MHRA Device Safety Information

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

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Summary

The MHRA's recommendations for using paclitaxel-coated devices in patients with intermittent claudication and critical limb ischaemia remains unchanged.

Background

In February 2020 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 remains 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 mortality risk generally outweighs the benefits. However, using these devices in patients with critical limb ischaemia remains an option in selected cases, where the benefits may outweigh the risks.

Peripheral arterial disease
In December 2018 a study (Katsanos et al) published findings which raised concerns over the use of paclitaxel-eluting balloons and stents in the treatment of patients with peripheral arterial disease and in particular the femoropopliteal artery in the leg. These devices are used to treat patients in which a build-up of deposits in the arteries restricts blood supply to leg muscles, also known as peripheral arterial disease (PAD).

Following this publication, an independent Expert Advisory Group (EAG) was formed to advise the MHRA. The group was made up of leading UK clinicians from specialist societies, including interventional radiology and vascular surgery, supported by MHRA scientists with toxicology and statistical expertise.

The EAG was asked to consider whether the publication's findings and device-specific clinical study results were statistically robust and whether there was any evidence of a causal relationship between the drug, paclitaxel, and increased mortality. It was also asked to provide recommendations to the MHRA on the benefits and risks of the use of these devices in the treatment of PAD.

The review concluded that the statistical analysis in the Katsanos paper was robust. The review also noted that there is a possible dose-dependent effect of the use of paclitaxel coated/eluting devices on mortality although no scientific or clinical explanation is currently available.

The report from the EAG in June 2019 recommended that these devices should not be used to treat patients with intermittent claudication (a pain in the leg caused by the lack of blood flow). This is a condition that may be treated effectively with other devices and therapies. The devices may still be considered in patients with critical limb ischaemia (severe obstruction of the arteries), where it is felt that the benefits outweigh the risks and taking NICE guidance into account. If these devices are used, there should be enhanced patient follow-up. These treatment decisions should be made through shared decision-making between the clinical team, the patient and their family or carers.

After receiving the recommendations, the MHRA acted to limit the current use of these devices in routine clinical care by publishing an alert. The MHRA continues to monitor and review this situation and we will update our advice if it changes.

Additionally, a general warning is now included in the instructions for use for all affected manufacturers of CE marked DCBs and DES products.

Critical limb ischemia (CLI)
In January 2020, another study by Katsanos et al raised additional concerns around using paclitaxel-coated balloons in infrapopliteal arteries in the treatment of critical limb ischemia patients (CLI), where the blood flow to the legs becomes severely restricted. The EAG was asked to consider if the results from this device-specific clinical study were statistically robust, and whether MHRA should update the current advice in light of these findings.

The EAG therefore reviewed the current evidence, which included evaluating several relevant published papers and anonymized individual patient data, as well as using MHRA statistical and toxicological knowledge to input into this evaluation. The EAG was also asked to assess any evidence of a causal relationship between the drug and the increased mortality or risk of amputation.

As a result of this review, the EAG cannot say that additional, specific, measures are needed for CLI patients. It also concluded that there is not enough evidence at the moment to explain any potential relationship between paclitaxel-coated device and mortality or amputation.

Action

Current recommendations
The EAG recommends revising the actions for clinicians so that they refer to usage in CLI patients. 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 potential 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 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. b) 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.

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.

For the patient
If you think you're affected, please contact your GP, vascular specialist or other healthcare professional.

The MHRA encourages anyone – patient, carer or healthcare professional, who knows of a safety problem or adverse event that is or might be linked to a medical device, to report to us. Patients can report via the Yellow Card scheme.

Patients requiring treatment for PAD/CLI can continue to be treated with alternative therapies and devices. However, for some patients, clinicians may consider using these devices if they believe this is the best option for the individual. The MHRA's 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.

MHRA actions
The EAG recommended that the process of informed consent on the use of paclitaxel-coated balloons and paclitaxel-eluting stents should include a risk-benefit discussion with patients on the uncertainty in long-term outcomes with these devices, and the current evidence of an increased mortality rate. To further enhance this, the MHRA is exploring the possibility of using decision aids to support shared decision-making between clinicians and patients and their families or carers.

The EAG also recommended more research to evaluate the causal relationship between paclitaxel devices and mortality; and continue to review evidence for a possible mechanistic basis.

In addition to this, and in line with the EAG's recommendations, the MHRA will consider the available evidence supporting the use of these devices for other conditions, such as neuro-intervention and AV fistula access.

The MHRA will continue to monitor these devices and take into account any further information we receive. This will allow us to take regulatory action and update our guidance where necessary.

MHRA and the EAG will also review evidence that emerges on potential systemic effects from other novel drug coated/eluting technologies that are used in the UK.

Enquiries and further information

Enquiries (and adverse incident reports) in Scotland should be addressed to:

Incident Reporting & Investigation Centre (IRIC)
NHS National Services Scotland
Gyle Square, 1 South Gyle Crescent, Edinburgh EH12 9EB
Tel: 0131 275 7575 Email: nss.iric@nhs.scot

Reporting options are available on the HFS website: How to report an Adverse Incident

Further information about reporting incidents can be found in CEL 43 (2009) or by contacting IRIC at the above address.

Information about medical device safety information produced by the MHRA can be found on the MHRA website here: https://www.gov.uk/drug-device-alerts/medical-device-safety-information-produced-by-the-mhra