South East London Area Prescribing Committee
Formulary recommendation

Reference	**009**
Intervention:	**GLP-1 receptor agonist (exenatide *twice daily* or lixisenatide) as add-on therapy for obese patients with type 2 diabetes mellitus in combination with insulin.**
Date of Decision	**March 2014**
Date of Issue:	**April 2014**
Recommendation:	**Amber, specialist initiation.** **Exenatide (*twice-daily*) or lixisenatide can be initiated by specialists for obese patients with type 2 diabetes mellitus in combination with insulin regimens where attempts to control HbA1c and weight with insulin alone in line with NICE have been inadequate.** Obese is defined in the NICE technology appraisals for GLP-1 agents as a Body Mass Index ≥ 35 kg/m2 in people of European descent (with adjustments for other ethnic groups) and who have health problems associated with this. **For shared care only when initiation criteria and the following have been met:** • **after the insulin regimen has been reviewed and the insulin dose has been adjusted,** • **after clinical benefit* of the addition of GLP-1 to the insulin has been shown in the individual at 6months after initiation,** • **If clinical benefit of the combination has not been demonstrated then the GLP-1 agent should be discontinued – stopping criteria should be made clear in the shared care guideline produced.** ***Clinical benefit assessment should include assessment of the following before and at 6 months after initiation of the combination therapy: (i) weight (either reduction or no gain), (ii) insulin dose (no increase or a reduction), and (iii) HbA1c results (1% reduction demonstrated).**
	NOTE. Exenatide *once-weekly* and liraglutide were also assessed for this indication by the committee and as they are not currently licensed they are not recommended for obese patients with type 2 diabetes mellitus in combination with insulin regimens.
Further Information	• Exenatide twice-daily and lixisenatide are only licensed as adjunctive therapy to basal insulin. Combination with other insulin regimens is supported where alternative regimens are clinically appropriate but would be classed as an unlicensed use. • At the point of initiation the current insulin regimen should be reviewed. Please note that where clinically appropriate, human NPH insulin should be first line choice with insulin analogues reserved for patients who meet the criteria stated in NICE clinical guideline 87. • Exenatide once-weekly and liraglutide are not recommended as adjunctive therapy to insulin. The committee will review this recommendation should relevant randomised controlled trial data

	become available for the use of these medicines as add-on therapy to insulin. People with type 2 diabetes currently receiving exenatide once-weekly or liraglutide as adjunctive therapy to insulin should have the option to continue their current treatment until they and their clinicians consider it appropriate to stop. • Local CCGs are advised update their local diabetes therapeutic pathways to reflect this recommendation.
Shared Care/Transfer of care document required:	Yes – existing shared care document for GLP-1 to be revised and approved before shared care in this scenario can be accepted. Ongoing review and stopping criteria and responsibility for this should be made explicit in the shared care guideline.
Cost Impact for agreed patient group	Based on the QOF data presented in the submission form, there are currently 2546 patients on GLP-1 therapy across the six CCGs. On the assumption that ABCD UK audit data are also representative of the South East London population, 929 patients are already on a GLP-1 receptor agonist combined with insulin (based on an average of 36.5% of GLP-1 therapy being combined with insulin). Assuming two thirds of these patients are on liraglutide, and one third on exenatide twice daily – the cost impact of current prescribing is about **£880,000**. The combination will increase usage by a further 33%, the estimated additional budget impact will be between **£226,000 and £302,000**, depending on which GLP-1 receptor agonist is prescribed.
Usage Monitoring & Impact Assessment	CCGs – epact data monitoring. Trusts – audit initiation of GLP1 as required.
Evidence reviewed	**References** 1. Scottish Medicines Consortium. Lixisenatide 10microgram/0.2mL, 20microgram/0.2mL solution for injection in pre-filled disposable pen (Lyxumia®) SMC No. (903/13). August 2013. 2. All Wales Medicines Strategy Group. Final Appraisal Recommendation – 3113: Lixisenatide (Lyxumia®) 10 micrograms and 20 micrograms solution for injection. November 2013. 3. Ryder B, and Thong K on behalf of the ABCD nationwide exenatide and nationwide liraglutide audit contributors. Findings from the Association of British Clinical Diabetologists (ABCD) nationwide exenatide and liraglutide audits. In Hot topics in diabetes, 5th edition, Vora J, ed. Synergy, London, 2012: 49-61. 4. Buse JB, et al. Use of twice-daily exenatide in basal insulin-treated patients with type 2 diabetes: a randomized, controlled trial. Ann Intern Med 2011; 154: 103-112. 5. Seino Y, et al. Randomized, double-blind, placebo-controlled trial of the once-daily GLP-1 receptor agonist lixisenatide in Asian patients with type 2 diabetes insufficiently controlled on basal insulin with or without a sulfonylurea (GetGoal-L-Asia). Diabetes Obes

	Metab 2012; 14: 910-917. 6. Riddle MC, et al. Adding once-daily lixisenatide for type 2 diabetes inadequately controlled with newly initiated and continuously titrated basal insulin glargine: a 24-week, randomized, placebocontrolled study (GetGoal-Duo 1). Diabetes Care 2013; 36: 2497-2503. 7. Riddle MC, et al. Adding once-daily lixisenatide for type 2 diabetes inadequately controlled by established basal insulin: a 24-week, randomized, placebo-controlled comparison (GetGoal-L). Diabetes Care 2013; 36 (9): 2489-96. 8. Thong KY, et al. Safety, efficacy and tolerability of exenatide in combination with insulin in the Association of British Clinical Diabetologists nationwide exenatide audit. Diabetes Obes Metab 2012; 13: 703–710. 9. All Wales Therapeutics and Toxicology Centre. AWMSG Secretariat Assessment Report. Lixisenatide (Lyxumia®q) 10 micrograms and 20 micrograms solution for injection. Reference number: 863. October 2013. 10. Hirsh IB, et al. Options for prandial glucose management in type 2 diabetes patients using basal insulin: addition of a short-acting GLP-1 analogue versus progression to basal-bolus therapy. Diabetes Obes Metab 2014; 16: 206–214. 11. Gupta PS, et al. Combined insulin and liraglutide therapy is associated with metabolic improvement and reduction in insulin dose in commonly prescribed insulin regimens: an ABCD liraglutide audit analysis. Poster abstract, ABCD Spring Meeting. April 2013.

NOTES:

a) Area Prescribing Committee recommendations and minutes are available publicly on member CCG public websites.
b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
c) Not to be used for commercial or marketing purposes. Strictly for use within the NHS