



# Summary of Investigation Results

May 19, 2020

Pharmaceuticals and Medical Devices Agency

## I. Summary of drug

|                        |                          |
|------------------------|--------------------------|
| [Non-proprietary name] | Insulin vial preparation |
| [Branded name]         | See Attachment           |
| [Approval holder]      | See Attachment           |
| [Indications]          | See Attachment           |

## II. Summary of Revision

Language concerning use of “syringes dedicated to insulin vials” should be added to the Important Precautions section.

## III. Investigation results and background of the revision

Cases of medical adverse events have been reported where use of general purpose syringes instead of syringes dedicated to insulin vials to formulate medication liquid from insulin vial preparations resulted in insulin overdose in the cases collected and released by the Project to Collect Medical Adverse Event Information, The Japan Council for Quality Health Care. MHLW/PMDA in consultation with expert advisors concluded that revision of the package insert was necessary.

## IV. Number of cases reported in Japan during the previous 5 fiscal years\*

A total of 19 cases involving insulin overdose that resulted from the use of general purpose syringes have been reported to date (See Appendix, only in Japanese).

\*Medical adverse events collected and released by the Project to Collect Medical Adverse Event Information, The Japan Council for Quality Health Care

## V. Proposed revision

For insulin preparations mentioned in 1-1) and 1-2), language concerning continuous subcutaneous insulin infusion therapy (CSII therapy) is included in the Dosage and Administration section together with a precaution regarding CSII therapy as well as use

of syringes dedicated to the insulin vials. Because the term to indicate the pump used in CSII therapy is different between insulin preparations mentioned in 1-1) and 1-2), 2 different revisions are proposed as follows:

- 1-1) Preparations without language concerning continuous subcutaneous insulin infusion (CSII) therapy in the OSAGE and ADMINISTRATION section (Attachment a., i.)

| Current                     | Revision   |
|-----------------------------|--|
| Important Precautions (N/A) | <p>Important Precautions</p> <p>Incorrect doses of insulin may be injected by confusing the number of units of insulin per milliliter of liquid (insulin units) with the volume of the liquid (mL). Syringes dedicated to the insulin vials that are calibrated in insulin units or other measurement units should be used to formulate or administer an injection liquid, except when the drug is used for continuous subcutaneous insulin infusion (CSII) therapy. In that case, the device that is specified in the user manual of the portable insulin infusion pump should be used.</p> |

- 1-2) Preparations with language concerning continuous subcutaneous insulin infusion (CSII) therapy in the DOSAGE and ADMINISTRATION section (Attachment b., g., h.)

| Current                     | Revision  |
|-----------------------------|---|
| Important Precautions (N/A) | <p>Important Precautions</p> <p>Incorrect doses of insulin may be injected by confusing the number of units of insulin per milliliter of liquid (insulin units) with the volume of the liquid (mL). Syringes dedicated to the insulin vials that are calibrated in insulin units or other</p> |



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|  |   |
|--|---|
|  | measurement units should be used to formulate or administer an injection liquid, except when the drug is used for continuous subcutaneous insulin infusion (CSII) therapy. In that case, the device that is specified in the user manual of the continuous subcutaneous infusion pump should be used. |
|--|---|

2) Preparations without language concerning continuous subcutaneous insulin infusion (CSII) therapy in the DOSAGE and ADMINISTRATION section (Attachment c., d., e., f., j., k.)

| Current                     | Revision  |
|-----------------------------|---|
| Important Precautions (N/A) | Important Precautions<br>Incorrect doses of insulin may be injected by confusing the number of units of insulin per milliliter of liquid (insulin units) with the volume of the liquid (mL). Syringes dedicated to the insulin vials that are calibrated in insulin units or other measurement units should be used to formulate or administer an injection liquid. |



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Attachment

|   | Non-proprietary name                        | Brand name (Marketing authorization holder)                        | Indications  |
|---|---|--|--|
| a | Insulin glulisine (genetical recombination) | Apidra Inj. 100 U/mL (Sanofi K.K.)                                 | Diabetes mellitus for which insulin therapy is indicated |
| b | Insulin lispro (genetical recombination)    | Insulin Lispro BS Injection HU 100 units/ml [Sanofi] (Sanofi K.K.) | Diabetes mellitus for which insulin therapy is indicated |
| c | Insulin glargine (genetical recombination)  | Lantus Inj. 100 U/mL (Sanofi K.K.)                                 | Diabetes mellitus for which insulin therapy is indicated |
| d | Insulin human (genetical recombination)     | Humulin N Injection 100 units/mL (Eli Lilly Japan K.K.)            | Diabetes mellitus for which insulin therapy is indicated |
| e | Insulin human (genetical recombination)     | Humulin R Injection 100 units/mL (Eli Lilly Japan K.K.)            | Diabetes mellitus for which insulin therapy is indicated |



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|   |  |  |  |
|---|--|--|--|
|   |  |  |  |
| f | Insulin human<br>(genetical<br>recombination)  | Humulin 3/7 Injection 100 units/mL<br>(Eli Lilly Japan K.K.) | Diabetes mellitus for which insulin therapy is indicated |
| g | Insulin lispro (genetical<br>recombination)    | Humalog Injection 100 units/mL<br>(Eli Lilly Japan K.K.)     | Diabetes mellitus for which insulin therapy is indicated |
| h | Insulin lispro (genetical<br>recombination)    | Lyumjev Injection 100 U/mL<br>(Eli Lilly Japan K.K.)         | Diabetes mellitus for which insulin therapy is indicated |
| i | Insulin aspart<br>(genetical<br>recombination) | Fiasp Injection 100 U/mL<br>(Novo Nordisk Pharma Ltd.)       | Diabetes mellitus for which insulin therapy is indicated |
| j | Insulin aspart<br>(genetical<br>recombination) | NovoRapid 100 U/mL<br>(Novo Nordisk Pharma Ltd.)             | Diabetes mellitus for which insulin therapy is indicated |
| k | Insulin human<br>(genetical<br>recombination)  | Novolin R 100 IU/mL<br>(Novo Nordisk Pharma Ltd.)            | Diabetes mellitus for which insulin therapy is indicated |