Integrated Impact Assessment Report for Clinical Commissioning Policies			
Policy Reference Number	ID019		
Policy Title	Mercaptamine hydrochloride for corneal cystine deposits in people aged older than 2 years Proposal		
Lead Commissioner	Sarah Watson	**Clinical Lead**	Detlef Bockenhaur
Finance Lead	Keith Moulds	**Analytical Lead**	Click here to enter text.

Integrated Impact Assessment – Index

About this Impact Assessment: instructions for completion and explanatory notes
• Each section is divided into themes. • Each theme sets out a number of questions. • All questions are answered by selecting a drop down option or including free text. • Free text boxes are provided to enable succinct relevant commentary to be added which explains the rationale for response or assumption. Please limit responses to 3 sentences of explanatory text. • Data in this document is either drawn from one of the relevant policy documents or a source for the information is provided. • Where assumptions are included where data is not available, this is specified.

Section A - Activity Impact	
A1 Current Patient Population & Demography / Growth	
A1.1 Prevalence of the disease/condition.	The prevalence of cystinosis is between 1 per 100,000 and 1 per 200,000 live births. There are 159 patients (84 children and 75 adults) in England who are currently receiving treatment with systemic cysteamine to treat crystals in other areas of the body and use the aqueous eye drops to treat corneal cystine deposits. In addition, 6 patients are registered with the Cystinosis Foundation UK with the rare form of ocular (non-nephropathic) cystinosis and currently use the aqueous eye drops only. The total number of people currently treated with eye drops for cystinosis in England is 165 [159 + 6]. *Source: Emma et al. 2014 / DPP section 6. Figures confirmed with experts from the PWG.*
A1.2 Number of patients currently eligible for the treatment according to the proposed policy commissioning criteria.	165 *Source: Recordati Rare Diseases internal data on number of treated patients and confirmed by clinical experts on the PWG.* The number for people eligible (as covered by the licence for this treatment) is 165.
A1.3 Age group for which the treatment is proposed according to the policy commissioning criteria.	**Other** The age group for which treatment is proposed is people aged 2 years or older with corneal crystal deposits caused by cystinosis. Corneal crystals appear as needle-shaped, highly reflective opacities. By 1 year of age, cystine crystals can be seen in the cornea by slit lamp. By approximately 7 years of age, the entire peripheral stroma (the thick, transparent middle

<table>
<tr><td></td><td>layer of the cornea) accumulates crystals, and by approximately 20 years of age, crystals can be seen in the entire corneal stroma.</td></tr>
<tr><td>A1.4 Age distribution of the patient population eligible according to the proposed policy commissioning criteria</td><td>Of the 165 people eligible for treatment, around 53% are adults (87 people) and 47% are children (78 people).
Source: Recordati Rare Diseases internal data</td></tr>
<tr><td>A1.5 How is the population currently distributed geographically?</td><td><u>Unevenly</u>
If unevenly, estimate regional distribution by %:<table><tr><td>North</td><td>39%</td></tr><tr><td>Midlands & East</td><td>34%</td></tr><tr><td>London</td><td>12.5%</td></tr><tr><td>South</td><td>14.5%</td></tr></table>Source: Recordati Rare Diseases internal data (Table 8 company submission)</td></tr>
<tr><td colspan="2">A2 Future Patient Population & Demography</td></tr>
<tr><td>A2.1 Projected changes in the disease/condition epidemiology, such as incidence or prevalence (prior to applying the new policy) in 2, 5, and 10 years?</td><td><u>Increasing</u>
Changes in incidence and prevalence are based on a constant estimate of cases diagnosed each year. This is shown in the table below.<table><tr><td>Projected change in epidemiology</td><td>Year 2</td><td>Year 5</td><td>Year 10</td></tr></table></td></tr>
</table>

Prevalence (a)	168	177	192
Incidence (b)	3	3	3
People eligible for mercaptamine hydrochloride	**171**	**180**	**195**

Source: Resource impact template – assumptions sheet. This is based Recordati Rare Diseases internal data on the number of treated patients.

A2.2 Are there likely to be changes in demography of the patient population and would this impact on activity/outcomes?

No

A2.3 Expected net increase or decrease in the number of patients who will be eligible for the service, according to the proposed service specification commissioning criteria, per year in years 2-5 and 10?

