Lixisenatide (Lyxumia): new GLP-1 mimetic for type 2 diabetes

Steve Chaplin BPharm, MSc and Frank Joseph MD, FRCP

Lixisenatide is a new GLP-1 mimetic for use in type 2 diabetes with oral agents and/or insulin. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse events, and Dr Frank Joseph discusses its place in therapy.

KEY POINTS

- Lixisenatide (Lyxumia) is a GLP-1 mimetic licensed for the treatment of type 2 diabetes in combination with oral glucose-lowering drugs and/or insulin
- Available as prefilled pens for subcutaneous injection; a month’s treatment at 20µg per day costs £54.14, less than exenatide (£68.24) or liraglutide (£78.48)
- In trials lasting 24 weeks, adjunctive lixisenatide reduced HbA1c by 0.36–0.75 per cent and at least doubled the proportion of patients achieving glycaemic control (HbA1c < 7.0 per cent) compared with placebo
- Another 24-week study showed lixisenatide to be noninferior to twice-daily exenatide in reducing HbA1c
- As with other GLP-1 mimetics, the commonest adverse effects are nausea and vomiting; these usually occur in the first three weeks, then diminish
- Lixisenatide may be preferred to twice-daily exenatide being noninferior, having better tolerability and only requiring one daily injection

The glucagon-like peptide-1 (GLP-1) mimetics exenatide and liraglutide (Victoza) are licensed for the treatment of type 2 diabetes in combination with oral glucose-lowering drugs and/or basal insulin when these, together with diet and exercise, do not provide adequate glycaemic control.

The recommended dose is 10µg once daily for 14 days, increasing to 20µg on day 15. Like twice-daily exenatide, it should be administered within an hour of a main meal; liraglutide can be injected independently of meal times (but at the same time each day).

When adding lixisenatide to established treatment, no dose adjustment of metformin is necessary but the dose of sulfonylurea and basal insulin may need to be reduced.

Dose adjustment is not necessary in older patients (though experience in those aged ≥75 is limited) or in those with hepatic impairment or mild renal impairment.

Lixisenatide should be used with caution in patients with moderate renal impairment and it is contraindicated in those with severe renal impairment.

Clinical trials

Phase 3 trials of lixisenatide included adults with type 2 diabetes with a median age of 54–59 years and median body mass index ranging from 29 to 33kg per m². Mean HbA1c at baseline was 8.0–8.5 per cent. The primary endpoint was the change in HbA1c after 24 weeks.

The effects on glycaemic control of adding lixisenatide to established treatment are summarised in Table 2. Compared with placebo, lixisenatide reduced HbA1c by 0.36–0.75 per cent and at least doubled the proportion of patients achieving glycaemic control (HbA1c < 7.0 per cent).

In patients taking insulin (for about three years), this was associated with a mean reduction in insulin dose of 5.6U (vs 1.9U with placebo) with or without...
GLP-1 mimetics are now an established treatment in the management of type 2 diabetes. As newer agents in this group have become available a variety of differences between them have been recognised: in dosing frequencies from once daily to once weekly; in formulation and delivery devices (prefilled pens vs injections that require mixing); reported differences in side-effect profiles and tolerability; reported variations in efficacy and potency; and last but not least, differences in cost.

**Duration of action**

The addition of lixisenatide, the most recent agent in this group, has now highlighted a further difference: that, based on pharmacokinetic and pharmacodynamic profiles, GLP-1 mimetics can be divided into ‘longer’ acting (once-weekly exenatide and liraglutide) and

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**Declaration of interests**

None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics
Lixisenatide has also been shown to be effective in patients whose diabetes is uncontrolled despite already being on a basal insulin. The postprandial glucose-lowering effect has been proposed as being beneficial in this situation, once the fasting hyperglycaemia has been dealt with by the basal insulin.4–6

Place in therapy
From a day-to-day clinical perspective, in situations where twice-daily exenatide might be considered then the data would suggest that lixisenatide may be preferred in being noninferior but having better tolerability and only requiring one injection a day, which is inherently better for adherence and patient satisfaction.

If liraglutide or once-weekly exenatide is the choice of treatment, then currently there are not enough efficacy or tolerability data to compare. There is an acquisition cost-based argument to be made, however, in that lixisenatide is 26–31 per cent less costly; however, the cost-effectiveness argument is yet to be made against these two agents. On-going trials should shed some light on these issues over the next few years.

Our own local experience, having recently replaced exenatide twice daily with lixisenatide, has been that it is well tolerated and, as with other GLP-1 mimetics, some patients show an early, exquisite response while others seem to show none. Our numbers are too small to draw any conclusions on efficacy as yet and, as with the national audits for exenatide and liraglutide, we will probably need a national audit of lixisenatide to look at real-life effects.

Lixisenatide does, however, provide us with a further option in our armamentarium in battling the ever-increasing incidence of type 2 diabetes.

References

Declaration of interests
Dr Joseph has received honoraria from NovoNordisk, Eli Lilly, Sanofi Aventis, Boehringer Ingelheim, AstraZeneca and MSD, and his department has received research grants from Sanofi Aventis, NovoNordisk and Eli Lilly.

Dr Joseph in consultant physician in diabetes and endocrinology, Countess of Chester Hospital NHS Foundation Trust