Integrated Impact Assessment Report for Clinical Commissioning Policies			
Policy Reference Number	1696		
Policy Title	**Cholic acid and chenodeoxycholic acid for treating inborn errors of bile acid synthesis (all ages)** Proposal **for routine commission** (ref A3.1)		
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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.	Inborn errors of bile acid synthesis are very rare, and there are limited data available on incidence and prevalence, particularly for specific subtypes. The European public assessment report [EPAR] for Kolbam states the prevalence of people with inborn errors of bile acid synthesis in the EU is 0.07 per 10,000. Chenodeoxycholic acid Leadiant (CDCA Leadiant) Sterol 27-hydroxylase deficiency presenting as CTX (cerebrotendinous xanthomatosis) A bibliographic study of the epidemiology of rare diseases estimated that there are about 200 people in Europe with CTX (EURODIS and ORPHANET: Rare diseases in numbers). NHS England data suggests that 26 patients with CTX are currently being treated with chenodeoxycholic acid Leadiant (CDCA), there are 3 patients awaiting treatment for inborn liver synthesis and NHS England assumes that 2 of these are people with CTX. The company submission states that there are 2 children with CTX currently being treated with Kolbam. Therefore the population group is estimated to be 30 (23 adults and 7 children).Over the 10-year period modelled we are expecting growth in the eligible population by around 15% as per the company submission. Cholic Acid NHS England data suggests that currently there are 31 patients treated with cholic acid with the company submission suggesting that there are 2

	patients receiving Kolbam off license instead of CDCA Leadiant. It is also assumed that 1 of the 3 patients awaiting treatment is for 3beta-HSD or 5beta-reductase .Therefore there are 30 eligible patients across the 2 Cholic Acid treatment groups. 3beta-HSD and 5 beta-reductase deficiency (Orphacol) The prevalence of 3beta-HSD and 5 beta-reductase deficiency is estimated to be 4.4 per 10 million which equates to 24 people in total. (The statement of product characteristics (SPC) for Orphacol estimates there are 3 to 5 cases per million for people with 3beta-HSD deficiency, and a tenfold lower prevalence for 5beta-reductase deficiency). NHS England data suggests that in the population of England that this rate is slightly higher than the average at around 4.9 per 10 million equating to 28 patients overall (22 adults and 6 children). It is assumed that 1 of the 3 patients awaiting treatment is an adult for Orphacol. It is assumed that the growth in the eligible population will be in line with general population growth, this equates to 1 extra person across the patient. AMACR (alpha-methylacyl-CoA racemase) and CYP7A1 (Cholesterol 7 alpha-hydroxylase) (Kolbam) The prevalence of AMACR and CYP7A1 is very low with only 24 cases confirmed worldwide. NHS England data suggests that this is 2 people in England (1 adults and 1 child). It is assumed that the growth in the eligible population will be in line with general population growth, we do not expect any additional people eligible for treatment over the period. Summary

	In summary, the total eligible population for both drugs in England is approximately **60** people, based on: • CTX: 30 people • 3beta-HSD deficiency and 5beta reductase deficiency: 28 people • AMACR: unknown, but unlikely to be more than 1 person • CYP7A1: unknown, unlikely to be more than 1 person *Source: Company submission for CDCA Leadiant / NHS England*
A1.2 Number of patients currently eligible for the treatment according to the proposed policy commissioning criteria.	Summary 60 patients in total as per A1.1. NHS England data suggest that 57 people are currently receiving CDCA Leadiant or cholic acid under interim agreement and that there are 3 patients awaiting treatment *CDCA Leadiant* All 30 patients as per A1.1 *Kolbam* All 2 patients as per A1.1. Please note that the draft policy proposition states that Kolbam should be used as a second line treatment for CTX. However it is assumed that those starting treatment with CDCA Leadiant for CTX would stay on this treatment indefinitely as per the clinical experts on the PWG.

	Orphacol All 28 patients as per A1.1 *Source: NHS England*
A1.3 Age group for which the treatment is proposed according to the policy commissioning criteria.	**Other** From 1 month onwards.
A1.4 Age distribution of the patient population eligible according to the proposed policy commissioning criteria	46 adults and 14 children *Source: NHS England / Company submission for CDCA Leadiant*
A1.5 How is the population currently distributed geographically?	**Unevenly** *Source: NHS England* Patients are treated in a range of providers across England. London – 33 Patients Midlands and East – 11 Patients North – 13 Patients South – 0 patients With 3 patients awaiting treatment with location unknown.

A2 Future Patient Population & Demography

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?

