



Melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic cancer in the liver

Interventional procedures guidance Published: 21 April 2021

www.nice.org.uk/guidance/ipg691

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment

or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the <u>Yellow Card Scheme</u>.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should <u>assess and reduce the environmental impact of implementing NICE recommendations</u> wherever possible.

1 Recommendations

- 1.1 Evidence on the safety of melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for cancer or metastases in the liver shows there are serious, well-recognised complications.
 - For patients with metastases in the liver from ocular melanoma, there is some
 evidence of short-term tumour response. For these patients, this procedure
 should only be used with special arrangements for clinical governance,
 consent, and audit or research. Find out what special arrangements mean on
 the NICE interventional procedures guidance page.
 - For patients with primary liver cancer or metastases in the liver that are not from ocular melanoma, evidence of efficacy is inadequate in quality and quantity. For these patients, this procedure should only be used in the context of research. Find out what <u>only in research means on the NICE</u> interventional procedures guidance page.
- 1.2 Clinicians wishing to do melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for patients with metastases in the liver from ocular melanoma should:
 - Inform the clinical governance leads in their healthcare organisation.

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- Give patients (and their families and carers as appropriate) clear written information to support <u>shared decision making</u>, including <u>NICE's information</u> for the public.
- Ensure that patients (and their families and carers as appropriate) understand the procedure's safety and efficacy, and any uncertainties about these.
- Audit and review clinical outcomes of all patients having the procedure. The
 main efficacy and safety outcomes identified in this guidance can be entered
 into NICE's interventional procedures outcomes audit tool (for use at local
 discretion).
- Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve.
- Healthcare organisations should:
 - Ensure systems are in place that support clinicians to collect and report data on outcomes and safety for every patient having this procedure.
 - Regularly review data on outcomes and safety for this procedure.
- 1.4 The procedure should only be done in specialist centres by a melanoma multidisciplinary team that includes an interventional radiologist, an anaesthetist, an oncologist and a clinical perfusion scientist trained and experienced in the procedure.
- Further research should be in the form of randomised controlled trials against current best practice, including other liver-directed and systemic therapies. It should report details of patient selection, concurrent therapies and techniques, and adverse events, including those related to chemotherapy.

2 The condition, current treatments and procedure

The condition

The most common types of primary liver cancer are hepatocellular carcinoma (also known as hepatoma) and cholangiocarcinoma. However, cancer in the liver has often metastasised from other sites such as the lung, colon, stomach and eye (particularly ocular melanoma, also known as uveal melanoma).

Current treatments

2.2 Treatment for primary or metastatic cancer in the liver depends on the location and stage of the cancer and how much liver function is preserved. Treatment options include surgical resection, thermal ablation, systemic chemotherapy, transarterial chemoembolisation, isolated hepatic perfusion and selective internal radiation therapy. In patients with primary liver cancer, surgical removal with curative intent and liver transplantation may be possible. For most patients with liver metastases, treatment with curative intent is not possible.

The procedure

- 2.3 Melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation is done under general anaesthesia. A high dose of melphalan chemotherapy is delivered directly into the hepatic artery. Blood leaving the liver is diverted out of the body and filtered to reduce the level of melphalan before being returned to the circulation. The aim is to allow high doses of melphalan chemotherapy to be used, which would otherwise not be tolerated because of severe systemic side effects.
- An infusion catheter is inserted into the femoral artery and guided into the hepatic artery. The femoral vein is cannulated and a multi-lumen, double-balloon

catheter is inserted into the inferior vena cava and across the hepatic veins. The balloons are inflated so that all blood leaving the liver through the hepatic veins enters the catheter rather than the systemic circulation. High doses of melphalan are infused directly into the liver through the hepatic artery infusion catheter over about 30 minutes. Blood leaving the liver passes through an extracorporeal filtration system to remove most of the melphalan and is returned to the circulation through a catheter in the internal jugular vein. Full anticoagulation with heparin is needed throughout the procedure.

The procedure causes significant changes in the patient's haemodynamic status, which must be managed by the anaesthetic team with support from a clinical perfusion scientist.

3 Committee considerations

The evidence

- 3.1 NICE did a rapid review of the published literature on the efficacy and safety of this procedure. This comprised a comprehensive literature search and detailed review of the evidence from 11 sources, which was discussed by the committee. The evidence included 1 randomised controlled trial, 1 non-randomised comparative study and 9 case series (including 2 studies looking at the same patient population). It is presented in table 2 of the interventional procedures overview. Other relevant literature is in the appendix of the overview.
- The committee considered the key efficacy outcomes to be: overall survival, progression-free survival, quality of life and downstaging of cancer.
- The committee considered the key safety outcomes to be: procedure-related complications (including bleeding, thrombosis and cardiovascular events), bone marrow or haematological toxicity, and death.
- 3.4 NICE received 1 submission from a patient organisation.

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Committee comments

- 3.5 The committee noted that the toxicity of the procedure is principally related to how efficiently the melphalan is removed and prevented from entering the systemic circulation.
- The technology has changed over time, and the newest filter may be associated with less haematological toxicity.
- 3.7 The procedure is used for unresectable liver cancer.

ISBN: 978-1-4731-4089-9

Endorsing organisation

This guidance has been endorsed by <u>Healthcare Improvement Scotland</u>.