropriate) with any difficulties they are having

- start treatment-dose anti-Staphylococcus aureus antibiotics
- restart prophylaxis after treatment, even if treatment has not been successful.

1.6.26 For people who are not taking prophylaxis and have a new Staphylococcus aureus infection (that is, previous respiratory sample cultures did not show Staphylococcus aureus infection):

- if they are clinically well, consider an oral anti-Staphylococcus aureus agent
- if they are clinically unwell and have pulmonary disease, consider oral or intravenous (depending on infection severity) broad-spectrum antibiotics that include an anti-Staphylococcus aureus agent.

1.6.27 Consider a long-term antibiotic to suppress chronic methicillin-sensitive Staphylococcus aureus (MSSA) respiratory infection in people whose pulmonary disease is stable.

1.6.28 For people with chronic MSSA respiratory infection who become clinically unwell with pulmonary disease, consider oral or intravenous broad-spectrum antibiotics (depending on infection severity) that include an anti-Staphylococcus aureus agent.

1.6.29 For people with new evidence of methicillin-resistant Staphylococcus aureus (MRSA) respiratory infection (with or without pulmonary exacerbation), seek specialist microbiological advice on treatment.

1.6.30 Do not routinely use antibiotics to suppress chronic MRSA in people with stable pulmonary disease.

1.6.31 If a person with cystic fibrosis and chronic MRSA respiratory infection becomes unwell with a pulmonary exacerbation or shows a decline in pulmonary function, seek specialist microbiological advice.

1.6.32 For guidance on preventing the spread of infection, refer to the NICE guideline on

healthcare-associated infections.

Pseudomonas aeruginosa

- 1.6.33 If a person with cystic fibrosis develops a new *Pseudomonas aeruginosa* infection (that is, recent respiratory secretion sample cultures showed no infection):
- if they are clinically well:
 - commence eradication therapy with a course of oral or intravenous antibiotics, together with an inhaled antibiotic
 - follow this with an extended course of oral and inhaled antibiotics
 - if they are clinically unwell:
 - commence eradication therapy with a course of intravenous antibiotics together with an inhaled antibiotic
 - follow this with an extended course of oral and inhaled antibiotics.
- 1.6.34 If eradication treatment is not successful despite treatment as recommended in 1.6.33, offer sustained treatment with an inhaled antibiotic. Consider nebulised colistimethate sodium as first-line treatment. (See recommendation 1.6.37 on using colistimethate dry powder for inhalation).
- 1.6.35 Depending on infection severity, use either an oral antibiotic or a combination of 2 intravenous antibiotics of different classes for people:
- who have chronic *Pseudomonas aeruginosa* infection (when treatment has not eradicated the infection) **and**
 - who become clinically unwell with a pulmonary disease exacerbation.
- 1.6.36 If a person with chronic *Pseudomonas aeruginosa* infection repeatedly becomes clinically unwell with pulmonary disease exacerbations, consider changing the antibiotic regimens used to treat exacerbations.
- 1.6.37 Colistimethate sodium dry powder for inhalation (DPI) is recommended as an

option for treating chronic pulmonary infection caused by *Pseudomonas aeruginosa* in people with cystic fibrosis only if:

- they would clinically benefit from continued colistimethate sodium but do not tolerate it in its nebulised form and thus tobramycin therapy would otherwise be considered **and**
- the manufacturer provides colistimethate sodium DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS.

[This recommendation is from the NICE technology appraisal guidance on colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis]

1.6.38 For people with chronic *Pseudomonas aeruginosa* infection who are clinically deteriorating despite regular inhaled colistimethate sodium, consider nebulised aztreonam, nebulised tobramycin, or tobramycin DPI (see recommendation 1.6.39 on using tobramycin DPI).

October 2017: note that this was an off-label use of all the drugs listed for children under 6. See NICE's information on prescribing medicines.

1.6.39 Tobramycin DPI is recommended as an option for treating chronic pulmonary infection caused by *Pseudomonas aeruginosa* in people with cystic fibrosis only if:

- nebulised tobramycin is considered an appropriate treatment, that is, when colistimethate sodium is contraindicated, is not tolerated or has not produced an adequate clinical response **and**
- the manufacturer provides tobramycin DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS.

[This recommendation is from the NICE technology appraisal guidance on colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis]

- 1.6.40 People currently using tobramycin DPI or colistimethate sodium DPI that is not recommended according to recommendations 1.6.37 or 1.6.39 should be able to continue treatment until they and their clinician consider it appropriate to stop. For children and young people this decision should be made jointly by the clinician, the child or young person and their parents or carers.

