PROTOCOL FOR PRESCRIBING LIRAGLUTIDE (VICTOZA) 6mg/ml SOLUTION FOR SUBCUTANEOUS INJECTION – 3ml PRE-FILLED PEN

This document should be read in conjunction with the current Summary of Product Characteristics
http://www.medicines.org.uk/

1. Approved Indication	Treatment of Type 2 diabetes mellitus in a **triple therapy regimen** in combination with metformin and a sulphonylurea or in combination with metformin and a glitazone in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies. **Patients must fit the criteria stated by NICE below.** Liraglutide can also be used as part of a dual therapy regimen (in combination with metformin or a sulphonylurea) if:- • The patient is intolerant of either metformin or a sulphonylurea, or treatment with metformin or a sulphonylurea is contraindicated **and** • The patient is intolerant of glitazones and DPP-4 inhibitors, or treatment with glitazones and DPP-4 inhibitors is contraindicated. • Treatment with liraglutide as part of a dual therapy regimen should only be continued if a beneficial metabolic response has been shown (defined as a reduction of a least 1 percentage point in HbA1c at 6 months). **The maximum approved dose of liraglutide is 1.2mg daily** Note: Liraglutide is **NOT** currently licensed for use in combination with insulin and so this is not indicated for use within this protocol.
2. Therapeutic use & Background	Liraglutide is a glucagon-like-peptide-1 (GLP-1) receptor agonist. It works by binding to the GLP-1 receptor to increase insulin secretion, suppress glucagon secretion, and slow gastric emptying. NICE guidance has been issued Liraglutide for the Treatment of Type 2 Diabetes Mellitus. TAG 203. October 2010. The information below is taken from the NICE guidance:- Consider adding liraglutide when the control of blood glucose remains or becomes inadequate (HbA1c ≥7.5%, or other higher level agreed with the individual) and the person has: • a body mass index (BMI) ≥ 35.0 kg/m^2 in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, or • a BMI < 35.0 kg/m^2 and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities. Only continue GLP-1 mimetic (liraglutide) therapy if the person has had a beneficial metabolic response (a reduction of at least 1% in HbA1c and a weight loss of at least 3% of initial body weight at 6 months). Discuss the potential benefits and risks of treatment with the person to enable them to make an informed decision. **Liraglutide may be initiated in Powys by GP's who are experienced in the treatment of Diabetes Mellitus and who currently initiate insulin. Treatment should be restricted to patients who fit the NICE guidance above.**
3. Contraindications / Special Warnings	Hypersensitivity to the active substance or to any of the excipients. Liraglutide should not be used in patients with:- • Type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. • Type 2 diabetes mellitus patients who require insulin therapy due to ß–cell failure. • End-stage renal disease or moderate to severe renal impairment (creatinine clearance <60ml/min). • Severe gastro-intestinal disease including gastroparesis, due to gastrointestinal adverse effects. • There is limited experience on the use of liraglutide in patients with congestive heart failure. • Pregnancy and breast feeding.

<table>
<tr><td>4.
Cautions</td><td>Intravenous or intramuscular injection of liraglutide is not recommended.

Clinical experience in patients >75 years old is limited.</td></tr>
<tr><td>5.
Typical Dosage Regimen (Adults)</td><td>Liraglutide should be initiated at a dose of 0.6mg once daily. The dose can be administered independently of food.
After at least one week, the dose can be increased to 1.2mg once daily.

NICE TAG (203) does not recommended doses of liraglutide above 1.2mg. Studies have shown little additional benefit but a greater incidence of adverse effects at this dose.
Liraglutide 1.8mg daily is NOT recommended for the treatment of people with type 2 diabetes.

If an injection is missed, a dose should be given if remembered within 12 hours of the due time. If it is more than 12 hours then the dose should be omitted and treatment continued at the next scheduled dose.

Each dose should be administered as a subcutaneous injection in the thigh, abdomen, or exceptionally the upper arm.

