Integrated Impact Assessment Report for Clinical Commissioning Policies			
Policy Reference Number	1679		
Policy Title	Lomitapide for homozygous familial hypercholesterolaemia Proposal **for routine commission** (ref A3.1)		
Lead Commissioner	Sarah Watson	**Clinical Lead**	Handrean Soran
Finance Lead	Craig Charlton	**Analytical Lead**	Click here to enter text.

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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.	The prevalence of homozygous familial hypercholesterolaemia (HoFH) in England is estimated to be 1 per 670,000 adults. There is no published incidence rate however the company have given an estimate (based on life prevalence/life expectancy) of 1 per 50 million population. Using these estimates, the current number of people in England with HoFH is 66. This is expected to increase by one person per year in line with the incidence rate over 10 years. There may be some reduction in the number of people with this condition over the time frame due to the high mortality rate, this is taken into account in the number of people continuing treatment each year in the resource impact model. *Source: Company submission Appendix 2 p66. Based on data from Sjouke (2014) Proportion of HoFH patients that clinically present. The incidence rate is estimated in the company submission p10 to equate to about 1 per 50 million.*
A1.2 Number of patients currently eligible for the treatment according to the proposed policy commissioning criteria.	The estimated number of people currently eligible for treatment is 47, of whom 34 people are eligible to receive long-term treatment with lomitapide. *Source: Company submission, Appendix 2, table 17 (pathway) – assumptions adjusted for expert opinion on people who are non-responsive to PCSK9 inhibitors.* Lomitapide should only be considered when HoFH is not adequately controlled by existing treatments and people are at high risk of cardiovascular events: • Approximately 22% (**14 people**) with HoFH have disease that is low density lipoprotein receptor (LDLR) negative (based on combining published data from registries in Spain, Sánchez-Hernández, 2016 and Alonso, 2016). LDLR negative disease does not respond to PCSK-9 inhibitors (France et al. 2016), these patients would be eligible for lomitapide. • The remaining 78% (51 people) would try a PCSK-9 inhibitor: ○ Approximately 30% of these 52 people would have disease that does not respond to treatment (Raal et al. 2017 (**15 people**) and therefore would be eligible for lomitapide.

	○ Approximately 70% of these 52 people would respond to PCSK9 (36 people) and 50% of these people would have disease that initially responds but does not reach the recommended low density lipoprotein cholesterol (LDL-C) target. This is an estimate by the company who market lomitapide and is adjusted to reflect the mid-point estimate, after discussion with clinical experts from the policy working group. These people will also be eligible for lomitapide (**18 people**). • The number of people eligible for lomitapide would be **47** (14+15+18). But of these 28% (based on the LOWER registry), would be unwilling or unable to commit to the low-fat diet required to take lomitapide, avoid alcohol, or because of co-morbidities resulting in liver toxicity concerns. Therefore it is estimated that **34** people (72% of those eligible for lomitapide) will be suitable for long term treatment. It is estimated this figure will remain reasonably consistent per year. **Please note: The actual number of people who receive treatment is different. This is based on uptake estimates from the company adjusted for clinical expert opinion and profiled over time, with any new cases offset in future years by people stopping treatment because of lack of effectiveness, adverse events or death. The resource impact model estimates the number of people receiving treatment over a 10 year period (see A3.3 below).**
A1.3 Age group for which the treatment is proposed according to the policy commissioning criteria.	**Adults** The company's summary of product characteristics states: The safety and efficacy of lomitapide in children < 18 years have not been established and the use of this medicinal product in children is therefore not recommended. No data are available. Therefore the population used is people aged 18 and over.
A1.4 Age distribution of the patient population eligible according to the proposed policy commissioning criteria	All adults (people aged 18 and over) who are eligible may receive lomitapide
A1.5 How is the population currently distributed geographically?	**Unevenly**

North	22%
Midlands & East	19%
London	31%
South	28%

Source: Company submission Part 3 – Budget and service impact p45.

The distribution is based on research conducted on behalf of Amryt Pharma in 2012. The company do not believe the geographical distribution of patients will have changed significantly since 2012.

