Australian Government
Department of Health
Therapeutic Goods Administration

Paclitaxel-coated products used in the peripheral arteries

Safety information: regulators review balloon and stent incidents

12 August 2019

Medical device regulators around the world are reviewing incidents associated with paclitaxel-coated products following the publication last December of a meta-analysis of randomised controlled trials in the Journal of the American Heart Association (JAHA) (https://www.ahajournals.org/doi/10.1161/JAHA.118.011245).

The JAHA meta-analysis concluded there was increased risk of death following application of paclitaxel–coated balloons and stents in the femoral and popliteal arteries of the lower limbs. It argued that further investigations were urgently warranted.

Paclitaxel-coated balloons and stents are used to improve blood flow to the legs and decrease the likelihood of repeat procedures to reopen blocked blood vessels.

US Food and Drug Administration (FDA)

Following publication of the JAHA meta-analysis, the US Food and Drug Administration (FDA) disseminated a letter to peripheral interventionalists and vascular medicine physicians (https://www.fda.gov/MedicalDevices/Safety/LetterstoHealthCareProviders/ucm629589.htm) alerting them to the issue. The FDA published a further update on 15 March (https://www.fda.gov/MedicalDevices/Safety/LetterstoHealthCareProviders/ucm633614.htm?utm_campaign=UPDATE%3A%20Treatment%20of%20Peripheral%20Arterial%20Disease%20with%20Paclitaxe Coated%20Balloons&utm_medium=email&utm_source=Eloqua) alerting health care providers that a preliminary analysis had shown a potentially concerning signal of increased long-term mortality in study subjects treated with paclitaxel-coated products compared to patients treated with uncoated devices. On 7 August 2019 the FDA published further information (https://www.fda.gov/medical-devices/letters-health-care-providers/august-7-2019-update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel) following its analysis of information provided to it at an advisory panel meeting in June 2019. The FDA has stated:

An analysis of trials related to late mortality in study participants treated with paclitaxel-coated devices compared to patients treated with uncoated devices identified that that there was a higher rate of mortality for the paclitaxel coated stents and balloons.

Medicines and Health products Regulatory Agency (MHRA)

The Medicines and Health products Regulatory Agency (MHRA) in the United Kingdom has also undertaken a review of the issue. Its expert advisory committee has provided advice in relation to further published recommendations for ongoing use on 4 June 2019 (https://www.gov.uk/drug-device-alerts/recommendations-for-ongoing-use-of-paclitaxel-drug-coated-balloons-dcbs-and-implantable-drug-eluting-stents-dess-in-the-treatment-of-patients-with-peripheral-artery-disease-pad-mda-2019-023?utm_source=fabd3291-0565-4604-9168-50ec2796b902&utm_medium=email&utm_campaign=govuk-notifications&utm_content=immediate). Their advice is to:

- Not use these devices in routine treatment of patients with intermittent claudication;
- Use these devices in patients with critical limb ischaemia is an appropriate option in accordance with NICE guidance;
- Assess the relative risks on an individual patient basis;
- Ensure informed consent includes a risk-benefit discussion regarding the uncertainty in long-term outcomes; and
- Patient follow-up should be life-long.

Therapeutic Goods Administration (TGA)

There are currently 10 paclitaxel-coated products included in the Australian Register of Therapeutic Goods (ARTG) and TGA staff have undertaken an appraisal of the JAHA meta-analysis and its methodology, along with other recent studies and meta-reviews. TGA data of adverse events in Australia have not shown a signal like the one described by the FDA. Adverse events reported to the TGA associated with these devices relate mostly to balloon and stent deployment issues. Most events occurred on the day of implantation and there have been no deaths reported.

Recommendations

Regulators including the TGA, MHRA and the US FDA are recommending that until further information is available, health care providers:

- Continue diligent monitoring of patients who have been treated with paclitaxel-coated balloons and paclitaxel-eluting stents.
- When making treatment recommendations and as part of the informed consent process, consider that there may be an increased rate of long-term mortality in patients treated with paclitaxel-coated balloons and paclitaxel-eluting stents.

- Discuss the risks and benefits of all available peripheral arterial disease (PAD) treatment options with your patients. For most patients, alternative treatment options to paclitaxel-coated balloons and paclitaxel-eluting stents should preferably be used until additional analysis of the safety signal has been performed.
- For some individual patients at particularly high risk for restenosis, clinicians may determine that the benefits of using a paclitaxel-coated product may outweigh the risks.
- Ensure patients receive optimal medical therapy for PAD and other cardiovascular risk factors as well as guidance on healthy lifestyles including weight control, smoking cessation, and exercise.[1]

Footnotes

[1] https://www.fda.gov/medical-devices/letters-health-care-providers/update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting (https://www.fda.gov/medical-devices/letters-health-care-providers/update-treatment-peripheral-arterial-disease-paclitaxel-coated-balloons-and-paclitaxel-eluting)

What to report? Please report adverse events, as well as near misses

The TGA encourages the reporting of any suspected adverse event or potential adverse event relating to a medical device. Adverse events can involve actual harm to a patient or caregiver, or a near miss that may have resulted in harm.

Some issues relating to medical devices that may lead to adverse events and prompt you to report include:

- mechanical or material failure
- design issues
- labelling, packaging or manufacturing deficiencies
- software deficiencies
- device interactions
- user/systemic errors.

Suspected adverse events or near misses can be reported directly to the TGA:

- **online** at Report a problem (//www.tga.gov.au/reporting-problems)
- **by emailing** iris@tga.gov.au (mailto:iris@tga.gov.au)
- **by mail** to IRIS, TGA, PO Box 100, Woden ACT 2606

- **by fax** to 02 6203 1713.

For more information about reporting, visit www.tga.gov.au (http://www.tga.gov.au) or contact the TGA's Medical Devices Branch on 1800 809 361.

Disclaimer

The Medical Devices Safety Update (MDSU) is aimed at health professionals and is intended to provide practical information on medical device safety, including emerging safety issues. The information in the MDSU is necessarily general and is not intended to be a substitute for a health professional's judgment in each case, taking into account the individual circumstances of their patients. Reasonable care has been taken to ensure that the information is accurate and complete at the time of publication. The Therapeutic Goods Administration gives no warranty that the information in this document is accurate or complete, and does not accept liability for any injury, loss or damage whatsoever, due to negligence or otherwise, arising from the use of or reliance on the information provided in this document.

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