**MHRA safety update - Insulins (all types): risk of cutaneous amyloidosis at injection site**

<https://www.gov.uk/drug-safety-update/insulins-all-types-risk-of-cutaneous-amyloidosis-at-injection-site>

**Background**

Insulin is used to treat all types of diabetes (including type 1 diabetes, type 2 diabetes and gestational diabetes). Patients who self-inject insulin are already advised to rotate injections within one area, and change injection sites completely every week or two (for example, from the abdomen to thigh), and to be aware that the injection site will affect blood sugar levels. A recent European review of reports of insulin-derived cutaneous amyloidosis at insulin injection sites concluded that there is a clear causal relationship between cutaneous amyloidosis and all insulins and insulin-containing products.

Insulin-derived amyloidosis is a specific form of localised cutaneous amyloidosis composed of insulin fibrils. It is likely caused by insulin accumulation at the injection sites, especially if these sites are used for repeated subcutaneous injections.

In the UK, up until the end of July 2019, 2 reports of cutaneous amyloidosis in patients receiving insulin therapy have been received via the MHRA’s Yellow Card Scheme. Literature suggests that cases of cutaneous amyloidosis may be under-reported and misdiagnosed as lipohypertrophy (a common increase in fat cells due to growth factor effect of insulin). Both conditions are characterised by lumps in the skin. However, where lipohypertrophy lesions are lobular and regress after stopping insulin injection, amyloid lesions are more solid and firm, do not regress quickly, and usually require surgical excision to treat

While amyloid lesions can delay insulin absorption and affect glycaemic control if used as a site for administration, the skin changes are thought to be localised. Although some cases of cutaneous amyloidosis were reported as of a serious nature, they were mostly reported as such due to hospital admission to resect an amyloid lesion. Aside from impact on glycaemic control, no other complications have been recognised. Lesions can be resected if the patient finds the lesion cosmetically unacceptable but this is usually a procedure that is not available on the NHS.

The Summaries of Product Characteristics and Patient Information Leaflets for all insulins and insulin-containing products are being updated to include this risk. Advice will also make clear the importance of site rotation and careful blood glucose monitoring following change of injection site to an unaffected area.

**Key recommendations**

**Health Care Professionals:**

* When reviewing patients always remind them to rotate injection sites within the same body region to reduce or prevent the risk of cutaneous amyloidosis and other skin reactions (for example, lipodystrophy)
* Consider cutaneous amyloidosis as a differential diagnosis to lipodystrophy when a patient presents with subcutaneous lumps at an insulin injection site
* Ensure that all people who inject insulin are taught to check for signs of developing cutaneous amyloidosis or lipohypertrophy and that they should report any abnormalities to their healthcare professional.
* If patients are injecting insulin into a ‘lumpy’ area a change in injection site may result in hypoglycaemia and hyperglycaemia. Patients should monitor their blood glucose levels more closely after a change in injection site. A dose adjustment of insulin or other antidiabetic medication may be needed to avoid hypoglycaemia.
* If a patient develops signs of cutaneous amyloidosis or lipohypertrophy advise them to avoid using that area for at least 3-6 months.
* Advise patients never to reuse needles as this increases the risk of developing cutaneous amyloidosis and other skin reactions.
* Only prescribe 4mm or 5mm needles especially for children, young people or very slim adults.
* Report serious adverse drug reactions associated with insulin to the [Yellow Card scheme](https://yellowcard.mhra.gov.uk/)
* A useful resource about insulin injection technique and download useful resources is: <http://fit4diabetes.com/united-kingdom/fit-technique-plus/>

**Community Pharmacy Teams:**

* Take every opportunity to counsel the patients who are using insulin to rotate their injection sites.
* Ask patients who use insulin if they have noticed any ‘lumps’ at their injection sites and to seek advice from their healthcare professional who supports them to manage their diabetes.
* If a patient is currently injecting insulin into a ‘lumpy’ area, before changing injection site they must consult their diabetes healthcare professional as a sudden change may result in hypoglycaemia.

**Advice to give to patients:**

* Insulin may not work very well if patients inject into an affected ‘lumpy’ area
* Patients must contact their healthcare professional if they are currently injecting insulin into a ‘lumpy’ area before changing injection site as a sudden change may result in hypoglycaemia.
* Patients should monitor their blood glucose levels more closely after a change in injection site and that their healthcare professional may make a dose adjustment of insulin or other antidiabetic medication.

**How to examine for lipohypertrophy and amyloidosis:**

<https://trenddiabetes.online/wp-content/uploads/2018/11/ITM-Guideline_v9-FINAL-251018.pdf>

* Always inspect for lipodystrophy in good light
* Gain consent to examine
* Look for changes in contour of skin
* Warm, clean hands
* Use water soluble gel
* Use tips of fingers
* Work towards suspected area of lipodystrophy with a light massage-like motion
* Push deep into tissue through fat to feel muscle below (if possible) then push forward toward until lipodystrophic tissue is felt
* Feel for a change in the subcutaneous tissue
* Document size and position of lipodystrophy
* Advise avoid using area for at least 3-6 months
* Re-examine at next visit

**Patient educational materials**

* Patient information leaflet from the TREND diabetes website:

<https://trenddiabetes.online/wp-content/uploads/2018/11/ITM-Toolkit_ITM_v8_PAGES-151018-FINAL.pdf>

* Patient information on the Diabetes UK website:

<https://www.diabetes.org.uk/guide-to-diabetes/managing-your-diabetes/treating-your-diabetes/insulin>