MHRA Device Safety Information

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Paclitaxel drug-coated balloons (DCBs) or drug-eluting stents (DESs): updated position on use in patients with critical limb ischaemia and intermittent claudication DSI/2022/003

Summary

The MHRA has updated its recommendations for using paclitaxel-coated devices in patients with intermittent claudication and critical limb ischaemia.

Background

In 2021 the MHRA reconvened the independent Expert Advisory Group (EAG) to review new evidence. Following the review, the MHRA's recommendations for using paclitaxel-coated devices in patients with intermittent claudication and critical limb ischaemia has been updated to take into account potential dose dependent effects of paclitaxel coated balloons and stents in patients.

Paclitaxel drug-coated balloons (DCBs) or drug-eluting stents (DESs) may continue to be used in patients with critical limb ischaemia (CLI) where the benefits may outweigh the risks. However, if the decision is made to use the devices in patients with CLI, a patient's exposure should be kept to a minimum. This includes:

- using the lowest dose devices available
- avoiding/reducing repeated exposure of paclitaxel coated devices e.g. from repeated procedures with drug coated devices.

The recommendations for intermittent claudication remain unchanged. Do not use paclitaxel drug-coated balloons (DCBs) or drug-eluting stents (DESs) in the routine treatment of patients with intermittent claudication, as the reported risk of longer-term increased mortality may outweigh the benefits.

Reconvening of EAG 2021

The MHRA published DSI/2021/001 in Feb 2021, issued in Scotland as MDSI(SC)2101, regarding the MHRA's position on the use of intermittent claudication and CLI.

The MHRA noted a further Katsanos study in summer 2021 raising concerns regarding the risk of major amputation following treatment with paclitaxel coated balloons in lower limb arteries. Prompted by this study, the EAG reconvened to review recent relevant evidence. The EAG's evaluation used the MHRA's in-house statistical and toxicological input.

The EAG was also asked to re-evaluate whether the recent evidence indicated a causal relationship between the drug and the increased mortality or risk of amputation.

Dose dependent effects

As part of the review undertaken by the EAG, information relating to the dosing of paclitaxel coated devices were noted3. This evidence suggested that a lower dose of paclitaxel may reduce the effects on all-cause mortality. The benefits of using a higher dose device were weighed against this.

As a result of this, the EAG recommends that paclitaxel DCBs or DESs may be used in patients with CLI where benefits such as quality of life outweigh the risks, but their exposure should be kept to a minimum by using the lowest dose devices available and where possible, reducing any theoretical risks from repeated exposure of paclitaxel coated devices, e.g. from repeated procedures with drug coated devices.

The evidence to explain the mechanism of action for any potential relationship between paclitaxel-coated devices and mortality or amputation is still inconclusive.

The MHRA will continue to monitor these devices and take into account any further information it receives. MHRA will take regulatory action and update its guidance when necessary.

Action

Current recommendations
The EAG recommends revising the actions for clinicians so that they refer to usage in CLI patients. The MHRA has acted on this recommendation to produce the following actions.

For the clinician

1. Do not use paclitaxel drug-coated balloons (DCBs) or drug-eluting stents (DESs) in the routine treatment of patients with intermittent claudication, as the mortality risk generally outweighs the benefits.

2. In patients with critical limb ischaemia, management should follow that outlined in the NICE guideline on Peripheral arterial disease: diagnosis and management (CG147).

3. Use of paclitaxel DCBs and DESs in patients with critical limb ischaemia remains an option in selected cases, where the benefits may outweigh the risks. This is because such patients generally have a higher risk of irreversible ischemic damage should restenosis occur, which may lead to limb loss and a lower life expectancy. Decisions on whether to use these devices should be made through shared decision-making between the patient, their family and carers and the clinical team.

4. Assess the relative risks on an individual patient basis, and if this supports use of a paclitaxel DCB or DES, ensure that:
   a. the patient's dose exposure should be kept to the minimum dose, to mitigate against potential dose-dependent effects. This includes taking into account, using the lowest dose where possible and avoiding repeated exposure of paclitaxel coated devices.
   b. the documentation of informed consent includes a risk-benefit discussion with the patient and their family or carers regarding the uncertainty in long-term outcomes with these devices, and the current evidence which indicates an increased risk of mortality.
   c. the patient receives clinically appropriate follow-up. This may include face-to-face or telephone consultations in the hospital or the community.

5. Ensure local procedures accounting for duty of candour are in place for the continued management of patients who have already been treated with paclitaxel DCBs an DESs. Consider the provision of information and advice to address any patient concerns arising from the current uncertainty in long-term outcomes associated with these devices. Treatment options should be determined through shared decision making between the patient, their family or carers and the clinical team. It is important that the patient and their family or carers are included in discussions around the risk and benefits of all available devices to allow them to make an informed decision.

6. Report any suspected or actual adverse incidents involving these devices through your healthcare institution's local incident reporting system and/or your national incident reporting authority as appropriate: England, Scotland, Northern Ireland, Wales.

Information for patients
Patients requiring treatment for peripheral arterial disease (PAD) and CLI can continue to be treated with alternative therapies and devices. However, in some cases, clinicians may consider using paclitaxel coated devices if they believe this is the best option for the individual, based on the patient's own circumstances. This may include, but not be limited to, quality of life considerations as well as known risks associated from repeated procedures.

The MHRA's revised advice allows clinicians to consider all the benefits and risks for each individual patient and to make the most appropriate treatment choice in collaboration with the patient and their family or carers. If you think you're affected, please contact your GP, vascular specialist or other healthcare professional.

Suggested onward distribution

Cardiology	Interventional radiology	Health & Safety
Catheterisation Labs	Operating Departments	Risk Management

Enquiries

Enquiries and adverse incident reports should be addressed to:

Incident Reporting & Investigation Centre (IRIC)
NHS National Services Scotland
Tel: 0131 275 7575 Email: nss.iric@nhs.scot

IRIC remit: general information about adverse incidents, safety alerts and IRIC's role can be found in CEL 43 (2009), *Safety of Health, Social Care, Estates and Facilities Equipment: NHS Board and Local Authority Responsibilities,* issued 30 October 2009.

Report an incident: Information on how to report an adverse incident

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