HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Insulin-containing medicines – Risk of cutaneous amyloidosis and potential for associated changes in glycaemic control

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) recently completed a review of the risk of injection site cutaneous amyloidosis associated with insulin-containing medicines. The review considered reports of cutaneous amyloidosis from the published literature and the European database of suspected adverse reactions, EudraVigilance. A number of spontaneous reports involving cutaneous amyloidosis described changes in glycaemic control, with subsequent recovery of glycaemic control reported following injection site rotation and implementation of correct injection technique.

Having considered the available data, the PRAC concluded that the cumulative evidence supports a causal relationship between insulin-containing medicines and cutaneous amyloidosis, with the potential for associated changes in glycaemic control. Based on the available evidence, the risk of cutaneous amyloidosis associated with insulin-containing medicines is considered to be a class effect.

Lipodystrophy is already a known side effect associated with insulin-containing medicines and the product information for these medicines contains a recommendation to rotate injection site to reduce the risk of lipohypertrophy. The product information (Summary of Product Characteristics (SmPC) and Package Leaflet (PL)) for insulin-containing medicines will now be updated to reflect the risk of cutaneous amyloidosis and to further highlight the need for injection site rotation.

Advice to Healthcare Professionals

- Injection site cutaneous amyloidosis has been reported in association with use of insulin-containing medicinal products.
- Patients should be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and cutaneous amyloidosis.
- There is a potential risk of delayed insulin absorption and worsened glycaemic control following insulin injections at sites of lipodystrophy or cutaneous amyloidosis.
- Blood glucose monitoring is recommended after a change in the injection site to an unaffected area, as sudden changes have been reported to result in hypoglycaemia.
- Dose adjustment of antidiabetic medications may need to be considered following a change in the injection site to an unaffected area.

Key Message

- Patients should be instructed to perform continuous rotation of the injection site to reduce the risk of developing lipodystrophy and injection site cutaneous amyloidosis.
- Blood glucose monitoring is recommended after a change in the injection site to an unaffected area, as sudden changes have been reported to result in hypoglycaemia. Dose adjustment of antidiabetic medications may also need to be considered.
- The product information for insulin-containing medicines will be updated to reflect current knowledge on the risk of cutaneous amyloidosis associated with injection.
- All reports of suspected adverse reactions should be reported to the HPRA via the available methods (www.hpra.ie/report).

** Insulin-containing medicines include Abasaglar, Actraphane, Actrapid, Apidra, Fiasp, Humalog, Humulin, Insulatard, Insulin Lispro Sanofi, Insuman, Lantus, Levemir, Liprolog, Mixtard, NovoMix, NovoRapid, Protaphane, Ryzodeg, Semglee, Suliqua, Toujeo, Tresiba and Xultophy. Further details are available on www.hpra.ie and www.ema.europa.eu.*