[This recommendation is from [the NICE technology appraisal guidance on colistimethate sodium and tobramycin dry powders for inhalation for treating pseudomonas lung infection in cystic fibrosis](#)]

Burkholderia cepacia complex

- 1.6.41 For people with cystic fibrosis who develop a new Burkholderia cepacia complex infection (that is, recent respiratory sample cultures showed no Burkholderia cepacia infection):
- whether they are clinically well or not, give antibiotic eradication therapy using a combination of intravenous antibiotics
 - seek specialist microbiological advice on the choice of antibiotics to use.
- 1.6.42 Be aware that there is no evidence to support using antibiotics to suppress chronic Burkholderia cepacia complex infection in people with cystic fibrosis who have stable pulmonary status. Discuss the possible risks (for example drug toxicity) of treating the infection with the person and their family members or carers (as appropriate).
- 1.6.43 For people with cystic fibrosis who have chronic Burkholderia cepacia complex infection (when treatment has not eradicated the infection) and who become clinically unwell with a pulmonary disease exacerbation:
- give a combination of oral or intravenous antibiotics
 - seek specialist microbiological advice on which antibiotics to use.
- 1.6.44 For people with cystic fibrosis who have chronic Burkholderia cepacia complex infection and declining pulmonary status:

- consider sustained treatment with an inhaled antibiotic to suppress the infection
- seek specialist microbiological advice on which antibiotic to use
- stop this treatment if there is no observed benefit.

Haemophilus influenzae

- 1.6.45 For people with cystic fibrosis who develop a Haemophilus influenzae infection (diagnosed by a positive respiratory sample culture) but do not have clinical evidence of pulmonary infection, treat with an appropriate oral antibiotic.
- 1.6.46 For people with cystic fibrosis who develop a Haemophilus influenzae infection (diagnosed by a positive respiratory sample culture) and are unwell with clinical evidence of pulmonary infection, treat with an appropriate antibiotic, given orally or intravenously depending on the severity of the illness.

Non-tuberculous mycobacteria

- 1.6.47 For people with cystic fibrosis who are clinically well but whose airway secretions are persistently positive for non-tuberculous mycobacteria, discuss with them and their family members or carers (as appropriate):
- the clinical uncertainties about non-tuberculous mycobacterial infection **and**
 - the possible benefits and risks (for example, drug toxicity) of treating it.
- 1.6.48 If a person with cystic fibrosis has a respiratory sample test positive for new non-tuberculous mycobacteria infection, repeat the test for confirmation.
- 1.6.49 If repeat testing confirms persistent non-tuberculous mycobacteria, do a chest CT scan to look for changes consistent with non-tuberculous mycobacteria disease.
- 1.6.50 Consider non-tuberculous mycobacterial therapy aimed at eradication for people

with cystic fibrosis:

- whose airway secretions persistently test positive for non-tuberculous mycobacteria **and**
- who are clinically unwell with pulmonary disease, or who have a chest CT scan showing changes consistent with non-tuberculous mycobacteria disease **and**
- whose pulmonary disease has not responded to other recommended treatments.

Seek specialist microbiological advice on which antibiotics to use and on the duration of treatment.

Aspergillus fumigatus complex

- 1.6.51 Do not routinely use antifungal agents to suppress chronic *Aspergillus fumigatus* complex respiratory infection (diagnosed by persistently positive respiratory secretion sample cultures) in people with cystic fibrosis and stable pulmonary status.
- 1.6.52 For people with cystic fibrosis with chronic *Aspergillus fumigatus* complex respiratory infection and declining pulmonary status:
- consider sustained treatment with an antifungal agent to suppress the infection
 - seek specialist microbiological advice on which antifungal agent to use
 - stop treatment or change to a different agent if there is no benefit.
- 1.6.53 For people with cystic fibrosis with elevated aspergillus serology (aspergillus-specific IgG and/or IgE) and declining pulmonary function despite optimised pulmonary treatment, think about treating for allergic bronchopulmonary aspergillosis or other aspergillus airway disease, especially if there are consistent chest X-ray or CT scan changes.

Unidentified infections

- 1.6.54 For people with cystic fibrosis who have a pulmonary disease exacerbation and no clear cause (based on recent respiratory secretion sample cultures):
- use an oral or intravenous (depending on the exacerbation severity) broad-spectrum antibiotic
 - continue collecting respiratory secretion samples, and change treatments if a pathogen is identified and a more appropriate treatment is available.