YR2 +/-	+6
YR3 +/-	+9
YR4 +/-	+12
YR5 +/-	+15
YR10 +/-	+30

Source: Resource impact template (assumptions input sheet).

Are these numbers in line with ONS growth assumptions for the age specific population? If not please justify the growth assumptions made.

No

Cystinosis is a rare inherited disease. The growth assumptions are based on a UK study on the incidence of genetic disorders in the West Midlands which was carried out between 1981-1991. The study recorded 21 new cases of cystinosis born in this time period (Source: Hutchesson, Bundey, Preece, Hall & Green 1998). An incidence (accounting for mortality) of net +3 patients per year has been assumed based on this study.

A3 Activity

A3.1 What is the purpose of new policy?

<u>Confirm routine commissioning position of an additional new treatment</u>

The purpose of the new policy is to propose licensed mercaptamine hydrochloride as a therapy for the treatment of corneal cystine deposits in adults and children from 2 years of age. Other than mercaptamine hydrochloride, there are no licensed treatments available. The current treatment for corneal cystine crystals is an unlicensed formulation of aqueous mercaptamine hydrochloride (0.55%) eye drops which are produced under the terms of a Specials' licence. There are many problems experienced by patients using this formulation which include the requirement to apply the drops 6 to 12 times per day (during waking hours) and to maintain its effectiveness, the formulation needs to be stored in a freezer at a temperature of -20C. If the policy is approved, a licensed product would be used for treatment, the burden on people would reduce, compliance is likely to improve, and this would allow for better treatment response.

A3.2 What is the annual activity associated with the existing pathway for the eligible population?

The annual activity is shown in the table below. This is the estimated number of people diagnosed and eligible for a treatment.

Source: DPP Section 3 / Resource impact template – assumptions input sheet

Year	Activity
0	165
1	168
2	171
3	174

4	177
5	180

A3.3 What is the estimated annual activity associated with the proposed policy proposition pathway for the eligible population?

Source: Resource impact template – assumptions input sheet

Estimated number of people eligible for treatment with mercaptamine hydrochloride and people who actually receive mercaptamine hydrochloride.

Year	Number of people eligible	Estimated percentage who take up mercaptamine hydrochloride	Cumulative number of people who take up / continue treatment	Number of people treated
Year 1	168	50%	85	**85**
Year 2	171	100%	171	**171**
Year 5	180	100%	180	**180**
Year 10	195	100%	195	**195**

The table above shows the number of people receiving treatment increasing and no people discontinuing the treatment. The reason for this is clinical experts from the PWG agree that local adverse events are transitory (resolve in a minute or some seconds after instillation), people usually get used to it. In practice (anecdotally), it is observed that those people who suffer from local adverse events and decide to interrupt treatment, resume treatment with viscous mercaptamine hydrochloride. The actual definite discontinuation rate is very low and, therefore given the small population, the resource impact assumes this to be zero.

A3.4 What is the estimated annual activity associated with the next best alternative comparator pathway for the eligible population? If the only alternative is the existing pathway, please state 'not applicable' and move to A4.	*Not applicable.* Please specify Mercaptamine hydrochloride (0.55%) viscous eye drops aims to fully replace unlicensed aqueous mercaptamine HCI 0.55% eye drops manufactured by the Guy's and St. Thomas's Hospital. There is no change to the existing pathway.
A4 Existing Patient Pathway	
A4.1 **Existing pathway:** Describe the relevant currently routinely commissioned: • Treatment or intervention • Patient pathway • Eligibility and/or uptake estimates.	All people with cystinosis (regardless of subtypes) can have corneal cystine crystals and can develop symptoms such as photophobia (light sensitivity), blepharospasm (involuntary closure of the eye), eye pain or diseases of the eye surface. Complications arising from cystine crystal deposits include corneal neovascularisation and various forms of keratopathies leading to visual impairment. Current treatment for corneal cystine crystals requires administration of aqueous mercaptamine hydrochloride eye drops which dissolve the cystine crystal deposits in the cornea of the eye. In England, there have previously been no licensed treatments for corneal cystine crystals, although unlicensed solutions of aqueous mercaptamine hydrochloride (0.55%) are produced under the terms of a 'Specials' licence and stored locally by NHS trusts. The eye drop solutions are produced locally in pharmacies or hospitals and have been used for many years for the management of eye symptoms of cystinosis [EPAR summary for the public 2016]. Patient pathway: Nephropathic cystinosis (affecting other areas of the body including the eyes and kidneys): Referral from local GP services to a local paediatrician or a nephrologist. If cystinosis is suspected, then a referral is made to a consultant nephrologist based at a tertiary centre with expertise in cystinosis for diagnosis. Treatment is initiated once there is confirmed nephropathic cystinosis upon testing (LCL levels test; corneal

