DATE:
June 2020

Field Safety Notice

[1] J Am Heart Assoc 2018;7:e011245

Paclitaxel-coated Balloons and Paclitaxel-Eluting Stents

Addition of a warning and a clinical summary section in the instructions for use (IFU) of paclitaxel-coated balloons and paclitaxel-eluting stents used in the treatment of peripheral arterial disease of the lower limbs.

List of affected Medical Devices:
BioPath™
ELUVIA™
IN.PACT Admiral™
IN.PACT Pacific™
Luminor
Lutonix®
Passeo-18 Lux
Ranger™
Ranger™ SL
SeQuent® Please OTW
Stellarex
Zilver® PTX®

Dear Healthcare Professional,

In December 2018, Katsanos et al published a meta-analysis on the "Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg"[1]. After the publication of this meta-analysis, Agence Nationale de Sécurité du Medicament et des produits de santé (ANSM), French competent authority, has requested of all manufacturers the addition of a warning and clinical summary related to the Katsanos Paclitaxel meta-analysis to European Instructions for Use (IFU)s. The meta-analysis authors describe an increased risk of death at 2 and 5 years following the application of paclitaxel-coated balloons and stents in the femoropopliteal artery in the studies analyzed.

The purpose of this communication is now to draw your attention to updates that will be made to the IFUs for these devices throughout Europe. These updates will include a warning and a summary of the Katsanos publication, provided in Appendix One and supplemented with the clinical data specific to each device concerned. Please note that the indications and contraindications of the concerned devices remain unchanged.

No product batch/lot is being recalled in relation to this field safety notice. As noted in Appendix One, "the benefits of paclitaxel-coated devices (e.g., reduced reinterventions) should be considered in individual patients along with potential risks (e.g., late mortality)". Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients. It is also important to remember that health professionals should inform patients and their follow- up physicians of the nature of the devices used during the procedure.

Please read this notice carefully and provide it to any relevant person in your organization.

If you have any questions or would like assistance regarding the content of this letter, please contact your usual representative of the company that supplies you with the devices concerned in your institution.

Yours sincerely,

B. Braun Melsungen AG
Biosensors Europe SA
Biotronik AG
Boston Scientific International S.A.
Cook Ireland LTD
Lutonix, Inc
LVD Biotech SL
Medtronic, Inc
Spectranetics Corporation

Appendix one: Wording for EU IFUs of the paclitaxel medical devices

Warning

A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients.

Summary of the meta-analysis

A meta-analysis of randomized controlled trials published in December 2018 by Katsanos et. al. identified an increased risk of late mortality at 2 years and beyond for paclitaxel-coated balloons and paclitaxel-eluting stents used to treat femoropopliteal arterial disease. In response to these data, the United States Food and Drug Administration (FDA) performed a patient level meta-analysis of long-term follow-up data from the pivotal premarket randomized trials of paclitaxel-coated devices used to treat femoropopliteal disease using available clinical data through May 2019. The meta-analysis also showed a late mortality signal in study subjects treated with paclitaxel-coated devices compared to patients treated with uncoated devices. Specifically, in the 3 randomized trials with a total of 1090 patients and available 5-year data, the crude mortality rate was 19.8% (range 15.9% - 23.4%) in patients treated with paclitaxel-coated devices compared to 12.7% (range 11.2% - 14.0%) in subjects treated with uncoated devices. The relative risk for increased mortality at 5 years was 1.57 (95% confidence interval 1.16 - 2.13), which corresponds to a 57% relative increase in mortality in patients treated with paclitaxel-coated devices. As presented at the June 2019 FDA Advisory Committee Meeting, an independent meta-analysis of similar patient-level data provided by VIVA Physicians, a vascular medicine organization, reported similar findings with a hazard ratio of 1.38 (95% confidence interval 1.06 - 1.80). Additional analyses have been conducted and are underway that are specifically designed to assess the relationship of mortality to paclitaxel-coated devices.

The presence and magnitude of the late mortality risk should be interpreted with caution because of multiple limitations in the available data, including wide confidence intervals due to a small sample size, pooling of studies of different paclitaxel-coated devices that were not intended to be combined, substantial amounts of missing study data, no clear evidence of a paclitaxel dose effect on mortality, and no identified pathophysiologic mechanism for the late deaths.

Paclitaxel-coated balloons and stents improve blood flow to the legs and decrease the likelihood of repeat procedures to reopen blocked blood vessels compared to uncoated devices. The benefits of paclitaxel-coated devices (e.g., reduced reinterventions) should be considered in individual patients along with potential risks (e.g., late mortality).

