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To: Commissioners of Prefectural Health Department (Bureau)

Director of Medical Device Evaluation Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)
Director of Pharmaceutical Safety Division,
Pharmaceutical Safety and Environmental Health Bureau,
Ministry of Health, Labour and Welfare
(Official seal omitted)

Self-inspection of Package Insert for Paclitaxel-coated Balloons and Stents in the Femoropopliteal Artery

Paclitaxel-coated balloons and stents in the femoropopliteal artery (hereinafter referred to as "PTX devices") have been used to reduce restenosis, etc., as a medical device for endovascular treatment of obstructive arteriosclerosis of lower extremities.

In terms of the safety of PTX devices, it has been reported overseas that clinical study data suggested that using the PTX devices may increase the risk of death, and it was necessary to perform a detailed assessment based on results of clinical studies in Japanese patients. Therefore, the Ministry of Health, Labour and Welfare (MHLW) has been examining the safety of PTX devices through the Health and Labour Sciences Research Grant (“Long-term Safety of Devices Utilizing Paclitaxel in the Femoropopliteal Artery (Principal Investigator: Masato Nakamura (Toho University)) since July 2019.

This time, the results of the special research based on the Health, Labour and Welfare Sciences Research Grants have been summarized, and a verification using clinical results in Japanese patients, etc., has shown no significant difference in the mortality rate for 5 years after treatment between the patient group and the control group (https://mhlw-grants.niph.go.jp/project/27636/1, only in Japanese).

Based on the results, Japanese Society for Vascular Surgery, Japanese Society of Interventional Radiology and Japanese Association of Cardiovascular Intervention and Therapeutics (hereinafter referred to as "3 academic societies") announced a statement describing that the decision on whether or not to use PTX devices should be made in consideration of the patient's

conditions and that informed consent based on the results in Japan and overseas should be obtained.

Therefore, based on the information described in the statement, we would like commissioners of prefectural health departments or bureaus to instruct the marketing authorization holders who manufacture and sell PTX devices under your jurisdiction to conduct voluntary inspections to ensure that the information is described in the package inserts of the PTX devices based on the latest knowledge obtained from articles, etc., pursuant to Article 63, Paragraph 2 of the Act.

Please note that this notification has been issued to professional organizations, Pharmaceuticals and Medical Devices Agency, and each marketing authorization holder.

In addition, the statement from 3 academic societies is available from the websites of the 3 academic societies.

Japanese Society for Vascular Surgery
http://www.jsvs.org/ja/info/pdf/2021012902.pdf (only in Japanese)
Japanese Society of Interventional Radiology
https://www.jsir.or.jp/wp-content/uploads/2015/03/PXT_210118.pdf (only in Japanese)
Japanese Association of Cardiovascular Intervention and Therapeutics
http://www.cvit.jp/files/news/2021/0129.pdf (only in Japanese)

Note

1. Target PTX devices

   Among drug-eluting femoral arterial stents and balloon dilation angioplasty catheters, the target medical devices are those to which paclitaxel has been applied.

2. Provision of necessary information before use of PTX devices

   The marketing authorization holders of the products described in 1 above should add the following contents to [Precautions] and [REFERENCES AND REFERENCE REQUEST] of the package insert so that healthcare professionals can confirm necessary information before use.

   (a) Describe the following items in [Important Precautions] of [Precautions].
   - This device should be used in consideration of risks and benefits in light of the patient's conditions.
   - Informed consent should be obtained based on the representative results in Japan (see [REFERENCES AND REFERENCE REQUEST]) in addition to overseas information.

   (b) [REFERENCES AND REFERENCE REQUEST]

- Katsanos K, et al., "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", Journal of the American Heart Association, 2018; 7:e011245
- the Health and Labour Sciences Research Grant (“Long-term Safety of Devices Utilizing Paclitaxel in the Femoropopliteal Artery (Principal Investigator : Masato Nakamura)
- "Statement on paclitaxel-coated balloons and stents in the femoropopliteal artery" (Japanese Society for Vascular Surgery, Japanese Association of Interventional Radiology, Japanese Association of Cardiovascular Intervention and Therapeutics)
- Nordanstig J, et al., "Mortality with Paclitaxel-Coated Devices in Peripheral Artery Disease", N Engl J Med, 2020; 383:2538-2546

3. Report of self-inspection results
   The above 2 should be handled by March 31, 2021. In addition, the results of self-inspection should be promptly reported to the Division of Safety for Medical Devices, Office of Manufacturing Quality and Vigilance for Medical Devices, Pharmaceuticals and Medical Devices Agency.

4. Regarding the products mentioned in the above 1, for which evaluation for approval is ongoing, the applicant should conduct the same inspection of the package insert (draft version) as in the above 2, and inform the application destination of the self-inspection results.