Immunomodulatory agents

- 1.6.55 For people with cystic fibrosis and deteriorating lung function or repeated pulmonary exacerbations, offer long-term treatment with azithromycin at an [immunomodulatory dose](#). October 2017: note that this was an off-label use. See [NICE's information on prescribing medicines](#).
- 1.6.56 For people who have continued deterioration in lung function, or continuing pulmonary exacerbations while receiving long-term treatment with azithromycin, stop azithromycin and consider oral corticosteroids.
- 1.6.57 Do not offer inhaled corticosteroids as an immunomodulatory treatment for cystic fibrosis.

1.7 Other monitoring, assessment and management

Nutritional interventions and exocrine pancreatic insufficiency

- 1.7.1 The cystic fibrosis specialist dietitian should offer advice on the benefits of optimal nutrition, and at the annual assessment review the person's:
- total nutritional intake, including energy intake (calories)
 - estimated nutritional needs

- pancreatic enzyme replacement therapy, if appropriate.

1.7.2 Encourage people to increase calorie intake by increasing portion size and eating high-energy foods if there is concern about their nutrition (including weight loss and inadequate weight gain).

1.7.3 If increased portion size and high-energy foods are not effective, consider a trial of oral nutritional supplements.

1.7.4 If attempts to increase calorie intake are not effective, consider:

- supplementation with enteral tube feeding **or**
- for adults, a short-term trial of an appetite stimulant (for example up to 3 months).

October 2017: note that this was an off-label use. See [NICE's information on prescribing medicines](#).

1.7.5 Test for exocrine pancreatic insufficiency in people with cystic fibrosis, using a non-invasive technique such as stool elastase estimation. If the test result is normal, repeat it if symptoms or signs suggesting malabsorption occur.

1.7.6 Offer oral pancreatic enzyme replacement therapy to people with exocrine pancreatic insufficiency. Adjust the dose as needed to minimise any symptoms or signs of malabsorption.

1.7.7 Consider an acid suppression agent (for example an H₂ receptor antagonist or a proton pump inhibitor) for people who have persistent symptoms or signs of malabsorption despite optimal pancreatic enzyme replacement therapy.

October 2017: note that this was an off-label use. See [NICE's information on prescribing medicines](#).

Distal intestinal obstruction syndrome

- 1.7.8 Be aware that a variety of conditions can cause acute abdominal pain and resemble distal intestinal obstruction syndrome in people with cystic fibrosis, for example:
- constipation
 - appendicitis
 - intussusception
 - cholecystitis.
- 1.7.9 Suspect distal intestinal obstruction syndrome in people with cystic fibrosis who have an acute onset of peri-umbilical or right lower quadrant abdominal pain and any of the following:
- a palpable mass in the right lower quadrant
 - faecal loading in the right lower quadrant on a plain abdominal X-ray, especially if associated with small intestine air-fluid levels
 - clinical features of partial or complete intestinal obstruction, such as vomiting (especially bilious) and abdominal distension.
- 1.7.10 For people who have an acute onset of peri-umbilical abdominal pain but no other clinical or radiological features of distal intestinal obstruction syndrome, consider further imaging, for example with an:
- abdominal ultrasound scan **or**
 - abdominal CT scan.
- 1.7.11 Manage suspected distal intestinal obstruction syndrome in a specialist cystic fibrosis centre, with supervision from specialists who have expertise in recognising and treating the condition and its complications.
- 1.7.12 Offer oral or intravenous fluids to ensure adequate hydration (and rehydration if needed) for people with distal intestinal obstruction syndrome.

- 1.7.13 Consider diatrizoate meglumine and diatrizoate sodium solution (Gastrografin) (orally or via an enteral tube) as first-line treatment for distal intestinal obstruction syndrome.
- 1.7.14 If diatrizoate meglumine and diatrizoate sodium solution (Gastrografin) is not effective, consider an iso-osmotic polyethylene glycol and electrolyte (PEG) solution (macrogols) (orally or via an enteral tube) as a second-line treatment.
- 1.7.15 Consider surgery as a last resort, if prolonged treatment with a PEG solution is not effective.
- 1.7.16 To reduce the risk of distal intestinal obstruction syndrome recurring:
- encourage people to drink plenty of fluids
 - optimise pancreatic enzyme replacement therapy (see [nutritional interventions and exocrine pancreatic insufficiency](#))
 - consider advising regular treatment with a stool-softening agent such as lactulose or a PEG solution.