Additional information regarding clinical data which will be adapted by each manufacturer in each IFU:
In the [insert pivotal study trial name], Kaplan Meier mortality estimates at 2, 3 and 5 years are [x], [x], and [x], respectively, for the YYY treatment device and [x], [x] and [x], respectively, for the ZZZ control device. Additional information regarding long-term outcomes can be found in Section (XX).

Attachment for VT-RAP-19-12-001

Lutonix® 014 Drug Coated Balloon PTA Catheter

Model: 9005

Product Codes:

LUTONIX® 014 Drug Coated Balloon PTA Catheter – EU				
9020515200040	9020515200120	9020510200080	9020510200150	9020513200100
9020515250040	9020515250120	9020510250080	9020510250150	9020513250100
9020515300040	9020515300120	9020510300080	9020510300150	9020513300100
9020515350040	9020515350120	9020510350080	9020510350150	9020513350100
9020515400040	9020515400120	9020510400080	9020510400150	9020513400100
9020515200080	9020515200150	9020510200100	9020513200040	9020513200120
9020515250080	9020515250150	9020510250100	9020513250040	9020513250120
9020515300080	9020515300150	9020510300100	9020513300040	9020513300120
9020515350080	9020515350150	9020510350100	9020513350040	9020513350120
9020515400080	9020515400150	9020510400100	9020513400040	9020513400120
9020515200100	9020510200040	9020510200120	9020513200080	9020513200150
9020515250100	9020510250040	9020510250120	9020513250080	9020513250150
9020515300100	9020510300040	9020510300120	9020513300080	9020513300150
9020515350100	9020510350040	9020510350120	9020513350080	9020513350150
9020515400100	9020510400040	9020510400120	9020513400080	9020513400150

Lutonix® 035 Drug Coated Balloon Catheter

Model: 9004

Product Codes:

LUTONIX® 035 Drug Coated Balloon PTA Catheter – EU				
9090475400020	9090475600120	9090410400080	9090410700040	9090413400150
9090475400040	9090475600150	9090410400100	9090410700060	9090413500020
9090475400060	9090475700020	9090410400120	9090410800020	9090413500040
9090475400080	9090475700040	9090410400150	9090410800040	9090413500060
9090475400100	9090475700060	9090410500020	9090410800060	9090413500080
9090475400120	9090475800020	9090410500040	9090410900020	9090413500100
9090475400150	9090475800040	9090410500060	9090410900040	9090413500120
9090475500020	9090475800060	9090410500080	9090410900060	9090413500150
9090475500040	9090475900020	9090410500100	9090410100020	9090413600020
9090475500060	9090475900040	9090410500120	9090410100040	9090413600040
9090475500080	9090475900060	9090410500150	9090410100060	9090413600060
9090475500100	9090475100020	9090410600020	9090410120020	9090413600080
9090475500120	9090475100040	9090410600040	9090410120040	9090413600100
9090475500150	9090475100060	9090410600060	9090413400020	9090413600120
9090475600020	9090475120020	9090410600080	9090413400040	9090413600150
9090475600040	9090475120040	9090410600100	9090413400060	9090413700020
9090475600060	9090410400020	9090410600120	9090413400080	9090413700040
9090475600080	9090410400040	9090410600150	9090413400100	9090413700060
9090475600100	9090410400060	9090410700020	9090413400120	

Lutonix® 014 PTCA Drug Coated Balloon Catheter

Model: 9001

Product Codes:

LUTONIX® 014 Drug Coated Balloon PTCA Catheter – EU				
9020138150009	9020138200040	9020138250030	9020138300020	9020138400015
9020138150012	9020138225009	9020138250040	9020138300030	9020138400020
9020138150015	9020138225012	9020138275009	9020138300040	9020138400030
9020138150020	9020138225015	9020138275012	9020138350009	9020138400040
9020138150030	9020138225020	9020138275015	9020138350012	9020138450009
9020138150040	9020138225030	9020138275020	9020138350015	9020138450012
9020138200009	9020138225040	9020138275030	9020138350020	9020138450015
9020138200012	9020138250009	9020138275040	9020138350030	9020138450020
9020138200015	9020138250012	9020138300009	9020138350040	9020138450030
9020138200020	9020138250015	9020138300012	9020138400009	9020138450040
9020138200030	9020138250020	9020138300015	9020138400012	