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

Projected change in epidemiology	**Year 2**	**Year 5**	**Year 10**
Prevalence	66	67	70
Incidence	1	1	1
Target population:			
Total adult HoFH patients with LDL-C levels above target (people eligible for lomitapide)	49	49	51
Number of people suitable for long term treatment (72%)	35	36	37

These figures are based on the company submission (referenced in 1.2 above, and adjusted after discussion with clinical experts from the policy working group according to people seen in clinical practice). **Of the 35-37 people suitable for long term treatment, a further assumption is made on people who take up treatment according to clinical expert opinion. Uptake is assumed to reach a maximum of 50% by year 4 (see A3.3 below and 'assumptions input sheet' of the resource impact template).**

<table>
<tr><td></td><td>Source: Company submission p10, incidence around 1 in 50 million people, this gives an increase of one person per year. In addition, if lomitapide is funded, the company anticipate there would be an increase in the prevalent HoFH population through an improved life expectancy. However a potential increase in patient numbers for this could not be modelled based on the information available today (p46 company submission).</td></tr>
<tr><td>A2.2 Are there likely to be changes in demography of the patient population and would this impact on activity/outcomes?</td><td><u>No</u>
The cities with tertiary referral centres may influence the distribution of patients.
Source: Company submission p46.</td></tr>
<tr><td>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.</td><td><table><tr><td>YR2 +/-</td><td>+1</td></tr><tr><td>YR3 +/-</td><td>+1</td></tr><tr><td>YR4 +/-</td><td>+1</td></tr><tr><td>YR5 +/-</td><td>+2</td></tr><tr><td>YR10 +/-</td><td>+3</td></tr></table>The figures above relate to people continuing treatment with lomitapide.
Source: Resource impact template based on assumptions in A1.2 above.

<u>Yes</u>
The ONS growth assumptions for the age specific population are the starting point for eligible population estimates.</td></tr>
<tr><td colspan="2">A3 Activity</td></tr>
</table>

<table>
<tr><td>A3.1 What is the purpose of new policy?</td><td><u>Confirm routine commissioning position of an additional new treatment</u>
The purpose of the new policy is to propose lomitapide as an adjuvant treatment for adults with homozygous familial hypercholesterolaemia. Lomitapide is indicated as an adjunct to a low-fat diet and other lipid-lowering medicinal products with or without LDL apheresis in adults with homozygous familial hypercholesterolaemia. Lomitapide is given if the disease progresses despite previous treatments, and provides an additional treatment option before the consideration of liver transplant.</td></tr>
<tr><td>A3.2 What is the annual activity associated with the existing pathway for the eligible population?</td><td>The estimated number of people currently receiving standard care (high dose statins and ezetimibe) is 47. This number is expected to increase steadily up to 51 by year 10.
Of the 47 people, it is assumed that 100% would need adjunctive treatment with apheresis.
A small percentage 11% (5 people) would also require add on treatment with evolocumab.

Source: Company submission Table 3 p16. Comparator treatments in current pathway of care - lomitapide is indicated as an adjunct treatment to a low fat diet and other lipid-lowering medicinal products with or without low density protein (LDL) apheresis in adult patients with homozygous familial hypercholesterolemia (HoFH). The percentage of people whose LDL-C levels are not adequately controlled by statins and/or ezetemibe is taken from the costing assumptions for NICE TA393 Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia and TA394 Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia, and also uses data from the company submission for ezetemibe (Sanofi). This is adjusted for NHSE data on current notifications for evolocumab. People who also need adjunctive treatment with apheresis is based on clinical expert opinion.</td></tr>
<tr><td>A3.3 What is the estimated annual activity associated with the proposed policy proposition pathway for the eligible population?</td><td>The estimated annual number of people eligible for lomitapide and the estimated number of people who actually receive lomitapide is shown below. This is an extract from the resource impact template.
Source: Estimates and assumptions are based on the company submission and clinical expert input.
People eligible for treatment with lomitapide and people who actually receive lomitapide
<table>
<tr><td>Year:</td><td>Number of people eligible</td><td>Number of people</td></tr>
</table>
</td></tr>
</table>

		treated
Year 1	48	17
Year 2	49	14
Year 5	49	17
Year 10	51	18

The number of people who actually receive treatment with lomitapide is lower because not all people eligible may take up treatment due to contraindications and the lifestyle restrictions imposed. Uptake is based on clinical expert opinion which suggests 50% uptake factored across the years. The number of people treated also takes into account that not all people are suitable for long term treatment (28% not suitable per A1.2 above), therefore there is a drop in year 2 reflecting this. The number of people treated in future years begins to rise steadily until 50% uptake is reached by year 4.