cystine crystals visible under slit lamp; possible genetic analysis of CTNS gene).

Non-nephropathic cystinosis (affecting the eyes only): Referral from GP to local ophthalmologist. Where there are ocular manifestations of cystinosis, referral is made to a consultant ophthalmologist and consultant nephrologist at a tertiary centre with expertise in cystinosis. Treatment is initiated once there is confirmed ocular cystinosis upon testing ((LCL levels test; corneal cysteine crystals visible under slit lamp; possible genetic analysis of CTNS gene; no clinical presentation with Fanconi syndrome).

For follow-up, patients are mainly seen by the nephrologist, endocrinologist, orthopaedics and for the eye condition, an ophthalmologist. Frequency depends on the clinical status of the patient and is therefore variable. Seeing the treating physician a couple of times a year is common.

The estimated number of people currently eligible and receiving treatment is shown in the table below:

Treatment	%	Year 1	Year 2	Year 5	Year 10
People who have aqueous mercaptamine hydrochloride	100%	168	171	180	195

Source: DPP / Recordati Rare Diseases submission/ Epidemiology data – see A2.1 above.

A4.2. What are the current treatment access and stopping criteria?	People with any cystinosis subtype are eligible for treatment since all people will develop corneal cystine crystals with corresponding symptoms and complications. In most instances, treatment is initiated in a tertiary centre with expertise in cystinosis and by a consultant nephrologist (systemic and eye treatment) or sometimes a consultant ophthalmologist (eye treatment). However, it is not uncommon for both nephropathic

	cystinosis treatment and eye-drop treatment to be initiated by an outlying regional paediatric nephrologist. Aqueous mercaptamine hydrochloride eye drops should be discontinued if the person experiences treatment emergent adverse effects or the person is unable to tolerate local adverse drug reactions (for example eye irritation, burning or stinging). Clinical expert input identifies that most people will encounter pain, redness and blurred vision from the eye drops, however these are transient in most people and non-harmful. People who stop will always have the option of restarting treatment to avoid build up of corneal crystals and the risk of corneal damage and visual loss. *Source: Recordati Rare Diseases / PWG clinical experts*
A4.3 What percentage of the total eligible population is expected to: a) Be clinically assessed for treatment b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	a) 100% b) 100% c) 100% d) 100% e) 100% *Source:* (a,b,c d & e) Eligible population receiving treatment - per Recordati Rare Diseases submission. Clinical experts have advised that all people would have treatment and continue the treatment to prevent sight loss. There are adherence issues with the frequency of having to administer the drops, however treatment can be restarted if doses are missed. Due to the variable nature of missed drops among individual people, the resource impact assumes all people take the recommended doses. This has also been assumed for the policy pathway.
A5 Comparator (next best alternative treatment) Patient Pathway (NB: comparator/next best alternative does not refer to current pathway but to an alternative option)	
A5.1 **Next best comparator**:	**No**

Is there another 'next best' alternative treatment which is a relevant comparator? *If yes, describe relevant* • *Treatment or intervention* • *Patient pathway* • *Actual or estimated eligibility and uptake*	*Source:* Please see A4.1 above.
A5.2 What percentage of the total eligible population is estimated to: a) Be clinically assessed for treatment b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	N/A
A6 New Patient Pathway	
A6.1 What percentage of the total eligible population is expected to: a) Be clinically assessed for treatment b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	a) 100% b) 100% c) 100% d) 100% e) 100% *Source:* (b) Per eligible population receiving treatment Recordati Rare Diseases submission, confirmed by PWG members; (c) assumption all eligible population choose treatment due to fewer doses needed per day. (d) People may recommence dosing regimen if they miss a dose. Resource impact assumes full compliance due to variable nature of compliance.