Liver disease

- 1.7.17 Perform a clinical assessment and liver function blood tests at the annual review for people with cystic fibrosis.
- 1.7.18 If liver function blood tests are abnormal, perform a liver ultrasound scan and consider ursodeoxycholic acid treatment. October 2017: note that this was an off-label use for adults. See [NICE's information on prescribing medicines](#).
- 1.7.19 Think about stopping ursodeoxycholic acid if liver function blood tests return to normal and clinical assessment and liver ultrasound scan show no liver disease.
- 1.7.20 If ursodeoxycholic acid is stopped, monitor for re-emergence of liver disease using clinical assessment and liver function blood tests.
- 1.7.21 Think about referring people with cystic fibrosis to a liver specialist if the liver

function blood test results are persistently abnormal despite treatment with ursodeoxycholic acid.

1.7.22 Refer people with cystic fibrosis to a liver specialist if they have any of the following:

- chronic progressive liver disease, based on clinical assessment, liver function blood tests or the findings on a liver ultrasound scan
- liver failure, based on clinical assessment and liver function tests
- portal hypertension, haematemesis, splenomegaly or findings on a liver ultrasound scan.

Cystic-fibrosis-related diabetes

1.7.23 Diagnose cystic-fibrosis-related diabetes using one of the following:

- continuous glucose monitoring (CGM)
- serial glucose testing over several days
- oral glucose tolerance testing (OGTT) – if OGTT is abnormal perform CGM or serial glucose testing over several days to confirm the diagnosis.

1.7.24 Test for cystic-fibrosis-related diabetes (as detailed in recommendation 1.7.23) in people with cystic fibrosis annually from 10 years of age.

1.7.25 Test for cystic-fibrosis-related diabetes at the end of the first and second trimesters of pregnancy, using CGM or OGTT.

1.7.26 Test for cystic-fibrosis-related diabetes in people with cystic fibrosis who are taking long-term systemic corticosteroids or receiving enteral tube feeding, using CGM or serial glucose monitoring.

1.7.27 Think about testing for cystic-fibrosis-related diabetes in people who still have any of the following despite optimised cystic fibrosis treatment:

- unexplained weight loss
- a deterioration in lung function as measured by spirometry
- increased frequency of pulmonary exacerbations
- excessive tiredness.

Bone mineral density

1.7.28 Consider dual energy X-ray absorptiometry (DXA) bone density scans for people with cystic fibrosis who have factors that put them at high risk of low bone mineral density, such as:

- frequent or long-term oral corticosteroid use
- frequent intravenous antibiotic use
- severe lung disease
- undernutrition
- previous low-impact fractures
- previous transplants
- post menopause.

1.7.29 Seek specialist advice for people with a bone mineral density standard deviation below -2.0 (Z score) or -2.5 (T score).

Exercise

- 1.7.30 Advise people with cystic fibrosis and their family members or carers (as appropriate) that regular exercise improves both lung function and overall fitness.
- 1.7.31 Offer people with cystic fibrosis an individualised exercise programme, taking into account their capability and preferences.

- 1.7.32 Regularly review exercise programmes to monitor the person's progress and ensure that the programme continues to be appropriate for their needs.
- 1.7.33 Provide people with cystic fibrosis who are having inpatient care with:
- an assessment of their exercise capacity
 - the facilities and support to continue their exercise programme (as appropriate), taking into account the need to prevent cross-infection (see [preventing cross-infection](#)) and local infection control guidelines.

Psychological assessment

- 1.7.34 At the annual review, the specialist clinical psychologist should include assessments of:
- general mental health and wellbeing
 - quality of life
 - any factors that are making treatment adherence difficult
 - indicators of emerging psychosocial problems
 - behaviours that affect health outcomes.
- 1.7.35 If a severe mental health condition is identified at any assessment performed by the cystic fibrosis clinical psychologist, refer the person with cystic fibrosis to a mental health practitioner. For guidance on treating mental health conditions, refer to the relevant NICE guideline.
- 1.7.36 For family members or carers of people with cystic fibrosis, the specialist clinical psychologist should:
- assess any cystic-fibrosis-related needs they have
 - support their psychological wellbeing
 - refer them to mental health practitioners as needed.