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.

The estimated number of people currently receiving standard care (high dose statins and ezetimibe) is 47. This number is expected to increase steadily up to 51 by year 10.

Of the 47 people, it is assumed that 100% would need adjunctive treatment with apheresis.

A small percentage 11% (5 people) would also require add on treatment with evolocumab

Source: Company submission Table 3 p16. Comparator treatments in current pathway of care - lomitapide is indicated as an adjunct treatment to a low fat diet and other lipid-lowering medicinal products with or without low density protein (LDL) apheresis in adult patients with homozygous familial hypercholesterolemia (HoFH). The percentage of people whose LDL-C levels are not adequately controlled by statins and/or ezetemibe is taken from the costing assumptions for NICE TA393 Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia and TA394 Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia, and also uses data from the company submission for ezetemibe (Sanofi). This is adjusted for NHSE data on current notifications for evolocumab. People who also need adjunctive treatment with apheresis is based on clinical expert opinion..

Click here to enter text.

A4 Existing Patient Pathway

A4.1 **Existing pathway:** Describe the relevant currently routinely commissioned:

- Treatment or intervention
- Patient pathway
- Eligibility and/or uptake estimates.

There are several treatments available for people with HoFH. These include:

- Dietary and lifestyle advice. This may include advice on smoking cessation, diet, weight loss and physical activity. This is usually given in combination with one or more medical treatments for HoFH.
- Statins. These drugs block the enzyme (a type of chemical) in a person's liver that helps to make cholesterol. This leads to a reduction in your blood cholesterol level. This is usually the first cholesterol lowering drug given to people with HoFH.
- Additional cholesterol-lowering drugs given in combination with statins: such as ezetimibe, fibrates, bile acid sequestrants, and PCSK-9 inhibitors.
- Lipoprotein apheresis. This involves using a machine to filter the blood and remove cholesterol. This is only offered to patients with HoFH and LDL-C that remains persistently high despite maximum medical therapy.
- Liver transplant, with or without a heart transplant. This may be considered if the disease progresses despite all the above described treatments. This procedure is performed very rarely for people with HoFH because of a lack of donor organs.

Existing patient pathway:
Once a person is diagnosed with HoFH they are given treatment to reduce LDL-C which includes lifestyle management (diet, exercise), lipid-lowering treatments including statins, ezetimibe and bile acid sequestrants. Evolocumab (a PCSK9 inhibitor) is given where people have not achieved LDL-C target. If their condition responds to this treatment, monitoring takes place for changes in LDL-C levels and cardiovascular disease. If a person's condition does not respond to a PCSK9, monitoring takes place for progressive heart disease along with assessment for liver transplant waiting list.

Source: Figure 1 company submission p15. The current pathway above summarises how existing treatments are used in England.

Eligibility and uptake estimates of current treatments are:

Treatment	%	Year 1	Year 2	Year 5	Year 10
People receiving high dose statins and ezetemibe	100	48	49	49	51

	People who also receive adjunctive apheresis	100	48	49	49	51
	People who also receive adjunctive treatment with evolocumab	11	5	5	5	6

