

**Macleod Diabetes & Endocrine Centre
Royal Devon & Exeter Hospital**

GLP-1 analogues with insulin in type 2 diabetes

For general advice on GLP-1 analogues, see our separate advice sheet.

Currently approved uses of GLP-1 analogues:

NICE and Formulary

- Only for add on to metformin and/or sulphonylurea, as an alternative to insulin.

Marketing licence

- These vary subtly (though not with any apparent logic) between the different GLP-1. Licences may change, and this document may become out-of-date. Consult BNF or www.medicines.org.uk if you wish to stick to licence.
- Exenatide (Byetta), liraglutide and lixisenatide are approved with basal insulin. Dulaglutide is approved with any insulin. Bydureon is not licensed with insulin.

Evidence:

- In patients with HbA1c moderately above target (mean 68 mmol/mol), addition of exenatide to insulin improved HbA1c by about 7 mmol/mol, and weight by about 3kg.
- We expect a greater benefit in patients with higher HbA1c, based on other studies.

Background

We think a trial of GLP-1 analogue with insulin is logical for carefully selected, overweight patients, who are on high-dose insulin but failing to achieve reasonable glycaemic control.

This is against Formulary advice. We do not wish to pressure primary care colleagues into prescribing against their judgement. However, the reality is that the combination is widely used, and we are quite often asked about it.

Our Specialist Nurses doing community clinics are sometimes asked whether to use GLP-1 analogues with insulin. Advising off-Formulary is sensitive, and in this situation, our nurses may give an opinion but the decision to prescribe remains with the primary care team.

Note that SGLT-2 inhibitors have both licence and NICE approval to use with insulin, are cheaper, and likely to be preferred by patients (tablets).

Consultants are happy to see patients to give an opinion. Treatment can be initiated here if you request, but is usually done in primary care. We can't take on on-going prescription.

A consultant referral is not required if the primary care team are happy to decide.

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Recommendation

Addition of GLP-1 analogue to insulin in primary care for type 2 diabetes

Patient selection

- Overweight, BMI>35, and more appropriate in heavier patients e.g. BMI>40.
- Insulin already at high dose. Total daily dose typically > 1.5 units/kg.
- Evidence that further insulin dose increase will not help, e.g. if insulin appears to cause weight gain without substantially improving blood sugars.
- Patient is prepared to increase number of daily injections.
- No contraindications to GLP-1 treatment, e.g. renal failure, risk of pancreatitis.

Method

- Start GLP-1 analogue in usual way, usually reduced dose initially and full dose thereafter. See our GLP-1 guidance for more detail.
- If HbA1c>70 mmol/mol (8.5%), start GLP-1 analogue with no adjustment of insulin.
- If HbA1c is <70 mmol/mol (8.5%), reduce insulin doses by around 25%. Review after 2 months, and increase insulin doses if blood glucose is above target.

Avoid unnecessary analogue insulin

- Take the opportunity to review the insulin. Many type 2 patients are on analogue insulin, which is expensive and gives little benefit. See analogue insulin guideline for more information.

Review

- Review at 6 months. Follow the usual criteria for continuation: HbA1c reduction of 11 mmol/mol and weight of 3%.
- If HbA1c reduction is not met, but insulin doses were reduced, consider increasing insulin doses and then re-assess.
- If insulin doses are reduced, this offsets the cost of the GLP-1. It may be reasonable to continue GLP-1 treatment if HbA1c and weight targets are not quite met.

Cost per month (as of Nov 2012)

- Exenatide (Byetta) £68 at 10 micrograms bd
- Liraglutide (Victoza) £78 at 1.2mg od
- Levemir Flexpen 10 units/day = £7.84 50 units/day = £39.20 100 units/day = £78.40
- Insulatard cartridge 10 units/day = £4.27 50 units/day = £21.37 100 units/day = £42.70
- Insulatard vial 10 units/day = £2.09 50 units/day = £10.45 100 units/day = £20.94