NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

OrganOx *metra* for liver transplant

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of OrganOx *metra* within its CE mark for preserving donor livers for transplant.

Background

Adults who need liver transplants are typically those with end-stage liver disease. Liver failure occurs when the liver is unable to repair itself and maintain its normal function. Liver failure can be caused by toxicity, viral hepatitis infections, autoimmune liver disease, alcohol related liver disease, non-alcoholic fatty liver disease and biliary cirrhosis. Symptoms of liver failure include a loss of appetite, yellowing of the skin, itching, loss of muscle and weight and passing of black stools. People with some types of primary liver cancer as well as some metabolic disorders may also require liver transplants.

People identified as needing a liver transplant are placed on a waiting list for a donor liver with an average waiting time of 3 to 4 months for adults (NHS B&T). People with black Asian and minority ethnic backgrounds are reported to have to wait longer for a successful match, due to a shortage of suitably matched donors by blood type (NHS B&T).

Transplants are carried out by specialist liver transplant surgeons in 1 of 7 adult units across the UK. Between April 2020 to March 2021,1,064 patients joined the liver transplant list. 712 of 870 livers donated in the UK in 2021 to 2022 were used including 86% of livers retrieved from donors after brain death and 65% from donors after circulatory death (NHS B&T).

Standard care for liver transplant involves removing the liver of a donor after brainstem death or circulatory death. A donor liver for transplant is usually preserved using static cold storage which involves flushing the donor liver with cold organ preservation solution which is transported in a cold storage icebox to minimise liver degradation for a maximum preservation time of 12 hours. It is not possible to do a formal functional assessment of the organ after retrieval from cold storage. Liver compatibility is instead based on the characteristics of the donor before retrieving the organ and the appearance of the organ. The liver discard rate in the UK between April 2020 to April 2021 was 38% (NHS B&T).

The use of normothermic and hypothermic machine perfusion devices for preservation of livers for transplant is by special arrangement only (NICE IPG636, 2019). Alternative preservation devices are currently available to the NHS including Organ Assists XVIVO Liver Assist device (capable of both hypothermic and normothermic perfusion) and the TransMedics Organ Care System Liver System (capable of normothermic perfusion).

The technology

OrganOx *metra* (OrganOx Limited) is a CE marked class IIa medical device intended to be used to sustain donor livers for transplantation. The device is a fully automated transportable normothermic organ perfusion device. It works by placing the liver in a sterile environment and continuously perfusing the organ with oxygenated blood, medicines, and nutrients at normal body temperature to mimic normal physiology. This can be done for up to 24 hours before transplant and aims to improve organ preservation, minimising liver injury and reducing the number of donor livers discarded. This also means the liver is functional, enabling assessment and evidence-based decision about whether to transplant.

The OrganOx *metra* is currently used across all NHS liver transplant centres in different arrangements. The device may be used in 'transport mode', which involves continuous normothermic perfusion, or in 'back to base mode' which involves normothermic perfusion on arrival at the recipient's hospital. For the purpose of this evaluation, we will be considering 'transport mode' only.

Decision problem:

Intervention	OrganOx *metra*
Population(s)	Adults requiring liver transplant

Comparators	• Standard care provided in the NHS (static cold storage)
	• Normothermic liver perfusion devices used in the NHS:
	  ○ OCS Liver system (TransMedics)
	  ○ XVIVO (Liver assist, Organ Assist)

Outcomes	The outcome measures to be considered include:
	• Utilisation: number of organs utilised versus discarded
	• Graft survival
	• Graft function:
	  • including early allograft dysfunction
	  • primary non function (which may include retransplantation or death within 7 days of transplantation).
	• Device-related adverse events.
	• Adverse effects of treatment
	• Acute kidney injury post transplantation
	• Hospital length of stay
	• Retransplant rates
	• Patient survival
	• Waiting times on transplant list
	• Health related quality of life (HR-QOL)