A4.2. What are the current treatment access and stopping criteria?	There are 200 lipid clinics in the UK. There are 6 tertiary centres in England. Around 60% of people with HoFH are treated at one of the six tertiary centres. The remaining 40% of people are treated at their local lipid clinics. Specific therapeutic targets for LDL-C lowering in HoFH are set by HEART UK and the European Atherosclerosis Society (EAS) at LDL-C of less than 2.5 mmol/L 100 mg/dL) for adults, or less than 1.8 mmol/L (70 mg/dL) in adults with clinical atherosclerotic cardiovascular disease. There is therefore generally a stepped approach to the treatment pathway – if patients have HoFH with LDL-C above these levels, this carries an increased risk of adverse cardiovascular events, and patients and their clinicians would consider adding the next treatment to reduce levels of LDL-C. The NICE guideline on the identification and management of familial hypercholesterolaemia, recommends statins as the initial treatment for all adults with familial hypercholesterolaemia (FH) in addition to dietary and lifestyle advice. The NICE guidance does not contain any other recommendations for specific medicines that should be given in combination with a statin for people with HoFH; it instead states that prescribing of medicines for adults with HoFH should be undertaken within a specialist centre. In clinical practice, ezetimibe with or without a bile acid sequestrant would first be added to a statin. The PCSK-9 inhibitor, evolocumab, would then be offered. However, France et al. 2016 states that evolocumab would only be given to patients who have HoFH that is either LDLR defective or unknown, because receptor negative patients do not respond to PSCK9 inhibitors (although if testing was not possible, this treatment may be tried first). Lipoprotein apheresis would then be offered, depending on the response to treatment and presence of coronary heart disease. If disease progression occurs despite treatment with lipid-lowering medication and lipoprotein apheresis, liver transplantation would be considered, although this is rare because of a lack of donor organs. *Source: Policy proposition section 8 and 9*
A4.3 What percentage of the total eligible population is expected to: a) Be clinically assessed for treatment	a) 100% b) 78% of people try a PCSK-9 inhibitor and 70% of these people will respond to a PCSK-9 inhibitor c) 100%

b) Be considered to meet an exclusion criteria following assessment c) Choose to initiate treatment d) Comply with treatment e) Complete treatment?	d) 100% e) 100% *Source: Company submission, Appendix 2, table 17 (pathway) – assumptions adjusted for expert opinion on people who are non-responsive to PCSK9 inhibitors.*
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**: 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*	**No** Lomitapide is thought to inhibit a protein in the body known as microsomal triglyceride transfer protein. This is involved in assembling fatty substances into larger particles, which are then released into the blood stream. The European public assessment report [EPAR] states that lomitapide represents a new class of drugs with a mechanism of action that differs from those of other classes of lipid-lowering medicines.
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	N/A

e) Complete treatment?	
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?	Per A4.3 above: a) 100% b) 78% of people try a PCSK-9 inhibitor and 70% of these people will respond to a PCSK-9 inhibitor c) 30% have disease that does not respond to a PCSK-9 inhibitor. Of the 70% who do respond to a PCSK-9 inhibitor, 50% respond initially but do not reach recommended LDL-C target – these groups choose to initiate other treatment d) Of the people eligible for lomitapide, 28% may be unwilling or unable to commit to a low fat diet, the remaining: e) 72% complete treatment *Source: Company submission, Appendix 2, table 17 (pathway) – assumptions adjusted for expert opinion on people who are non-responsive to PCSK9 inhibitors.*
A6.2 Specify the nature and duration of the proposed new treatment or intervention.	**Life long** Around 72% of people eligible who will receive lomitapide will be suitable for long term treatment. *Source: Company submission p64 and Table 17.*
A7 Treatment Setting	
A7.1 How is this treatment	*Select all that apply:*

delivered to the patient?	<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> Lomitapide capsules would be delivered to the patient at home. However it is envisaged by the company that initiation treatment with lomitapide, initial monitoring and dose changes would be carried out at the tertiary treatment centres (or in conjunction with them, e.g. via telephone consultation). Once a person is stabilised on lomitapide, then repeat prescriptions could be provided locally (and delivered via home delivery).
A7.2 What is the current number of contracted providers for the eligible population by region?	<table><tr><td>NORTH</td><td>1</td></tr><tr><td>MIDLANDS & EAST</td><td>2</td></tr><tr><td>LONDON</td><td>2</td></tr><tr><td>SOUTH</td><td>1</td></tr></table>

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	

Aggregate Contract Monitoring *	☐
Patient level contract monitoring	☐
Patient level drugs dataset	☐
Patient level devices dataset	☐
Devices supply chain reconciliation dataset	☐
Secondary Usage Service (SUS+)	☐
Mental Health Services DataSet (MHSDS)	☐
National Return**	☐
Clinical Database**	☐
Other**	☒

**If National Return, Clinical database or other selected, please specify: Lomitapide is distributed via home delivery. If required, the company Amryt Pharma can provide anonymised data on a number of people taking lomitapide (including number of new starters, people stopping treatment and number continuing treatment).