<table>
<tr><td></td><td>(e) Clinical opinion / Recordati Rare Diseases – adverse effects generally minor (stinging up to a minute after instillation) people usually resume treatment – discontinuation rate is very low.</td></tr>
<tr><td>A6.2 Specify the nature and duration of the proposed new treatment or intervention.</td><td><u>Life long</u></td></tr>
<tr><td colspan="2">A7 Treatment Setting</td></tr>
<tr><td>A7.1 How is this treatment delivered to the patient?</td><td>Select all that apply:
<table><tr><td>Emergency/Urgent care attendance</td><td>☐</td></tr><tr><td>Acute Trust: inpatient</td><td>☐</td></tr><tr><td>Acute Trust: day patient</td><td>☐</td></tr><tr><td>Acute Trust: outpatient</td><td>☒</td></tr><tr><td>Mental Health provider: inpatient</td><td>☐</td></tr><tr><td>Mental Health provider: outpatient</td><td>☐</td></tr><tr><td>Community setting</td><td>☒</td></tr><tr><td>Homecare</td><td>☒</td></tr><tr><td>Other</td><td>☐</td></tr></table>
The treatment can be delivered via hospital pharmacies, hospital outpatient pharmacies, retail pharmacies and/or referral into primary care. Some people may receive treatment via homecare arrangements.</td></tr>
</table>

A7.2 What is the current number of contracted providers for the eligible population by region?	NORTH Royal Manchester Children's Hospital (both) Royal Liverpool Children's Hospital (Alder Hey) Nephro (Cystagon only)	2	1 ophthalmology only, 1 both ophthalmology and nephrology
	MIDLANDS & EAST Birmingham Women's and Children's Hospital/QE Hospital Birmingham (adults) Yes (both) Newcastle Royal Victoria Hospital Nephro (Cystagon only) Nottingham Children's Hospital Nephro (Cystagon only)	3	2 ophthalmology only, 1 ophthalmology and nephrology
	LONDON Great Ormond Street Hospital Yes (both)	2	both ophthalmology and nephrology

	Evelina Children's Hospital/ Guy`s Hospital (Adults) (both)		
	SOUTH Southampton University Hospital (both) Bristol Royal Hospital for Children (both)	2	both ophthalmology and nephrology

Key tertiary centres with specialists in cystinosis in England. Source: company - Recordati Rare Diseases

A7.3 Does the proposition require a change of delivery setting or capacity requirements?	**No**
A8 Coding	
A8.1 Specify the datasets used to record the new patient pathway activity. *expected to be populated for all commissioned activity	*Select all that apply:*

Aggregate Contract Monitoring *	☐
Patient level contract monitoring	☐
Patient level drugs dataset	☒
Patient level devices dataset	☐

	<table><tr><td>Devices supply chain reconciliation dataset</td><td>☐</td></tr><tr><td>Secondary Usage Service (SUS+)</td><td>☐</td></tr><tr><td>Mental Health Services DataSet (MHSDS)</td><td>☐</td></tr><tr><td>National Return**</td><td>☐</td></tr><tr><td>Clinical Database**</td><td>☐</td></tr><tr><td>Other**</td><td>☒</td></tr></table>**If National Return, Clinical database or other selected, please specify: Mercaptamine hydrochloride (cystadrops) is currently only available on prescription within the EU. UK prescribing data could be used to record activity. Please see European public assessment report (EPAR Cystadrops). In addition, this formulation of mercaptamine hydrochloride is a high cost drug excluded from tariff. Activity could therefore be captured in the high cost drug dataset for routine commissioning. A requirement for data to be collected via Blueteq could also be introduced.
A8.2 Specify how the activity related to the new patient pathway will be identified.	*Select all that apply:* <table><tr><td>OPCS v4.8</td><td>☐</td></tr><tr><td>ICD10</td><td>☐</td></tr><tr><td>Treatment function code</td><td>☐</td></tr><tr><td>Main Speciality code</td><td>☐</td></tr><tr><td>HRG</td><td>☐</td></tr><tr><td>SNOMED</td><td>☐</td></tr><tr><td>Clinical coding / terming methodology used by clinical profession</td><td>☒</td></tr></table>