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. Guidance will only be issued in accordance with the CE marking. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Subgroups	If the evidence allows the following subgroups will be considered: • Marginal organs (donor livers not previously considered suitable for transplant without normothermic perfusion, these might include circulatory death donors, older donors, donors with steatotic livers). • Complex recipients (these might include people who have previously had a transplant or those with fulminant liver failure with haemodynamic instability).
Other considerations	OrganOx *metra* is currently used across all 7-specialist adult liver transplant centres: Royal Free Hospital and Kings College Hospital London, Queen Elizabeth Hospital Birmingham, St James's University Hospital Leeds, Freeman Hospital Newcastle, Addenbrookes Hospital Cambridge, Edinburgh Royal Infirmary. Changes in the UK to allocate donor livers to improve equity of access have resulted in a substantial increase in the need to transport organs using charter flights. The 24-hour preservation period enabled by this device may allow more livers to be transported in the UK by road, offering a more environmentally sustainable alternative to SCS in organ transplant. This improved preservation period may also assist in reducing health inequalities, allowing people to be considered irrespective of the location of the donor location.
Related NICE recommendations	Related Guideline: Clinical Guideline Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation [CG135], 2016. Cirrhosis in over 16s: assessment and management 2016 NICE guideline NG50

	Non-alcoholic fatty liver disease: assessment and management 2016. NICE Guideline NG49 Related Technology appraisals: Everolimus for preventing organ rejection in liver transplantation. Technology appraisal guidance [TA348], 2015. Related Interventional Procedures: Extracorporeal whole liver perfusion for acute liver failure. Interventional procedures guidance [IPG690], 2021. Ex-situ machine perfusion for extracorporeal preservation of livers for transplantation 2019. NICE interventional procedures guidance IPG636 Normothermic extracorporeal preservation of hearts for transplantation following donation after brainstem death. Interventional procedures guidance [IPG549], 2016. Living-donor liver transplantation. Interventional procedures guidance [IPG535], 2015 Living-donor liver transplantation 2015. NICE interventional procedures guidance IPG535 Quality standard: Liver disease 2017. NICE quality standard on liver disease QS152 NICE Advice: OrganOx metra for liver transplant. Medtech innovation briefing [MIB275], 2021.
Related National Policy	The NHS Long Term Plan, 2019. Living Donor Liver Transplantation, by the British Transplantation Society and British association for the studies of the liver, 2015. Organ donation and transplantation to 2030: meeting the need, NHS Blood and Transplant, 2020 NHS England manual for prescribed specialised services 2018-2019, Liver transplantation service 69, page 197

Questions for consultation

- Where do you consider OrganOx *metra* in transport mode will fit into the existing care pathway for liver transplantation? Will there be certain clinical

circumstances when OrganOx *metra* in transport mode would be considered inappropriate?
- Would the technology be a candidate for managed access?
- Do you consider OrganOx *metra* to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?
- Does the XVIVO (Liver assist, Organ Assist) device provide normothermic perfusion in transport mode? Does the OCS Liver system (TransMedics) device provide normothermic perfusion in transport mode? Are these devices used in the NHS and should they be considered as a comparator? Are there any other devices available in the NHS that offer normothermic liver perfusion in transport mode that should be considered in this evaluation?
- Are the subgroups suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom OrganOx *metra* is expected to be more clinically effective or cost effective that should be considered separately?
- Are the outcomes listed appropriate? Are there any other outcomes you would consider key to include? And what follow up periods would be appropriate to capture these outcomes?
- Do you consider that the use of OrganOx *metra* can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?
- What would be an appropriate time horizon to capture the QALY benefits of the OrganOx *metra*?
- Please identify the nature of the data which you understand to be available to enable the committee to take account of the benefits of the OrganOx *metra.*

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:
- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which OrganOx *metra* is indicated for.
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.
- Is it accurate that some groups of individuals wait longer for liver transplants (including those with Black, Asian or minority ethnic groups)? Would you expect the use of the OrganOx *metra* could improve equality of access in any way?

To help NICE prioritise topics to appraise this technology through its single technology appraisal process (STA). We welcome comments on the appropriateness of appraising this topic through this process. Information on the Institutes technology appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).