Increasing

It is estimated that the prevalence of CTX will increase by 15% over the 10-year period. For 3-beta-HSD & 5beta reductase and AMACR & CYP7A1 deficiencies we expect growth to be in line with the growth the general population.

Source: Company submission for CDCA Leadiant

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

Not known

Potential changes in demography are unknown

Source: N/A

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?

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

	Inborn error bile acid synthesis subtype		
	CTX (CDCA Leadiant)	3beta-HSD & 5beta reductase deficiencies (Orphacol)	AMACR & CYP7A1 (Kolbam)
YR2 +/-	+1	-	-
YR3 +/-	+1	-	-
YR4 +/-	+2	-	-
YR5 +/-	+2	-	-

	<table><tr><td>YR10 +/-</td><td>+5</td><td>+1</td><td>-</td></tr></table> *Source: Company submission for CDCA Leadiant / NHS England* **No** The company submission believes that the population groups with inborn liver synthesis disorders will increase by 15% over the period for CTX and the clinical experts have advised that they think in the 3beta-HSD & 5beta reductase and AMACR and CYP7A1 deficiencies that the growth will be in line with the growth in the general population.
A3 Activity	
A3.1 What is the purpose of new policy?	**Other** There are currently 57 people on cholic acid or chenodeoxycholic acid who had already started on the treatments when they were previously available as off label treatments, these patients are being funded temporarily through individual funding requests whilst polices to support commissioning are being developed. This began for Cholic Acid in April 2016 and Chenodeoxycholic Acid in April 2017. The policy looks at the long-term treatment of these people, the incident population and people awaiting treatment (3 people currently)
A3.2 What is the annual activity associated with the existing pathway for the eligible population?	The estimated annual number of people across the 5 relevant subpopulations of inborn liver synthesis deficiency groups are estimated to be as below: All Ages

	<table><tr><th></th><th>CTX (CDCA Leadiant)</th><th>3beta-HSD and 5 beta-reductase (Orphacol)</th><th>AMACR and CYP7A1 (Kolbam)</th><th>Total</th></tr><tr><td>YR1</td><td>31</td><td>28</td><td>2</td><td>60</td></tr><tr><td>YR2</td><td>31</td><td>28</td><td>2</td><td>61</td></tr><tr><td>YR5</td><td>32</td><td>28</td><td>2</td><td>62</td></tr><tr><td>YR10</td><td>35</td><td>29</td><td>2</td><td>66</td></tr></table> *Source: NHS England* There are currently 57 people known to be on either CDCA Leadiant or cholic acid as of March 2018. NHS England is also aware of 3 people awaiting treatment. We expect all of these people to continue or be offered the treatment. We are expecting growth of around 15% across the CTX group and growth in line with the general population in the other 2 groups.
A3.3 What is the estimated annual activity associated with the proposed policy proposition pathway for the eligible population?	Please see A3.2, all patients who be eligible for treatment.
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 *Source: PWG* CDCA Leadiant and cholic acid are the only available treatments.
A4 Existing Patient Pathway	

A4.1 **Existing pathway:** Describe the relevant currently routinely commissioned: • Treatment or intervention • Patient pathway • Eligibility and/or uptake estimates.	Currently there are 57 people on either cholic acid (31) or chenodeoxycholic acid (26). NHS England agreed to fund existing patients from April 2017 whilst the policy was developed. Patients presenting after that date have to apply for treatment through the IFR process. Less than 5 patients are waiting for treatment currently. *Source: NHS England/PWG*
A4.2. What are the current treatment access and stopping criteria?	The treatment is only available to people already being treated with CDCA Leadiant and cholic acid (through individual funding requests). At present NHS England will not fund treatment for any people currently not on the treatment. *Source:* NHS England/PWG
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?	If not known, please specify a) 100% b) 0% c) 100% d) 100% e) 100% *Source: PWG 26th March*
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** – People with inborn errors of bile acid synthesis currently receive cholic acid or chenodeoxycholic acid in NHS practice.

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: PWG 26th March*
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?	Total estimated eligible a) N/A b) N/A c) N/A d) N/A e) N/A *Source: PWG 26th March*
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?	If not known, please specify a) 100% b) 0% c) 100% d) 100% e) 100% *Source:* PWG 26th March
A6.2 Specify the nature and duration of the proposed new treatment or intervention.	**Life long**

	Chenodeoxycholic acid Leadiant (CDCA Leadiant) CDCA Leadiant is a lifelong treatment. The treatment is taken orally daily. It is available in 250mg capsules. For adults the starting dose is 750mg over 3 doses and can be increased to a maximum dose of 1,000mg daily. For children the starting dose is 5mg per kg divided into 3 doses per day. It can be increased to up to 15mg per kg per day over 3 doses if needed. When the dose calculated is not a multiple of 250mg, the nearest dose below the maximum over 15mg per kg per day should be selected. Cholic Acid Orphacol Orphacol is a lifelong treatment. The treatment is taken orally. It is available in 50mg and 250mg capsules. The minimum dose for all ages is 50mg and the dose should not exceed 500mg. The dose is adjusted in 50mg steps, the dose range is 5mg to 15mg per kg per day. Kolbam Kolbam is a lifelong treatment. The treatment is taken orally. It is available in 50mg and 250mg capsules.