A8.2 Specify how the activity related to the new patient pathway will be identified.	<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> SMOMED/SCTID drug code: 23592411000001102
A8.3 **Identification Rules for Drugs:** How are drug costs captured?	**Already specified in current NHS England Drugs List document** If the drug has already been specified in the current NHS England Drug List please specify drug name and drug indication: Lomitapide. Category: Lipid regulating drugs
A8.4 **Identification Rules for Devices:** How are device costs captured?	**Not applicable**
A8.5 **Identification Rules for Activity:**	**Not captured by an existing specialised service line**

<table>
<tr><td>How are activity costs captured?</td><td>If the activity is not captured please specify whether the proposed identification rules have been documented and agreed with the Identification Rules team. <u>No</u></td></tr>
<tr><td colspan="2">A9 Monitoring</td></tr>
<tr><td>A9.1 Contracts
Specify any new or revised data flow or data collection requirements, needed for inclusion in the NHS Standard Contract Information Schedule.</td><td><u>None</u>
Per company submission – table 13.</td></tr>
<tr><td>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 monitoring required, for example reporting or use of prior approval systems.</td><td><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>The company recommends monitoring of lomitapide use in agreement with the tertiary centres. There is a consensus on lomitapide use already produced by the majority of English centres – UK consensus on lomitapide positioning (company submission Table 13 / Appendix 6).</td></tr>
<tr><td>A9.3 Business intelligence
Is there potential for duplicate reporting?</td><td><u>No</u></td></tr>
</table>

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** If no, will one be developed? The company can provide anonymised data on the number of people taking lomitapide (including number of new starters, any patients stopping lomitapide, and number continuing treatment.
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.)	There are around 200 lipid clinics in England and 6 tertiary lipid centres. Around 60% of people with HoFH are managed at tertiary centres with the remaining 40% managed by their local lipid clinic. *Source: Company research data – see Table 11 company submission.*
B1.2 Will the proposition change the way the commissioned service is organised?	**No**

<table>
<tr><td></td><td>Source: Company submission table 12; no change is anticipated to the organisation of commissioned services.</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>
Source: Company submission table 12; no changes required to the organisation of care.</td></tr>
<tr><td colspan="2">B2 Geography & Access</td></tr>
<tr><td>B2.1 Where do current referrals come from?</td><td><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>
People who have HoFH are referred by their GP or local lipid clinic based on LDL-C levels or family history or by a cardiologist following a major adverse cardiac event (MACE) leading to the diagnosis of HoFH.</td></tr>
<tr><td>B2.2 What impact will the new policy have on the sources of referral?</td><td><u>No impact</u></td></tr>
<tr><td>B2.3 Is the new policy likely to improve equity of access?</td><td><u>No impact</u>
No relevant equity issues identified.</td></tr>
</table>

B2.4 Is the new policy likely to improve equality of access and/or outcomes?	**Increase** People who have HoFH do not currently have access to this treatment in routine commissioning.
B3 Implementation	
B3.1 Will commissioning or provider action be required before implementation of the proposition can occur?	**No action required**
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?	**No - go to B3.4**
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></td></tr>
<tr><td>B3.10 Specify how revised provision will be secured by NHS England as the responsible commissioner.</td><td><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>
</table></td></tr>
</table>

	Price-based selection process to maximise cost effectiveness	☐
	Any qualified provider	☐
	National Commercial Agreements e.g. drugs, devices	☐
	Procurement	☐
	Other	☐

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

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.	Initial treatment (3 months) Cost per pack (list price) including VAT £21,318 (28 capsules same price for 5,10 and 20mg) Cost per pack after initial treatment £17,765 (no VAT applies) After a person is stabilised on lomitapide, treatment is delivered to the home, therefore no VAT applies. All patients who require daily doses equating to >1 pack per month are not charged for extra packs of product. The recommended vitamin/mineral supplements are provided free of charge by Amryt Pharma. The drug is initiated at tertiary centres where prescriptions attract VAT. The first 3 months of treatment for lomitapide are assumed in the resource impact to have VAT. Other drugs used in addition to lomitapide: Evolocumab (420mg every 2 weeks £204.12 (incl VAT) per pre-filled syringe)