1.8 Preventing cross-infection

- 1.8.1 For recommendations on preventing and controlling infection, see [the NICE guidelines on infection control in primary and community care and healthcare-associated infections](#), and [the NICE quality standard on infection prevention and control](#).
- 1.8.2 To prevent cross-infection among people with cystic fibrosis in outpatient and inpatient care, use microbiological surveillance and a local infection control strategy that includes cohorting.
- 1.8.3 Inform people with cystic fibrosis, their family members or carers (as appropriate) and staff involved in their care about the risk of cross-infection and how to avoid it.
- 1.8.4 Each specialist cystic fibrosis clinic should be organised to prevent cross-infection. Separate people individually during the clinic, including by organising:
- the use of communal areas
 - attendance at diagnostic, treatment and pharmacy facilities.
- 1.8.5 Keep people with transmissible or chronic *Pseudomonas aeruginosa* or *Burkholderia cepacia* complex infection separate from people who do not have these infections, for example by using separate outpatient clinics.
- 1.8.6 Consider keeping people with cystic fibrosis who have intermittent isolation of *Pseudomonas aeruginosa* separate from people who do not have this infection, for example by using separate outpatient clinics. Help people with cystic fibrosis plan their inpatient attendance to avoid contact with each other, for example when they use:
- hospital restaurants, schools and recreation areas
 - diagnostic, treatment and pharmacy facilities (see [information and support](#)).
- 1.8.7 During inpatient care, give people with cystic fibrosis individual rooms with en-suite facilities.

Terms used in this guideline

Immunomodulatory dose

A dose of a drug that is less than the minimum inhibitory dose.

Outreach care

A model of care in which the specialist multidisciplinary cystic fibrosis team provide outpatient clinics in local hospitals.

Pulmonary exacerbation

The sudden or recent worsening of clinical symptoms or signs. This is frequently caused by an acute pulmonary infection.

Pulmonary infection

In people with cystic fibrosis, this can be diagnosed based on symptoms or signs, or by identifying pathogens in respiratory secretion samples.

Shared-care model (network cystic fibrosis clinic)

When a local hospital cares for people with cystic fibrosis, with oversight, support and direct involvement from members of a specialist cystic fibrosis multidisciplinary team.

Telemedicine

Providing clinical services remotely, using phone and video messaging to communicate with the patient.

Young people

Aged 12 to 17 years.

Context

Cystic fibrosis is a multi-system genetic disorder affecting the lungs, pancreas, liver and intestine. It can have a significant impact on life expectancy and quality of life. The current median age of those who have died is 28 years and the median predicted survival is 45.1 years.

Diagnosis is primarily made during newborn screening. The median age at diagnosis is 2 months, and 1 in every 2500 babies born in the UK has cystic fibrosis. Approximately 60% of people on the UK cystic fibrosis registry are aged over 16 years.

Many different mutations are responsible for cystic fibrosis. The UK registry shows that 90.8% of people with cystic fibrosis have one known genotype; however 8.9% of people have at least one unknown genotype.

Lung function is often reduced in cystic fibrosis. The typical measure of lung function is forced expiratory volume in 1 second (FEV₁). FEV₁ is a key predictor of life expectancy in people with cystic fibrosis, and optimising lung function is a major goal of care.

Lung infections are a cause of significant morbidity in cystic fibrosis. Chronic infection (for example with *Staphylococcus aureus* and *Pseudomonas aeruginosa*) may need long-term use of antibiotics.

There is variation across the country in the multidisciplinary team structures used, the arrangements services make for providing care, and in the resources available to support services. Particular problems may arise with smaller shared-care clinic arrangements. In some centres, both inpatient and outpatient facilities are limited. For example, there may be problems in arranging admission to single rooms with en-suite facilities. If adequate protocols are not in place, then there is a risk of cross-infection.

By making robust recommendations based on the available evidence and best practice in cystic fibrosis care, this guideline will help improve care for this highly complex condition.

Recommendations for research

The committee has made the following recommendations for research. The committee's full set of recommendations for research are detailed in the [full guideline](#).

1 Liver disease

Should all children with meconium ileus receive ursodeoxycholic acid from diagnosis?

Why this is important

Liver disease is the third most common cause of mortality in people with cystic fibrosis, and around 10 to 30% of people with cystic fibrosis will develop cystic-fibrosis-related liver disease. Children with meconium ileus are at an increased risk of liver disease, and starting treatment with ursodeoxycholic acid from diagnosis may reduce this risk. Ursodeoxycholic acid appears safe, is well tolerated and cheap. Routine use could increase people's overall quality of life and reduce the need for subsequent treatment for liver disease, but more research is needed into the effectiveness and safety of this treatment.

