Teriparatide in pen injectors or cartridges: multidose formulations which must not be drawn into a syringe

The pens and cartridges that contain *teriparatide* are designed for 28 doses. Overdoses have been reported following administration, by mistake, of the entire contents of the pen or cartridge as a single injection after drewing it into a syringe.

Teriparatide is a recombinant fragment of parathyroid hormone. In the European Union, it is authorised as a solution for subcutaneous once-daily injection for the treatment of osteoporosis in patients at high risk of fracture. *Teriparatide* mainly carries a risk of gastrointestinal disorders, orthostatic hypotension, vertigo, anaphylaxis, hypercalcaemia, and possibly bone tumours (1).

Pre-filled pens, or cartridges to insert into a pen. As of 28 July 2021, four proprietary medicinal products based on *teriparatide* were marketed in France. The originator product, Forsteo° (available since the 2000s) and the generic Livogiva° (available since early 2021) are presented in the form of ready-to-use, prefilled multidose pens. The generics Movymia° and Terrosa° (available since mid-2019 and late 2020 respectively) are presented as multidose cartridges to be inserted into specific pens, which are sometimes sold separately as Movymia Pen° and Terrosa Pen° respectively (2).

The needles, which must be changed after each injection, are not supplied, neither in the boxes of ready-to-use prefilled pens, nor in those containing the pens designed for use with the cartridges (2).

The daily dose to be injected is 20 micrograms of *teriparatide* (corresponding to 80 microlitres of solution), which is prominently displayed on the labelling for all 4 brands. The prefilled pens and the cartridges are designed for 28 days of treatment and hence 28 doses. They contain a total of 600 micrograms of *teriparatide* in 2.4 ml of injectable solution, except for the prefilled Livogiva° pen, which contains 675 micrograms in 2.7 ml (for 28 days of treatment) (2).

As of 28 July 2021, the total volume, or the total quantity of *teriparatide* per pen or cartridge, is specified on the box of most brands, but this information is sometimes not prominently displayed.

Inappropriate withdrawal and injection of the entire contents of the pen or cartridge. The pen injectors are devices provided for precise measurement of the doses to be injected by a healthcare professional or by a patient after instruction. Although seemingly simple, they nevertheless carry a risk of dosing errors, especially when a syringe is used inappropriately to draw off a dose from a cartridge or directly from a prefilled pen (3). This handling error has occurred since the 2000s with the prefilled Forsteo° pen. Some healthcare professionals, lacking the needles needed for use of the prefilled pen, have drawn and then injected the entire contents of the pen, i.e. 28 doses. Since 2005, the summary of product characteristics (SPC) states that these overdoses are associated with nausea, "weakness" (not otherwise specified), drowsiness and hypotension (2,4,5). Tachycardia has also been associated with such overdoses. This type of error continues to be reported, and led the French Health Products Agency (ANSM) to issue a safety alert in 2021, citing all proprietary drugs based on *teriparatide*, but without specifying the exact circumstances in which errors occurred (6,7).

Some healthcare professionals who only had *teriparatide* (Movymia°) cartridges without the Movymia Pen°, used a syringe to draw and then administer the entire volume contained in the cartridge, i.e. 28 times the daily dose (6). According to the company EG Labo, from whom we requested information, 7 cases were reported between mid-2019 and early 2021, which resulted in vomiting and mild to significant fatigue. The causes identified by the company were: a shortage of Movymia Pen° with only the cartridge being dispensed; lack of awareness of the existence of the Movymia Pen°; and healthcare professionals assuming similarity with other injectable products, without reading the package leaflet. The company has plans to add the following to the boxes: "*28 doses – To be used only with the Movymia Pen°*" (8). The instruction *"Do not transfer the drug to a syringe"* is included in the package leaflet for all 4 drugs, but it should also be present on the boxes, the pens and the cartridges (2).

In practice Drawing the contents of a cartridge or prefilled pen into a syringe carries a risk of dosing errors. For every treatment with *teriparatide*, it is important to prescribe and dispense all of the components needed for administration, including the needles for the pen injector and, where appropriate, the correct pen for the cartridges that are prescribed. It is advisable to warn patients that these components should be stored and transported together.

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