	The recommended daily dose of Kolbam is 10mg to 15mg per kg It should not exceed 15mg per kg per day and the lowest dose should be chosen. Please be aware the current availability of Kolbam in England is currently limited. *Source: Clinical evidence reviews*
A7 Treatment Setting	
A7.1 How is this treatment delivered to the patient?	*Select all that apply:* Emergency/Urgent care attendance ☐ Acute Trust: inpatient ☒ Acute Trust: day patient ☒ Acute Trust: outpatient ☒ Mental Health provider: inpatient ☐ Mental Health provider: outpatient ☐ Community setting ☐ Homecare ☒ Other ☐ Please specify: It is anticipated that the drug will be delivered to people through an outpatient setting and subsequently by homecare. There may be some

	cases where patients are treated as an inpatient or through a day case unit.
A7.2 What is the current number of contracted providers for the eligible population by region?	<table><tr><td>NORTH</td><td>8</td></tr><tr><td>MIDLANDS & EAST</td><td>3</td></tr><tr><td>LONDON</td><td>6</td></tr><tr><td>SOUTH</td><td>0</td></tr></table> *Source: NHS England, people currently treated*
A7.3 Does the proposition require a change of delivery setting or capacity requirements?	**No** Please specify: The vast majority of eligible people are already being treated presently with either CDCA Leadiant or cholic acid. The treatment is to be taken at home and it would not require any additional outpatient appointments. *Source: PWG 26th March*
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:* <table><tr><td>Aggregate Contract Monitoring *</td><td>☒</td></tr><tr><td>Patient level contract monitoring</td><td>☒</td></tr><tr><td>Patient level drugs dataset</td><td>☒</td></tr><tr><td>Patient level devices dataset</td><td>☐</td></tr><tr><td>Devices supply chain reconciliation dataset</td><td>☐</td></tr></table>

	<table><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:
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?	**<u>Already specified in current NHS England Drugs List document</u>** If the drug has already been specified in the current NHS England Drug List please specify drug name and drug indication: the drugs are currently included on the list as Chenodeoxycholic acid for Cerebrotendinous xanthomatosis and primary biliary cirrhosis Cholic acid for inborn errors of primary bile acid synthesis Neither drug is routinely commissioned.

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 correctly captured by an existing specialised service line (NCBPS code within the PSS Tool** If activity costs are already captured please specify the specialised service code and description (e.g. NCBPS01C Chemotherapy). NCBPSC23 specialist paediatric liver disease / NCBPS36Z Metabolic disorders If activity costs are already captured please specify whether this service needs a separate code. **No** If the activity is captured but the service line needs amendment please specify whether the proposed amendments have been documented and agreed with the Identification Rules team **N/A** If the activity is not captured please specify whether the proposed identification rules have been documented and agreed with the Identification Rules team. **No**
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)**	*Select all that apply:*

For treatments which are tariff excluded drugs or devices not covered by the Zero Cost Model, specify the pharmacy or device monitoring required, for example reporting or use of prior approval systems.	<table><tr><td>Drugs or Device MDS</td><td>☐</td></tr><tr><td>Blueteq</td><td>☒</td></tr><tr><td>Other prior approval</td><td>☐</td></tr></table> Please specify: Individual funding request (IFR) is used at present, it is anticipated that Blueteq would be used if the policy was approved.
A9.3 **Business intelligence** Is there potential for duplicate reporting?	**No**
A9.4 **Contract monitoring** Is this part of routine contract monitoring?	**Yes**
A9.5 **Dashboard reporting** Specify whether a dashboard exists for the proposed intervention?	**No** If no, will one be developed? 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?	**No**
Section B - Service Impact	
B1 Service Organisation	
B1.1 Describe how the service is currently organised? (i.e. tertiary centres, networked provision etc.)	Patients with these rare conditions are treated in a number of specialist liver and metabolic units across the country.

