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N o t i f i c a t i o n
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To: Commissioner of Prefectural Health Department (Bureau)

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

Director of Pharmaceutical Safety Division, Pharmaceutical Safety and Environmental Health Bureau, Ministry of Health, Labour and Welfare (MHLW)

Revision of Precautions to the Package Inserts of Drug-eluting Coronary Stent or Drug-coated Balloon Dilatation Catheter for Coronary Angioplasty

Following the recent compilation of the JCS 2018 Guideline on Revascularization of Stable Coronary Artery Disease and the JCS 2018 Guideline on Diagnosis and Treatment of Acute Coronary Syndrome Guidelines by a joint research group organized by related academic societies, the following revision of the PRECAUTIONS in the package insert of drug-eluting coronary stent or drug-coated balloon dilatation catheter for coronary angioplasty has been instructed to the relevant marketing authorization holders (MAHs). Commissioners of the prefectural health bureaus and departments are requested to appropriately circulate the information among medical institutions or other concerned parties under your supervision.

1. The WARNINGS section of the package insert of drug-eluting coronary stent or drug-coated balloon dilatation catheter for coronary angioplasty should be revised according to the Appendix.

2. The package inserts revised in line with the instruction as 1 above should be uploaded in the package insert information page for medical devices (only in Japanese) of the Pharmaceuticals and Medical Devices Agency (PMDA).

3. Responses to the instructions 1, 2, and dissemination to medical institutions and other related parties of the information on the revision of package insert should be completed within 3 months after the release of this notification and the completion should be notified to the Division of Safety for Medical Devices, Office of Manufacturing Quality and Vigilance for Medical Devices, PMDA.

4. Marketing authorization applicants for drug-eluting coronary stents or drug-coated balloon dilatation catheters for coronary angioplasty under review should notify the reviewing agency of their intention to revise the proposed package inserts submitted for the review.

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(Appendix)

PRECAUTIONS in the package insert should be revised in line with the Table 1 and Table 2 below for drug-eluting coronary stents and drug-coated balloon dilatation catheters for coronary angioplasty, respectively.

Table 1

Current (Deleted language is strike-through lined.)	Revised (Added language is underlined.)
WARNINGS • ~~Dual antiplatelet therapy (DAPT) is recommended by the clinical studies for at least xx month(s) after the operation (see the section of "CLINICAL STUDY RESULTS")~~ ~~Note 1)~~~~.~~ Periodical follow-up should be performed as needed by the patient conditions and whether administration of the antiplatelet drug should be prolonged or not is determined in full consideration of risks of adverse reactions such as haemorrhage as well as the background factors of the patient and the anatomical features of the lesion, since there have been reports on late stent thrombosis – a critical malfunction – more than 1 year after stent replacement. Meanwhile, it should be noted that concomitant use of an antiplatelet drug or an anticoagulant drug may lead to a greater risk of haemorrhage. ~~Note 1) Describe the rationale for the recommended period in the CLINICAL STUDY RESULTS section.~~	WARNINGS • Antiplatelet therapy (APT) after the operation should be properly performed based on the latest guidelines such as the JCS 2018 Guideline on Revascularization of Stable Coronary Artery Disease and the JCS 2018 Guideline on Diagnosis and Treatment of Acute Coronary Syndrome Guidelines of the Japanese Circulation Society, as well as other relevant information. Periodical follow-up should be performed as needed by the patient conditions and whether administration of the antiplatelet drug should be prolonged or not is determined in full consideration of risks of adverse reactions such as haemorrhage as well as the background factors of the patient and the anatomical features of the lesion, since there have been reports on late stent thrombosis – a critical malfunction – more than 1 year after stent replacement. Meanwhile, it should be noted that concomitant use of an antiplatelet drug or an anticoagulant drug may lead to a greater risk of haemorrhage (see the CLINICAL STUDY RESULTS section for the period of dual antiplatelet therapy (DAPT) recommended by the clinical studies.)

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Table 2

Current (Deleted language is strike-through lined.)	Revised (Added language is underlined.)
WARNINGS • Dual antiplatelet therapy (DAPT) is recommended by the clinical studies for at least xx month(s) after the operation (see the section of CLINICAL STUDY RESULTS) Note 2). After the recommended period, DAPT ~~should be performed adequately after confirmation of the period recommended by the stent placement~~. Periodical follow-up should be performed as needed by the patient conditions and whether administration of the antiplatelet drug should be prolonged or not is determined in full consideration of risks of adverse reactions such as haemorrhage as well as the background factors of the patient and the anatomical features of the lesion. Meanwhile, it should be noted that concomitant use of an antiplatelet drug and an anticoagulant drug may lead to a greater risk of haemorrhage. Note 2) Describe the rationale for the recommended period in the CLINICAL STUDY RESULTS section.	WARNINGS • Dual antiplatelet therapy (DAPT) is recommended by the clinical studies for at least xx month(s) after the operation (see the section of CLINICAL STUDY RESULTS) Note 2). After the recommended period by the clinical studies, DAPT <u>should be performed based on the latest guidelines such as the JCS 2018 Guideline on Revascularization of Stable Coronary Artery Disease and the JCS 2018 Guideline on Diagnosis and Treatment of Acute Coronary Syndrome Guidelines of the Japanese Circulation Society, as well as other relevant information.</u> Periodical follow-up should be performed as needed by the patient conditions and whether administration of the antiplatelet drug should be extended or not is determined in full consideration of risks of adverse reactions such as haemorrhage as well as the background factors of the patient and the anatomical features of the lesion. Meanwhile, it should be noted that concomitant use of an antiplatelet drug and an anticoagulant drug may lead to a greater risk of haemorrhage. Note 2) Describe the rationale for the recommended period in the CLINICAL STUDY RESULTS section.