	Ezetemibe - (10mg once daily – 28 tab pack £31.57 (incl VAT) Statins – non-proprietary, variable dose. Annual cost per person used (NICE CG71 Table 5 costing report) The annual cost of adjunctive treatments is calculated in the unit costs page of the resource impact template. VAT is applied in resource impact page of the template.
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 %)	Lomitapide is a high cost drug (BNF category: Lipid regulating drugs) and is excluded from tariff. There may be costs associated with liver function monitoring. These are: £163 MRI scan (2017/18 Tariff 2017/18 RD03Z MRI Age 19 and over with contrast) £5 – Fib 4 (NICE Clinical Guideline NG50 – full guideline) £50 Acoustic force radiation imaging (NICE Clinical Guideline NG50 Cirrhosis in over 16s: assessment and management – full guideline) £45 Fibrotest (NICE Clinical Guideline NG50 – full guideline) £111 - Enhanced liver fibrosis test (ELF test) (NICE clinical guideline NG50 – full guideline) £3 – C-Reactive protein test (NICE Clinical Guideline NG50 – full guideline) £327 Outpatient appointment to a hepatologist (treatment code 306 - WF01B First attendance)

	£134 Outpatient hepatologist (WF01A follow up attendance). The monitoring and follow up of people treated with lomitapide may be undertaken in outpatient haematology; the relevant codes and prices are: Treatment function code 303 WF01B (first attendance) £244 WF01A follow up attendance £109 These are using 2017/18 National tariff prices. Due to the small number of people treated, these costs are not anticipated to be significant. These costs have been included in the resource impact assessment (unit costs page) and given as totals in C2.1 below.
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.	No additional costs covered by local tariff are anticipated (company submission Table 14 p53).
C1.6 **Other Activity Costs not covered by National or Local Tariff** Include descriptions and estimates of all key costs.	No additional activity costs not covered by National or Local tariff are anticipated.
C1.7 Are there any prior approval mechanisms required either during	**No** The company do not anticipate a prior approval scheme would be required. If required, this should be agreed

implementation or permanently?

with the tertiary care centres and the company recommends this is based around the current consensus they have put forward shown in Appendix 6 of the company submission.

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?

	Drug costs **(list price)** (NHSE impact) £	Monthly / quarterly monitoring and follow up (CCG impact) £	Annual tests (CCG impact) £	Total £
YR1	231,579	1,700	838	£234,117
YR2	231,579	518	838	£232,935
YR3	231,579	518	838	£232,935
YR4	231,579	518	838	£232,935
YR5	231,579	518	838	£232,935

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

No changes are currently expected in year 6 to 10 which would impact on the model.

Costs for monitoring and tests which are assumed to have impact on CCGs are included above for completeness to show the total costs of lomitapide on the NHS. These costs are uplifted by an averaged MFF.

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 annual cost of treatment to NHS England over 10 years **using list prices**. These exclude monitoring and adverse events which are not identified as having significantly different costs to current

<table>
<tr>
<td></td>
<td>treatment options.
Estimated budget impact to NHSE – list prices
<table>
<tr><th></th><th>Net resource impact including VAT £000s</th></tr>
<tr><td>Year 1</td><td>2,165</td></tr>
<tr><td>Year 2</td><td>3,265</td></tr>
<tr><td>Year 5</td><td>3,937</td></tr>
<tr><td>Year 10</td><td>4,180</td></tr>
</table>
NB VAT applies to treatment initiated at tertiary centres. It is assumed people receive their first 3 months of prescriptions at tertiary centres until they are stable on lomitapide. After this period it is delivered to the home and VAT no longer applies. VAT in later years (Yrs 2, 5 and 10) reflects new people starting treatment in these years.</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"></td>
</tr>
</table>

C4 Overall cost impact of this policy to the NHS as a whole

C4.1 Specify the budget impact of the proposal on other parts of the NHS.

Budget impact for CCGs:

Cost saving

Budget impact for providers:

Cost pressure

Please specify:

There is no cost impact for CCGs because services fall within specialised commissioning. There are potential savings for CCGs. This is due to a reduced number of people having apheresis or reduced frequency of apheresis in some people from weekly / fortnightly to monthly. The estimated cost of weekly apheresis per year is around £13,500. This is taken from:

National Tariff 2017/18 code SA16Z 'Plasma exchanges 20 or more' Combined day case / ordinary elective spell tariff including average MFF uplift **1.0809 (£12,478 x 1.0809)**

For providers additional monitoring and follow up is needed and additional tests. Due to the small number of people who may receive treatment, this activity is not anticipated to have significant impact on capacity and costs.

