Ministry of Health, Labour and Welfare

Safety Division, Pharmaceutical and Food Safety Bureau

Translated by **Pharmaceuticals and Medical Devices Agency**

Office of Safety I

July 21, 2015

Notification

PFSB/ELD/OMDE Notification No. 0721-3
PFSB/SD Notification No. 0721-3

To: Representatives (of the Companies listed in Appendix 1)

Counsellor of Minister's Secretariat, Ministry of Health, Labour and Welfare
(Evaluation and Licensing of Medical Device/Cellular and Tissue-based Products)

Director of Safety Division, Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Revision of the Precautions in the Package Insert of Medical Devices and In Vitro Diagnostics for Blood Glucose Measurements Using Enzymatic Electrodes

The measurement principles of glucose analyzers can be broadly divided into assays using enzymatic electrodes and enzyme colorimetric assays. Glucose analyzers include self-monitoring blood glucose (SMBG) meters, automated analyzers, and glucose assay kits for blood tests and for self-monitoring (refers to medical devices and in vitro diagnostics that measure blood glucose levels and hereinafter are referred to as "blood glucose meters, etc."). Until now, measurements of blood glucose levels using any measurement principles during administration of pralidoxime iodide tended to be higher than the actual blood glucose levels (i.e. false high values). Therefore, revisions of the precautions had been advised based on the PFSB/SD Notification No. 0907001 "Regarding Instructions on Revision of the "Precautions" in the Package Insert of Blood Glucose Meters" and PFSB/SD Notification No. 0907003 "Regarding Revisions of the "Precautions" in the Package Inserts" of the Notification of the Safety Division, Pharmaceutical and Food Safety Bureau, MHLW, dated September 7, 2007.

Based on recent findings, blood glucose meters using enzymatic electrodes as a measurement principle are influenced by serum iodide ion concentration. In addition, there was a case report of false high values of blood glucose suggesting a contamination of residual iodine antiseptics on patient's skin when collecting blood. Therefore, "Precautions" in the package insert should be revised in order to give the alert regarding blood collection methods, etc.

This notification is issued to advise the Marketing Authorization Holders dealing with these products to revise the "Precautions" in the respective package insert as explained as follows and asks for your cooperation in making this information widely known to medical institutions, etc.

1. In the “Important Precautions” section in the Precautions in the package inserts of glucose analyzers and SMBG meters that use enzymatic electrodes, the following text should be added:

   Avoid collecting blood from sites using topical preparations that include iodine. (It may cause false high values.)

2. In the “Important Precautions” section in the Precautions of the package insert of automated analyzers, etc. that use enzymatic electrodes to measure blood glucose, the following text should be added:

   Avoid collecting blood from sites using topical preparations that include iodine when measuring blood glucose. (It may cause false high values.)

3. In the “Operating Precautions” of the package insert of in vitro diagnostics used when enzymatic electrodes are used to measure blood glucose, the following text should be added as an interfering substance:

   If there is a substance that releases iodide ions in the measured sample, it may result in false high values.

4. The revised package inserts of blood glucose meters, etc. as advised in the abovementioned items 1 to 3 should be uploaded on Information Services on the website of the Pharmaceuticals and Medical Devices Agency (hereinafter referred to as “PMDA”) as information on package inserts for medical devices or in vitro diagnostics.

5. The respective Marketing Authorization Holders should report to the Medical Device Safety Division, Office of Safety 1, PMDA by August 21, 2015, regarding the actions taken for abovementioned items 1 to 4 in addition to the information provided in the revised package insert to the medical institutions, etc.
   In addition, blood glucose meters, etc. that can theoretically explain how it is not influenced by iodide ions should immediately be reported to the Medical Device Safety Division.

6. For any related products under application for approval, the applicant should report to the PMDA that the revision will be made in the respective package insert (draft).

(Appendix 1)

IL Japan Co., Ltd.

Arkray, Inc.

Alere Medical Co., Ltd.

Abbott Japan Co., Ltd.

Gunze Limited

Johnson & Johnson K.K.

Siemens Healthcare Diagnostics K.K.

Nipro Corporation

Nova Biomedical K.K.

Bayer Yakuhin Ltd.

Panasonic Healthcare Co., Ltd.

ForaCare Japan Co., Ltd.

HORIBA, Ltd.

Radiometer K.K.

Roche Diagnostics K.K.