Treatment of Peripheral Arterial Disease with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality - Letter to Health Care Providers

January 17, 2019

Dear Peripheral Interventionalists and Vascular Medicine Physicians:

We are writing to inform you that the FDA is evaluating recent information regarding the potential for increased long-term mortality after use of paclitaxel-coated balloons and paclitaxel-eluting stents to treat peripheral arterial disease (PAD) in the femoropopliteal artery.

A **recent meta-analysis (https://www.ahajournals.org/doi/10.1161/JAHA.118.011245)** of randomized trials published in the Journal of the American Heart Association (JAHA) suggests a possible increased mortality rate after two years in PAD patients treated with paclitaxel-coated balloons and paclitaxel-eluting stents compared to patients treated with control devices (non-coated balloons or bare metal stents). The specific cause for this observation is yet to be determined.

BACKGROUND

Paclitaxel-coated balloons and paclitaxel-eluting stents are intended to treat de novo or restenotic lesions in the femoropopliteal artery. The balloon and stent work to mechanically open the obstructed vessel. Paclitaxel is released from the balloon or stent to prevent scar tissue formation in the blood vessel that can re-obstruct the artery (restenosis).

In the U.S., paclitaxel-coated balloons are also marketed for the treatment of stenotic lesions in dysfunctional native arteriovenous dialysis fistulae. While paclitaxel-coated stents have been approved for use in the treatment of coronary artery disease, no paclitaxel-coated balloons or paclitaxel-eluting stents are currently marketed for this use.

RECOMMENDATIONS

The FDA recommends that health care providers:

- Continue surveillance of patients who have been treated with paclitaxel-coated balloons and paclitaxel-eluting stents per the current standard of care.
- In clinical decision-making, discuss the risks and benefits of all available treatment options for PAD with your patients.

- Report any adverse events or suspected adverse events experienced with the use of paclitaxel-coated balloons and paclitaxel-eluting stents. Voluntary reports can be submitted through **MedWatch, the (http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm)FDA Safety Information and Adverse Event Reporting program (http://www.fda.gov/Safety/MedWatch/HowToReport/default.htm)**. Device manufacturers and user facilities must comply with the applicable **Medical Device Reporting (MDR) regulations (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/default.htm)**. Health care personnel employed by facilities that are subject to **FDA's user facility reporting requirements (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/PostmarketRequirements/ReportingAdverseEvents/default.htm)** should follow the reporting procedures established by their facilities. Prompt reporting of adverse events can help the FDA identify and better understand the risks associated with medical devices.

FDA ACTIONS

The FDA is currently evaluating available long-term follow-up data to determine if there are any long-term risks associated with paclitaxel-coated products. This will include an evaluation of long-term follow-up data from studies that supported approval of paclitaxel-coated balloons or paclitaxel-eluting stents in the U.S. and other available data sets. This review will focus on causes of death, the paclitaxel dose delivered, and patient characteristics that may impact clinical outcomes. Additional statistical analyses will be performed to clarify the presence and magnitude of any long-term risks. We are working with manufacturers of paclitaxel-coated balloons and paclitaxel-eluting stents to better understand this issue.

There are a number of paclitaxel-coated balloons or paclitaxel-eluting stents approved or under study for peripheral vascular use in the U.S. Currently, the FDA believes that the benefits continue to outweigh the risks for approved paclitaxel-coated balloons and paclitaxel-eluting stents when used in accordance with their indications for use.

The FDA will communicate with the public as new information becomes available.

CONTACT US

If you have questions about this communication, please contact the Division of Industry and Consumer Education (DICE) at **DICE@FDA.HHS.GOV (mailto:DICE@FDA.HHS.GOV)**, 1-800-638-2041 or 301-796-7100.

Sincerely,
/s/
William Maisel, MD, MPH
Chief Medical Officer
Center for Devices and Radiological Health
U.S. Food and Drug Administration

ADDITIONAL RESOURCES

- **Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (JAHA, December 6, 2018) (https://www.ahajournals.org/doi/10.1161/JAHA.118.011245)**

More in Letters to Health Care Providers

FDA in Brief: FDA alerts health care professionals of possible increased risk of death associated with specific drug-containing balloons and stents in certain patients with peripheral arterial disease

January 17, 2019

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"A critical part of our medical product safety umbrella are our tools for collecting and analyzing emerging data about potential new safety risks of devices in the postmarket setting. We've invested heavily in these capabilities, to achieve a robust system that can quickly analyze emerging risks, and give us the information we need to intervene to prevent harm to patients. Today, we issued such a communication to health care professionals about possible risks to certain patients with peripheral arterial disease being treated with a type of drug-containing balloon or stent. The identification of this risk, and our work to notify patients and providers, reinforces why post-market surveillance is so important and why our continued investment in these capabilities is a key part of our work to protect patients. In this case, the specific cause of the increased risk of death found in a recently published study is yet to be determined, but we're reviewing all available information quickly and thoroughly and will communicate as soon as we know more. In the meantime, we urge health care professionals to carefully monitor patients with peripheral arterial disease who are using these devices," said FDA Commissioner Scott Gottlieb, M.D. "Keeping Americans safe is our top priority, regardless of whether we are operating in a business as usual setting or not. Even though the agency is currently facing a lapse in appropriations, we're continuing our important work to help ensure the safety of medical products, including medical device postmarket surveillance."

Today the FDA issued a **Letter to Health Care Providers (/MedicalDevices/Safety/Letter-stoHealthCareProviders/ucm629589.htm)** about a recent **publication (https://www.ahajournals.org/doi/10.1161/JAHA.118.011245) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)** in the Journal of the American Heart Association that suggests a possible increased risk of death at two years and beyond in patients with a type of peripheral arterial disease (PAD) who were treated with vascular balloons coated with a drug called paclitaxel or stents that release paclitaxel in the femoropopliteal artery in the leg, compared to patients treated with control devices (non-coated balloons or bare metal stents). Paclitaxel-coated balloons and paclitaxel-eluting stents are approved to treat obstructed lesions in arteries of the legs. The authors of the paper analyzed data from previously conducted randomized-controlled trials.

The letter recommends doctors continue to monitor patients who have been treated with these devices and discuss the benefits and risks of all available treatment options for patients with PAD. At this time, the FDA believes that the benefits continue to outweigh the risks for

approved paclitaxel-coated balloons and paclitaxel-eluting stents when used as indicated. In addition, the agency encourages prompt reporting of adverse events or suspected adverse events experienced with these devices through its **MedWatch (/Safety/MedWatch/HowToReport/default.htm)** reporting system.

The FDA is currently evaluating available long-term follow-up data—including from studies that supported approval of the devices and other available data sets—to determine if there are any long-term risks associated with paclitaxel-coated products. The agency is also conducting additional statistical analyses to clarify the presence and magnitude of any long-term risks, and is working directly with manufacturers of these devices to better understand this issue.

The FDA will communicate publicly as more information becomes available.

Related Information

- **FDA Letter to Health Care Providers: Treatment of Peripheral Arterial Disease with Paclitaxel-Coated Balloons and Paclitaxel-Eluting Stents Potentially Associated with Increased Mortality (/MedicalDevices/Safety/LetterstoHealthCareProviders/ucm629589.htm)**
- **JAHA: Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (https://www.ahajournals.org/doi/10.1161/JAHA.118.011245) (http://www.fda.gov/AboutFDA/AboutThisWebsite/WebsitePolicies/Disclaimers/default.htm)**

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More in FDA In Brief (/NewsEvents/Newsroom/FDAInBrief/default.htm)