2 Airway clearance techniques

How effective are daily airway clearance techniques in maintaining lung function in infants and children with cystic fibrosis?

Why this is important

There has been debate about the level of physiotherapy needed to preserve lung health since healthcare systems started diagnosing cystic fibrosis through newborn screening. Some clinical teams teach parents airway clearance techniques and recommend using them daily, but others use alternatives such as parental respiratory assessment tools with structured exercise. Routine airway clearance from diagnosis takes up a lot of time and places considerable responsibility on the parents and carers. These techniques are also difficult to perform, particularly with an infant or young child who does not understand what is happening. It is important to find out whether daily airway clearance techniques

are helping to maintain lung health or are creating an unnecessary burden on parents and carers. Future research should look at the impact on the lives of parents, family members and carers, as well as long-term clinical outcomes for infants and children with cystic fibrosis.

3 Monitoring pulmonary disease

Is lung clearance index a useful and cost-effective tool for the routine assessment and monitoring of changes in pulmonary status in people with cystic fibrosis?

Why this is important

Assessing the severity of lung disease is difficult in younger children. Not all children under 5 years can do spirometry tests and they are not sufficiently sensitive in people with good lung function, where CT scans can show pulmonary status changes before spirometry changes. A simple, sensitive and reproducible measurement such as lung clearance index allows assessment of respiratory status in people with cystic fibrosis, and could improve clinical decision-making.

4 Psychological assessment

What is the most effective measure of psychological functioning to use as a test for thresholds of concern in people with cystic fibrosis?

Why this is important

There are no validated tools to assess psychological and behavioural problems in people with cystic fibrosis, and these would be useful to validate generic measures (for example for depression and anxiety). People with a long-term physical health condition are more likely to present with mental health problems. NHS England highlights that prevention of mental health problems is the most cost-effective service that can be provided. To prevent mental health problems, all people with cystic fibrosis would need to have their mental health status routinely and regularly assessed. People with cystic fibrosis would benefit, therefore, from having a routine test that would show who needs psychological intervention. This would allow early intervention to maintain or improve quality of life, prevent mental health problems from developing, and improve health outcomes through an improvement in wellbeing.

5 Monitoring for cystic-fibrosis-related diabetes

What is the most effective strategy to detect diabetes in people with cystic fibrosis?

Why this is important

Diabetes develops and presents very differently in people with cystic fibrosis. Although annual testing for cystic-fibrosis-related diabetes is recommended in this guideline for people over 10 with cystic fibrosis, there is a lack of evidence on how to diagnose the condition. There is currently variation in practice, with cystic fibrosis centres using different combinations of the oral glucose tolerance test, HbA1c, serial glucose testing, and continuous glucose monitoring systems. Identifying which strategy is most effective for early identification of cystic-fibrosis-related diabetes would help teams start prompt treatment and prevent the clinical decline associated with the condition.

6 Mucoactive agents

What is the most clinically and cost-effective dose of rhDNase (dornase alfa; recombinant human deoxyribonuclease) for people with cystic fibrosis?

Why this is important

People with cystic fibrosis often have complex treatment schedules, which can include multiple nebulised treatments. Taking daily rhDNase increases the burden on them. Because of this, it is essential to find out whether rhDNase needs to be taken this often to provide clinical benefit. There is some evidence that alternate-day rhDNase is just as effective, and if this is confirmed then overall treatment adherence may improve and cost savings would be made. The current evidence base is mostly small, underpowered, short-term trials, in people who have had this treatment before. Consequently, it is not clear what the long-term impact of different doses of rhDNase are for people with cystic fibrosis. It may be cost effective to switch to alternate-day rhDNase if it is shown to be as effective as daily rhDNase.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see [NICE's topic page on cystic fibrosis](#).

For full details of the evidence and the guideline committee's discussions on the 2018 recommendations, see the [full guideline](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources to help you put this guideline into practice](#). For general help and advice on putting our guidelines into practice, see [resources to help you put NICE guidance into practice](#).

Update information

Minor changes since publication

October 2022: We added text to indicate that pulse oximetry may be less reliable in people with dark skin. We also added a link to the NHS patient safety alert on the risk of harm from inappropriate placement of pulse oximeter probes. See recommendation 1.6.9.

October 2021: We added a link to NICE's shared decision making guideline in recommendation 1.2.8.

November 2017: details of marketing authorisation in footnote 1 corrected.

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