A8.3 **Identification Rules for Drugs:** How are drug costs captured?	**Not already specified in current NHS England Drugs List document**
A8.4 **Identification Rules for Devices:** How are device costs captured?	**Not applicable.**
A8.5 **Identification Rules for Activity:** How are activity costs captured?	**Already captured by an existing specialised service line (NCBPS code) within the PSS Tool but needs amendment** If activity costs are already captured, please specify the specialised service code and description (e.g. NCBPS01C Chemotherapy). NCBPS23N OPHTHALMOLOGY CHILDREN NCBPS37Z OPHTHALMOLOGY ADULTS It is unlikely that people with corneal cystine deposits would be specifically identified within the full data set, however this is where activity would be captured.
A9 Monitoring	
A9.1 **Contracts** Specify any new or revised data flow or data collection requirements, needed for inclusion in the NHS Standard Contract Information Schedule.	**None**
A9.2 **Excluded Drugs and Devices (not covered by the Zero Cost Model)** For treatments which are tariff excluded drugs or devices not covered by the Zero Cost Model, specify the pharmacy or device	*Select all that apply:* Drugs or Device MDS ☐ Blueteq ☒

monitoring required, for example reporting or use of prior approval systems.	Other prior approval ☐
A9.3 **Business intelligence** Is there potential for duplicate reporting?	**No**
A9.4 **Contract monitoring** Is this part of routine contract monitoring?	**No**
A9.5 **Dashboard reporting** Specify whether a dashboard exists for the proposed intervention?	**No**
A9.6 **NICE reporting** Are there any directly applicable NICE or equivalent quality standards which need to be monitored in association with the new policy?	**Yes** If yes, specify how performance monitoring data will be used for this purpose. The quality standard on Serious eye disorders (QS180) was published in February 2019. The quality standard covers preventing sight loss in adults.
Section B - Service Impact	
B1 Service Organisation	
B1.1 Describe how the service is currently organised? (i.e. tertiary centres, networked provision etc.)	In most instances, treatment for both adults and children is initiated in a tertiary centre with expertise in cystinosis and by a consultant nephrologist who can initiate both systemic treatment and eye treatment. Eye treatment may sometimes be initiated by a consultant ophthalmologist at a tertiary centre with expertise in cystinosis. There are

<table>
<tr><td></td><td>nine tertiary centres with expertise in cystinosis in England. However, it is not uncommon for both nephropathic cystinosis treatment and eye drop treatment to be initiated by an outlying regional paediatric nephrologist.
Source: Recordati Rare Diseases submission confirmed by PWG members</td></tr>
<tr><td>B1.2 Will the proposition change the way the commissioned service is organised?</td><td><u>No</u></td></tr>
<tr><td>B1.3 Will the proposition require a new approach to the organisation of care?</td><td><u>No change to delivery of care</u></td></tr>
<tr><td colspan="2">B2 Geography & Access</td></tr>
<tr><td>B2.1 Where do current referrals come from?</td><td>Select all that apply:
<table><tr><td>GP</td><td>☒</td></tr><tr><td>Secondary care</td><td>☐</td></tr><tr><td>Tertiary care</td><td>☐</td></tr><tr><td>Other</td><td>☐</td></tr></table>A person or infant is likely to initially present with symptoms of cystinosis to GP services. Referral is then made to a local paediatrician or nephrologist. In the case of ocular cystinosis, referral is made to a local ophthalmologist. A confirmed diagnosis will normally be made by a consultant nephrologist based at a tertiary centre with expertise in cystinosis when referral is made due to a clinical suspicion of cystinosis.</td></tr>
</table>

