

Warning: dangers of insulin at 200 units per ml



For some years, *insulin* has only been available in the European Union at a concentration of 100 units per millilitre, in order to prevent any risk of error, especially for patients travelling to different countries within the European Union (1).

In October 2012, the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) issued a recommendation in favour of the authorisation of the first *insulin* at a strength of 200 units per millilitre for self-injection by patients with diabetes.

The company that requested the marketing authorisation claimed that there is a growing need for high-strength *insulin* to enable the administration of high doses in a single injection, particularly for very obese diabetic patients.

The recommendation concerned a new "second-generation" *insulin* analogue: *insulin degludec* (Tresiba[®]) (a)(2).

On 17 December 2012, before the decision on whether to grant marketing authorisation for Tresiba[®] was due to be signed, *Prescrire* sent an open letter to the head of the European Commission's Medicinal Products Unit, the directors of the European Medicines Agency (EMA) and the French drug regulatory agency (ANSM), and to other relevant heads of department within the World Health Organization (WHO) and the European Pharmacopoeia (3).

In this letter, *Prescrire* warned of the dangers of over-hasty authorisation of *insulin degludec* at a strength of 200 units per ml. This concentration of *insulin* exposes patients to a risk of medication error through overdose, and therefore to the risk of severe and potentially fatal hypoglycaemia (3).

In particular, *Prescrire* asked the European Commission to ensure that the risks inherent in the introduction of a new concentration of *insulin* have been properly taken into account: high-quality, clearly differentiated labelling and packaging; packaging tested by patients and carers representative of the population likely to use the product, including patients with diabetes-related visual impairment; clarification on the correlation between the various types of *insulin* unit; etc. (3).

In addition, data from the US suggest an increased cardiovascular risk with *insulin degludec*. *Prescrire* decried the fact that the delicate transition towards the coexistence of two concentrations of *insulin* would be made using a new drug, whose risks are relatively unknown, rather than a better established *insulin* (3).

On 21 January 2013, the European Commission signed the marketing authorisation for *insulin degludec* 200 units per ml (4).

The European Commission responded to *Prescrire*'s letter by explaining that: unlike the US drug regulatory agency

(FDA), the EMA had not detected an increased cardiovascular risk with *insulin degludec*; patient "education programmes" ought to "minimise" the risk of error; and that *insulin degludec* would undergo post-marketing surveillance, just like any drug placed on the European market (5).

Healthcare professionals, patients and carers will need to be extremely vigilant and put procedures in place to reduce the risk of error when using these insulins (6).

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a- We shall be publishing a critical appraisal of the clinical evaluation of insulin degludec in an upcoming issue.

Selected references from *Prescrire*'s literature search.

- 1- *Prescrire* Rédaction "Insulines: harmonisation à 100 U/ml au 30 mars 2000" *Rev Prescrire* 2000; **20** (204): 197.
- 2- EMA "European Medicines Agency recommends approval of first higher-strength insulin for treatment of patients with diabetes mellitus in the EU (EMA/CHMP/2012)" 19 October 2012: 2 pages.
- 3- *Prescrire* Rédaction "Quel besoin d'une insuline à 200 Unités par ml? Pourquoi avec un analogue nouveau et encore peu connu?" Open letter to the European Commission; Paris, 17 December 2012. www.prescrire.org accessed 18 December 2012: 4 pages.
- 4- Reuters "Novo Nordisk gets green light for Tresiba in Europe" 21 January 2013; 1 page.
- 5- European Commission – Health and Consumers Directorate-General "Letter to *Prescrire* about the marketing authorisation of insulin-degludec containing medicinal products" Brussels, Ref. Ares (2013)542228 - 4 April 2013: 4 pages.
- 6- *Prescrire* Rédaction "Utilisation de l'insuline: des erreurs évitables" *Rev Prescrire* 2013; **33** (360): 746-751.