Irish Medicines Board
Earlsfort Centre
Earlsfort Terrace
Dublin 2
Ireland
Attn.: Niamh Arthur

12 December 2006
Ref.: Pilar Carrero

NovoRapid®/Levemir® Medication Errors

Dear

Novo Nordisk A/S is committed to patient safety and proper medication usage. An ongoing surveillance of our post-marketing reports reveals that, in some cases, patients have incorrectly used our insulin products, namely NovoRapid® and Levemir®, to treat their diabetes. These errors have primarily occurred due to maladministration of NovoRapid instead of Levemir in their pre-filled (FlexPen®) and 3 ml cartridge (Penfill®) presentations. Although these cases have been rare to very rarely observed, unwarranted substitutions of insulin products have the potential to cause poor glycaemic control and hypoglycaemia.

This notification relates to **NovoRapid®** (insulin aspart, [rDNA origin]) and **Levemir®** (insulin detemir, [rDNA origin]) and the potential for medication errors involving:

- **NovoRapid® FlexPen®** *substituted* for **Levemir® FlexPen®** or *viceversa*.
- **NovoRapid® Penfill®** *substituted* for **Levemir® Penfill®** or *viceversa*.

Novo Nordisk insulin products have been demonstrated to be safe and effective when used according to the Prescribing Information. To help ensure patient safety, we have implemented the following important safety measures:

- Colour-branded labeling. Our insulin analogue line is colour-branded with a distinct colour bar on the white packaging, 3 ml cartridges (Penfill), and pre-filled devices (FlexPen) to clearly differentiate our different insulin products. The FlexPen devices are also colour-branded on the push-button:

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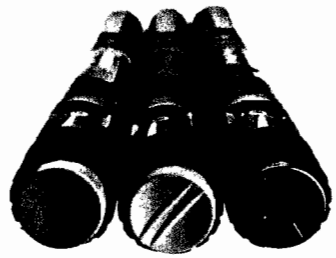
- **NovoRapid®**, our rapid-acting insulin analogue, has an orange bar.
- **Levemir®,** our long-acting insulin analogue, has a green bar.

- Tactile labeling. Our insulin analogue FlexPen devices are fitted with a tactile-coding system on the push-button that helps the user distinguish between different kinds of insulin.
- Promotional material. Our promotional material clearly delineates the function and brand names of our insulin products.

Below pictures illustrate the diligence with which e.g. the FlexPen® devices are differentiated.



Despite these safety measures, ongoing surveillance of our post-marketing reports has revealed that, in some cases, patients have incorrectly used our insulin products (NovoRapid® and Levemir®) to treat their diabetes. We would like to inform you that Novo Nordisk has closely monitored this type of incidents.

An analysis of adverse events reported in relation to medication errors due to maladministration of NovoRapid® instead of Levemir® was performed based on data from the Novo Nordisk A/S Global Safety Database, Argus. The analysis covered the period since Levemir® was launched (1 March 2004) up to October 2, 2006. Conclusions from this analysis are summarised below:

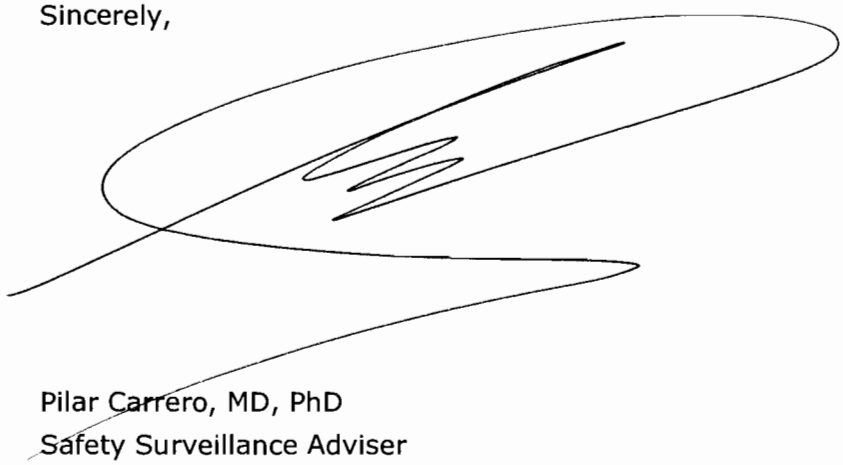
- No medication error cases due to maladministration of NovoRapid® instead of Levemir® were identified prior to January 2006
- Most cases occurred in subjects recently introduced to NovoRapid®/Levemir® basal-bolus regimen
- FlexPen® cases: Some subjects attributed the error to the similar appearance of the device
- Penfill® cases: Some subjects switched insulin product because NovoRapid® and Levemir® are both clear solutions
- Distribution is similar within age groups (Only 37% cases state age information)
- Approximately 80% of the cases were reported as non-serious adverse events

- The reporting rates are Rare (<1/1,000; >1/10,000) in UK, Ireland and Australia, and Very Rare (<1/10,000) in Europe (except UK and Ireland), USA, and Canada

Although these cases have been rare to very rarely observed, Novo Nordisk has concluded that measures mitigating the potential risk should be considered.

For that purpose, Novo Nordisk has started an evaluation of different options to improve colour differentiation between FlexPen® devices. Novo Nordisk expects to conclude on this analysis by March 2007.

Sincerely,



Pilar Carrero, MD, PhD
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