B2.2 What impact will the new policy have on the sources of referral?	**No impact**
B2.3 Is the new policy likely to improve equity of access?	**No impact**
B2.4 Is the new policy likely to improve equality of access and/or outcomes?	**Increase** The current standard of care requires using an unlicensed aqueous formulation of mercaptamine hydrochloride eye drops to be used every waking hour (but can be reduced to every other waking hour at physician's discretion) 6-10 times a day or 10-12 times a day depending on the treatment consensus (Emma, et al 2014). This is because the aqueous formulation has a very short cornea contact time due to eye blinking and the production / renewal of tear fluid. Many patients lack compliance and thereby fail to achieve effectiveness. In addition, the storage conditions of viscous mercaptamine hydrochloride allow for room temperature storage in contrast to the aqueous formulation eye drops which require refrigeration after each use. There is a lack of compliance with cold storage affecting stability and thus effectiveness because mercaptamine is highly unstable when exposed to heat and light. Viscous mercaptamine hydrochloride eye drops overcomes this challenge by allowing longer cornea penetration time thereby enabling 4 times a day regime. This has higher adherence rates (based on the 5-year OCT-1 study; Labbe et al 2014). Patient experts have explained how the frequent need to administer the current eye drops formulation dominates their lives. Going out for the day becomes an incredibly complex operation. Where the person being

	treated is a young child, having to carry enough eyedrops (which need to be kept cool), continually needing to interrupt activities and administer the drops, and ensuring compliance with a complex medical regime is not compatible with an active daily life. The treatment fulfils an unmet need for a medication which is effective and improves the quality of life of people with cystinosis.
B3 Implementation	
B3.1 Will commissioning or provider action be required before implementation of the proposition can occur?	**Service organisation action** Work to identify services is subject to a separate service specification proposal. In the interim, centres with some expertise would be required to identify any actions needed before implementation of the proposal can occur.
B3.2 **Time to implementation:** Is a lead-in time required prior to implementation?	**No - go to B3.4**
B3.3 **Time to implementation:** If lead-in time is required prior to implementation, will an interim plan for implementation be required?	
B3.4 Is a change in provider physical infrastructure required?	**No**
B3.5 Is a change in provider staffing required?	**No**

<table>
<tr><td>B3.6 Are there new clinical dependency and/or adjacency requirements that would need to be in place?</td><td><u>No</u></td></tr>
<tr><td>B3.7 Are there changes in the support services that need to be in place?</td><td><u>No</u></td></tr>
<tr><td>B3.8 Is there a change in provider and/or inter-provider governance required? (e.g. ODN arrangements / prime contractor)</td><td><u>No</u></td></tr>
<tr><td>B3.9 Is there likely to be either an increase or decrease in the number of commissioned providers? If yes, specify the current and estimated number of providers required in each region</td><td><u>No change</u>
No change to current service provision is anticipated due to the rarity of the condition and small number of patients.</td></tr>
<tr><td>B3.10 Specify how revised provision will be secured by NHS England as the responsible commissioner.</td><td>Select all that apply:
<table><tr><td>Publication and notification of new policy</td><td>☒</td></tr><tr><td>Market intervention required</td><td>☐</td></tr><tr><td>Competitive selection process to secure increase or decrease provider configuration</td><td>☐</td></tr><tr><td>Price-based selection process to maximise cost effectiveness</td><td>☐</td></tr><tr><td>Any qualified provider</td><td>☐</td></tr><tr><td>National Commercial Agreements e.g. drugs, devices</td><td>☐</td></tr><tr><td>Procurement</td><td>☐</td></tr><tr><td>Other</td><td>☐</td></tr></table></td></tr>
</table>

	There is parallel work currently happening to identify a service specification for cystinosis. In the interim the highly specialist team involves identification of providers.
B4 Place-based Commissioning	
B4.1 Is this service currently subject to, or planned for, place-based commissioning arrangements? (e.g. future CCG lead, devolved commissioning arrangements, STPs)	**No**
Section C - Finance Impact	
C1 Tariff/Pricing	
C1.1 How is the service contracted and/or charged? Only specify for the relevant section of the patient pathway	*Select all that apply:*

Drugs	Not separately charged – part of local or national tariffs	☐
	Excluded from tariff – pass through	☐
	Excluded from tariff - other	☒
Devices	Not separately charged – part of local or national tariffs	☐
	Excluded from tariff (excluding ZCM) – pass through	☐
	Excluded from tariff (excluding ZCM) – other	☐
	Via Zero Cost Model	☐
Activity	Paid entirely by National Tariffs	☐

		Paid entirely by Local Tariffs	☐
		Partially paid by National Tariffs	☐
		Partially paid by Local Tariffs	☐
		Part/fully paid under a Block arrangement	☐
		Part/fully paid under Pass-Through arrangements	☐
		Part/fully paid under Other arrangements	☒