<table>
<tr><td></td><td>Source: NHS England</td></tr>
<tr><td>B1.2 Will the proposition change the way the commissioned service is organised?</td><td><u>No</u>
Please specify:
There will be minimal impact on the current service organisation.
Source: PWG 26th March</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>
Please specify:
There will be minimal impact on the current approach to the organisation with 57 of 60 eligible people currently being treated.</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>Please specify:
Most referrals are from secondary or tertiary care but it is known of at least 1 person that is treated in a primary care setting.</td></tr>
<tr><td>B2.2 What impact will the new policy have on the sources of referral?</td><td><u>No impact</u>
Please specify:
The impact on current working practice will be minimal.</td></tr>
</table>

B2.3 Is the new policy likely to improve equity of access?	**Increase** Please specify: People who present with the conditions will not be eligible for treatment, therefore the new policy would improve equity of access. *Source: NHS England*
B2.4 Is the new policy likely to improve equality of access and/or outcomes?	**Increase** Please specify: Please specify: all newly presenting patients who meet the criteria in the policy will be eligible for treatment; currently newly presenting patients have to go through the IFR process. *Source: NHS England*
B3 Implementation	
B3.1 Will commissioning or provider action be required before implementation of the proposition can occur?	**No action required** Please specify: 57 of 60 people with the conditions are already being treated and the other 3 people are known to NHS England.
B3.2 **Time to implementation:** Is a lead-in time required prior to implementation?	**No - go to B3.4** If yes, specify the likely time to implementation:
B3.3 **Time to implementation:** If lead-in time is required prior to implementation, will an interim plan for implementation be required?	**No - go to B3.4** If yes, outline the plan:
B3.4 Is a change in provider physical infrastructure required?	**No** Please specify:

<table>
<tr><td>B3.5 Is a change in provider staffing required?</td><td><u>No</u>
Please specify:</td></tr>
<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>
Please specify:</td></tr>
<tr><td>B3.7 Are there changes in the support services that need to be in place?</td><td><u>No</u>
Please specify:</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>
Please specify:</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>

The impact on current working practice will be minimal.</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></table></td></tr>
</table>

	Other ☐ Please specify:
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** Please specify: These are expensive treatments prescribed from a small number of centres and would be a burden to CCGs if they had to assume the commissioning responsibility for these drugs
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	☐

Drugs - Both Chenodeoxycholic acid and cholic acid are on the NHS England excluded drug list and therefore would be excluded from tariff as pass through.

The small number of additional MRI and outpatient appointments are covered by national tariff. These appointments will only be for the incident population and those patients waiting for treatment presently.

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.

It is assumed that all the below treatments will be homecare and therefore be VAT free.

Adults

Chenodeoxycholic Acid – £153,302 per year, a pack of 100 tablets at £14,000. Based on a dose of 250mg, 3 times a day.

Orphacol – £160,888 per year, a pack of 30 tablets at £6,630. Based on a dose of 250mg, twice a day.

	Kolbam – £137,592 per year, a pack of 90 tablets at £11,340. Based on an average dose of 250mg, 3 times a day. **<u>Children</u>** Chenodeoxycholic Acid – £101,920 per year, a pack of 100 tablets at £14,000. Based on a dose of 250mg, twice a day. Orphacol – £80,444 per year, a pack of 30 tablets at £6,630. Based on a dose of 250mg, once per day. Kolbam – £91,728 per year, pack of 90 tablets at £11,340. Based on an average dose of 250mg, 2 times a day. **All of the above costs are at list price and do not include VAT**
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.	N/A
C1.4 **Activity Costs covered by National Tariffs** List all the HRG codes, HRG descriptions, national tariffs (excluding MFF), volume and other key costs (e.g. specialist top up %)	**<u>All prices national tariff 18/19 excluding market forces factor (MFF)</u>** Magnetic resonance imaging scan of 1 area without contrast, 19 years or over RD01A - £114 Magnetic resonance imaging scan of 1 area without contrast, between 6 and 18 years RD01B - £120

	Magnetic Resonance Imaging Scan of 1 Area, without Contrast, 5 years and under RD01C - £132 Hepatobiliary & Pancreatic Surgery outpatient follow up single professional - WF01A - £105 Hepatology follow up outpatient single professional WF01A - £134 Neurology follow up outpatient single professional WF01A - £172 Paediatric Neurology follow up outpatient single professional WF01A - £363
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.	N/A
C1.6 **Other Activity Costs not covered by National or Local Tariff** Include descriptions and estimates of all key costs.	N/A
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?