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 an estimated resource impact to the commissioner (NHSE) from implementing the policy. The table below shows the total impact to the NHS as a whole split between NHSE and CCGs. The cost of lomitapide is at list prices, therefore the actual resource impact to NHSE is likely to be lower.

Year	Cost impact NHSE £000s	Cost/ (saving) impact CCGs £000s	NHS impact £000s
1	2,165	(93)	2,072
2	3,265	(54)	3,211
5	3,937	(92)	3,845

	<table><tr><td>10</td><td>4,180</td><td>(97)</td><td>4,083</td></tr></table> The figures reflect a gradual uptake of lomitapide reaching 50% of people eligible for long term treatment by year 4. In year 2 the CCG saving attributed in reduced costs of apheresis is lower due to a part year effect of monitoring and follow up costs of lomitapide falling into year 2 from year one. This assumes monitoring and follow up costs are met by CCGs and takes into account people starting lomitapide part way through the year if the policy is approved.
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?	**Yes** Some people who frequently undergo apheresis may be able to increase the amount of time they spend in work as a result of reduced need for frequent apheresis. This could reduce the impact on social care costs may allow people to improve their work prospects.
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?	As HoFH patients reduce their LDL-C levels, it is anticipated their life expectancy may increase, and therefore absolute numbers of HoFH patients will increase over time. This will increase the resource impact. There is also uncertainty about the incidence of newly diagnosed HoFH patients in the future. Most of this uncertainty is likely to have an impact in 5 to 10 years. However the disease is rare, with an expected incidence of approximately 1 new case per year in England, which will limit the expected resource impact. The resource impact model assumes a maximum uptake of 50% based on clinical expert opinion. **The cost of 50% uptake in year 5 to NHSE is estimated to be £3.9 million (C4.2 above)**. **If uptake reaches 100% in the medium term (by year 5), the NHSE resource impact could be around £9.5 million (at list prices)**.
C6.2 How can these risks be mitigated?	Monitoring of lomitapide use can be established in agreement with tertiary centres. SNOMED / SCTID could be used to identify total activity for HoFH and trend analysis could be used to assess whether the correct questions are being asked to ensure proper use within the policy. A patent access scheme may help to mitigate risk. The policy could be approved after publication of relevant clinical effectiveness evidence.
C6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total cost scenarios?	Questions were given to the policy working group asking for their input to the resource impact assumptions and to the uptake of treatment to inform scenarios. The main adjustment identified, related to the uptake of lomitapide over time. Clinical opinion assumes that uptake will reach 50% by year 4. An uptake of 35% is assumed in year 1 because there may be a backlog of people awaiting treatment with lomitapide.
C6.4 What scenario has been approved and why?	Expert clinical opinion is that uptake is expected to be 35% in year 1 and will reach a maximum of 50% by year 4. This is because some people may have contraindications and cannot take up lomitapide. There are also lifestyle restrictions imposed such as a low fat diet and other lifestyle modifications which may prevent people taking up the treatment.
C7 Value for Money	
C7.1 What published evidence is available that the treatment is cost	**A cost-effectiveness evidence review has not been undertaken.**

<table>
<tr><td>effective as evidenced in the evidence review?</td><td></td></tr>
<tr><td>C7.2 Has other data been identified through the service specification development relevant to the assessment of value for money?</td><td>
<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>
D’Erasmo L et al. 2017 studied the efficacy of lomitapide in the treatment of HoFH in 15 patients. The study reports that during follow-up, 8 of 10 patients receiving apheresis (80%) stopped this treatment due to marked LDL-C reduction. No severe adverse events were recorded.
Due to the rarity of HoFH it was not possible to conduct robust outcome studies. Modelled data has shown that even with a conservative reduction in LDL-C of 38%, there is a potential to extend lives by a median of 11 years. This is because lomitapide may translate into reduction in cardiovascular events. Due to limited data, the number of events on a per person basis is difficult to estimate, and there is no data to accurately model this.
</td></tr>
<tr><td colspan="2">C8 Cost Profile</td></tr>
</table>

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.	Not applicable