C1.2 **Drug Costs** Where not included in national or local tariffs, list each drug or combination, dosage, quantity, **list** price including VAT if applicable and any other key information e.g. Chemotherapy Regime. NB discounted prices or local prices must not be included as these are subject to commercial confidentiality and must not be disclosed.	The **NHS list price** is £1,038 per vial (including VAT) for 7 days' supply. Estimated annual cost = £54,124. NHS England may stipulate that the treatment is prescribed through outsourced outpatient pharmacy or arrangements with specialist centres for home delivery. The resource impact assumes VAT at 20% is applicable to 85% of prescriptions. Around 15% of people are receiving the policy treatment via homecare. A homecare administrative charge of 10% has been assumed in line with previous NHSE policies.
C1.3 **Device Costs** Where not included in national or local tariff, list each element of the excluded device, quantity, **list or expected** price including VAT if applicable and any other key information. NB: Discounted prices or local prices must not be included as these are subject to commercial confidentiality and must not be disclosed.	Not applicable
C1.4 **Activity Costs covered by National Tariffs**	HRG codes, descriptions and tariffs applicable. (Please note these apply to both the current pathway and the new pathway). There are no

List all the HRG codes, HRG descriptions, national tariffs (excluding MFF), volume and other key costs (e.g. specialist top up %)	additional appointments expected in the proposed new pathway, therefore no additional costs are estimated). 2019/20 Tariff– non-specialist services TFC 130 Outpatient ophthalmology – first attendance £133 TFC 130 Outpatient ophthalmology – follow up £58 (2 per year) TFC 216 Paediatric ophthalmology – first attendance £133 TFC 216 Paediatric ophthalmology – follow up £79 (2 per year) BZ88A Retinal Tomography 19 years and older £96 (1 needed) BZ88A Retinal Tomography 18 years and under - £117 BZ24G Non-surgical ophthalmology without interventions CC score 0-1 £343 (1 needed for 20% of patients).
C1.5 **Activity Costs covered by Local Tariff** List all the HRGs (if applicable), HRG or local description, estimated average tariff, volume and any other key costs. Also indicate whether the Local Tariff(s) is/are newly proposed or established and if newly proposed how is has been derived, validated and tested.	Not applicable
C1.6 **Other Activity Costs not covered by National or Local Tariff** Include descriptions and estimates of all key costs.	Not applicable
C1.7 Are there any prior approval mechanisms required either during implementation or permanently?	**No**
C2 Average Cost per Patient	

C2.1 What is the estimated cost per patient to NHS England, in years 1-5, including follow-up where required?

YR1	£21,972
YR2	£48,700
YR3	£48,700
YR4	£48,700
YR5	£48,700

Are there any changes expected in year 6-10 which would impact the model?

The above estimated cost per person figures include VAT (at 20%) or homecare admin costs (at 10%).
There are cohorts of patients in Leeds and in the Midlands who are currently supplied the policy treatment via homecare. This is reflected in the resource impact work (15% of people receiving the drugs via homecare with the rest receiving treatment via their hospital prescriber). The admin costs have been applied to the cost of the current comparator treatment based on commissioner information. Homecare costs have been applied to the policy treatment based on information from the company.
The year 1 costs are lower because a part year effect of the annual treatment cost is assumed (50%). This allows for the timing of when the policy may be agreed in year, and when it is implemented.

C3 Overall Cost Impact of this Policy to NHS England

C3.1 Specify the budget impact of the proposal on NHS England in relation to the relevant pathway.

Cost pressure

The table below shows the estimated resource impact in years 1,2,5 and 10 (including VAT where applicable). The resource impact excludes the cost of assessment, monitoring and follow up costs which are not identified as being significantly different from the current costs associated

<table>
<tr><td></td><td>with cystinosis and unlicensed formulations of mercaptamine hydrochloride.