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

	CTX (CDCA Leadiant)	3beta-HSD and 5 beta-reductase (Orphacol)	AMACR and CYP7A1 (Kolbam)
Year 1	£TBC	£TBC	£TBC
Year 2	£TBC	£TBC	£TBC
Year 3	£TBC	£TBC	£TBC
Year 4	£TBC	£TBC	£TBC
Year 5	£TBC	£TBC	£TBC

If yes, please specify:

There is a slight increase in numbers of people with CTX relative to population growth because of an estimated increase in prevalence. For the other 2 groups' growth is expected to be in line with population growth.

C3 Overall Cost Impact of this Policy to NHS England

<table>
<tr>
<td>C3.1 Specify the budget impact of the proposal on NHS England in relation to the relevant pathway.</td>
<td><u>Cost pressure</u>

Please specify:

<table>
<tr><th></th><th>Chenodeoxycholic Acid</th><th>Orphacol</th><th>Kolbam</th><th>Total</th></tr>
<tr><td>Year 1 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
<tr><td>Year 2 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
<tr><td>Year 5 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
<tr><td>Year 10 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</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>N/A</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>N/A</td>
</tr>
<tr>
<td colspan="2">C4 Overall cost impact of this policy to the NHS as a whole</td>
</tr>
</table>

<table>
<tr>
<td>C4.1 Specify the budget impact of the proposal on other parts of the NHS.</td>
<td>Budget impact for CCGs: The cost of reimbursing providers for additional tests and outpatient appointments for new appointments is not expected to be significant, less than £1,000 per year nationally.
<u>Cost neutral</u>
Budget impact for providers: There may be some additional tests and outpatient appointments for people newly starting treatment, these numbers are not expected to be significant, less than £1,000 per year nationally.
<u>Cost neutral</u>
The additional pressure on CCG’s will be the cost of reimbursing the providers for the additional tests and appointments as set out in the starting and monitoring as part of potential stopping criteria.</td>
</tr>
<tr>
<td>C4.2 Taking into account responses to C3.1 and C4.1, specify the budget impact to the NHS as a whole.</td>
<td><u>Cost pressure</u>
Please specify:

The below table shows the annual cost of treatment in years 1,2,5 and 10 using list prices and exclusive of VAT

<table>
<tr><th></th><th>Chenodeoxycholic Acid</th><th>Orphacol</th><th>Kolbam</th><th>Total</th></tr>
<tr><td>Year 1 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
<tr><td>Year 2 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
<tr><td>Year 5 (£) m</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
<tr><td>Year 10 (£)</td><td>£TBC</td><td>£TBC</td><td>£TBC</td><td>£TBC</td></tr>
</table>
</td>
</tr>
</table>

C4.3 Where the budget impact is unknown set out the reasons why this cannot be measured	N/A
C4.4 Are there likely to be any costs or savings for non-NHS commissioners and/or public sector funders?	**No** There is minimal impact on current practice.
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 epidemiology of inborn liver synthesis deficiencies are uncertain. The company submission for chenodeoxycholic acid Leadiant has predicted 15% growth over the period. However 57 of 60 known people with the condition are already on the treatments.
C6.2 How can these risks be mitigated?	A prior approval mechanism will be used to ensure chenodeoxycholic acid, Orphacol and Kolbam are used at the correct point in the pathway, and trend analysis could be used to assess whether the correct questions are being asked to ensure proper use within the policy. Blueteq will also be used to monitor the uptake of the treatments.

C6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	The scenario for profile of uptake was discussed with clinical experts at the policy working group meeting. It was highlighted that initial uptake could be as high as 100% of the eligible population. We have used a growth rate of 15% for CDCA Leadiant patients over the 10-year period which is modelled in the resource impact template and growth in line with population growth for the cholic acid patients.
C6.4 What scenario has been approved and why?	The scenario of uptake in the resource impact template was agreed with clinical experts at the policy working group on the 26th March 2018. We have used this scenario because it is based on clinical experience and knowledge of each patient group.
C7 Value for Money	
C7.1 What published evidence is available that the treatment is cost effective as evidenced in the evidence review?	**A cost-effectiveness evidence review has not been undertaken.** .
C7.2 Has other data been identified through the service specification development relevant to the assessment of value for money?	*Select all that apply:* Available pricing data suggests the treatment is equivalent cost compared to current/comparator treatment ☐ Available pricing data suggests the treatment is lower cost compared to current/comparator treatment ☐ Available clinical practice data suggests the new treatment has the potential to improve value for money ☐ Other data has been identified ☐ No data has been identified ☒

	The data supports a high level of certainty about the impact on value	☐
	The data does not support a high level of certainty about the impact on value	☐
C8 Cost Profile		
C8.1 Are there non-recurrent capital or revenue costs associated with this policy?	**No**	
C8.2 If yes, confirm the source of funds to meet these costs.	N/A	