Estimated budget impact at list prices<table><tr><td>Year</td><td>£000</td></tr><tr><td>1</td><td>1,866</td></tr><tr><td>2</td><td>8,328</td></tr><tr><td>5</td><td>8,766</td></tr><tr><td>10</td><td>9,496</td></tr></table></td></tr>
<tr><td>C3.2 If the budget impact on NHS England cannot be identified set out the reasons why this cannot be measured.</td><td>Not applicable.</td></tr>
<tr><td>C3.3 If the activity is subject to a change of commissioning responsibility, from CCG to NHS England, has a methodology for the transfer of funds been identified, and calculated?</td><td>Not applicable</td></tr>
<tr><td colspan="2">C4 Overall cost impact of this policy to the NHS as a whole</td></tr>
<tr><td>C4.1 Specify the budget impact of the proposal on other parts of the NHS.</td><td>Budget impact for CCGs:
<u>No impact on CCGs</u>
Budget impact for providers:
<u>No impact on providers</u>
Please specify:</td></tr>
</table>

	The treatment and associated costs of mercaptamine hydrochloride fall within NHS specialised commissioning and would be commissioned by NHS England.
C4.2 Taking into account responses to C3.1 and C4.1, specify the budget impact to the NHS as a whole.	**Cost pressure** Please specify: The figures in C3.1 show that there is a resource impact to the commissioner (NHS England) from implementing the policy. The cost of mercaptamine hydrochloride is at list price.
C4.3 Where the budget impact is unknown set out the reasons why this cannot be measured	Not applicable.
C4.4 Are there likely to be any costs or savings for non-NHS commissioners and/or public sector funders?	**Unknown** Please specify:
C5 Funding	
C5.1 Where a cost pressure is indicated, state known source of funds for investment, where identified, e.g. decommissioning less clinically or cost-effective services.	CPAG prioritisation reserve.
C6 Financial Risks Associated with Implementing this Policy	
C6.1 What are the material financial risks to implementing this policy?	The treatment is high cost at between £45 and £49k more per person per year than the unlicensed comparator (depending on whether it is prescribed via the tertiary centre or delivered to the persons home as part

	of homecare arrangements). The published prevalence figures compared with actual known, diagnosed and treated patients differ considerably. The company has therefore used physician and patient association reported patient numbers.
C6.2 How can these risks be mitigated?	Blueteq could be used to ensure mercaptamine hydrochloride is used in accordance with the policy, and trend analysis could be used to look at the pattern of people continuing treatment and new people starting treatment over time. This should fall after prevalent cases are treated (estimated to occur from year 3). A discount could be agreed with the company and the service specification could require tertiary centres to have homecare arrangements to reduce the cost of treatment.
C6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	The resource impact assumes all people would have the licensed treatment if the policy is approved and that VAT is applicable to 85% of people treated. This is a maximum cost scenario.
C6.4 What scenario has been approved and why?	The maximum cost scenario has been used because it is anticipated that production of the unlicensed aqueous mercaptamine hydrochloride (made in hospital pharmacies) would eventually cease due to lack of demand if the policy is approved. The people who require the treatment are a very small population with specific needs that are not addressed with the current unlicensed option.
C7 Value for Money	
C7.1 What published evidence is available that the treatment is cost effective as evidenced in the evidence review?	**There is no published evidence of cost-effectiveness** The clinical evidence review for this technology found no studies relating to cost effectiveness.

<table>
<tr><td>C7.2 Has other data been identified through the service specification development relevant to the assessment of value for money?</td><td>Select all that apply:<table>
<tr><td>Available pricing data suggests the treatment is equivalent cost compared to current/comparator treatment</td><td>☐</td></tr>
<tr><td>Available pricing data suggests the treatment is lower cost compared to current/comparator treatment</td><td>☐</td></tr>
<tr><td>Available clinical practice data suggests the new treatment has the potential to improve value for money</td><td>☐</td></tr>
<tr><td>Other data has been identified</td><td>☐</td></tr>
<tr><td>No data has been identified</td><td>☐</td></tr>
<tr><td>The data supports a high level of certainty about the impact on value</td><td>☐</td></tr>
<tr><td>The data does not support a high level of certainty about the impact on value</td><td>☒</td></tr>
</table></td></tr>
<tr><td colspan="2">C8 Cost Profile</td></tr>
<tr><td>C8.1 Are there non-recurrent capital or revenue costs associated with this policy?</td><td><u>No</u></td></tr>
<tr><td>C8.2 If yes, confirm the source of funds to meet these costs.</td><td>Not applicable</td></tr>
</table>