• Elderly: No dose adjustment is required based on age, however therapeutic experience in patients ≥75 years of age is limited.
• Renal Impariment:
o No dosage adjustment in necessary in patients with mild renal impairment (creatinine clearance (GFR) ≤60 – 90ml/min)
o Liraglutide should not be used in patients with creatinine clearance <60ml/min (lack of data).
• Hepatic Impairment:
o Not recommended in mild, moderate or severe liver impairment (lack of data)</td></tr>
<tr><td>6.Drug Interactions For a comprehensive list consult the BNF or SPC</td><td>The effect of liraglutide in slowing gastric emptying may reduce the extent and rate of absorption of orally administered medicinal products. Patients receiving medicinal products which have either a narrow therapeutic ratio or those which require careful clinical monitoring (including warfarin) should be followed closely.

• Sulphonylureas: Increased risk of hypoglycaemia. Consider a reduction in the dose of sulphonylurea. Blood glucose monitoring may be required initially.
• Insulin: The combination with liraglutide has not been evaluated and therefore cannot be recommended.
• Warfarin: It is not know if a clinically significant interaction occurs. The INR should be closely monitored during initiation and dose increase of liraglutide therapy in patients on warfarin and/or coumarol derivatives.</td></tr>
<tr><td>7.
Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult SPC or BNF</td><td>Adverse reaction frequency are classified using the following convention:
Very common (≥ 10%), common (≥ 1% and < 10%); uncommon (≥ 0.1% and < 1%).
<table>
<tr><th>Clinical condition</th><th>Management</th></tr>
<tr><td>GI: Nausea, and diarrhoea (very common) Vomiting constipation, abdominal pain, dyspepsia (common)</td><td>May diminish after a few days or weeks on continued treatment. Could try short course anti-emetic but if no improvement stop. Reassess after a few weeks.
It is worth checking that liraglutide is being used correctly and recommending smaller meal portion sizes.</td></tr>
<tr><td>CNS: Headache, dizziness (common)</td><td></td></tr>
<tr><td>Respiratory: Nasopharyngitis (common)</td><td></td></tr>
<tr><td>Metabolic: Hypoglycaemia</td><td>Especially in combination with sulphonylureas. May require blood glucose monitoring initially.</td></tr>
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	Other: Pancreatitis (rare) — Discontinue immediately and discuss with Specialist **Other:** Altered renal function (incidence not known) — Significant change – review treatment The patient should be advised to report any of the following signs or symptoms without delay: **Symptoms of acute pancreatitis (persistent, severe abdominal pain)** Liraglutide is a black triangle drug (at the time of writing) Any adverse reaction to a black triangle drug should be reported to the CHM via the 'yellow card' scheme.
8. Baseline investigations	Baseline bodyweight and HBA1c.
9. Monitoring	**Daily blood glucose monitoring is not routinely required but for patients taking a sulphonylurea, where a dose adjustment of the sulphonylurea may be necessary, it may be appropriate for patients initiating liraglutide to monitor their blood glucose on a daily basis for the first 2 months.**

Monitoring	Frequency	Results	Action
HbA1c	**Every 3 months for the first 6 months then every 6 months**	At 6 months: at least a 1% reduction	*Review treatment if this is not achieved*
Bodyweight		At 6 months: At least a 3% reduction	*Review treatment if this is not achieved*
Blood Pressure			*Review treatment or refer if there are any significant changes*
U&Es, eGFR		Significant change	

10. Pharmaceutical aspects	Needles will need to be prescribed and a sharps box provided. One liraglutide pen (18mg in ml) will last for 30 days at a dose of 0.6mg daily A pack of 2 pens will be required per month for the 1.2mg daily dose Store in a refrigerator (2°C – 8°C). Do not freeze. Shelf life 2 years. Store away from the freezer compartment. After first use: Store below 30°C or store in a refrigerator (2°C – 8°C). Do not freeze. Keep the cap on the pen in order to protect from light. Do not store with the needle attached.
11. Contact information	**Diabetes Specialist Nurses:-** • **South – Jenny Jarvis - 01874 615637** • **Mid – Patricia Powell - 01597 828717** • **North – Sally Ann Jones - 01686 617360**
12. Criteria for shared care for non-initiating GP's	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated and established by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements.
13. Responsibilities of initiating prescriber	• Initiate treatment. • Undertake baseline monitoring. • Dose adjustments. • Monitor patient's initial reaction to and progress on the drug. • Ensure that the patient has an adequate supply of medication. • Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug.

	For Secondary Care providers operating under shared care - provide GP with • Diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. • Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment • Advice on when to stop this drug. Provide patient with relevant drug information and instruction:(if appropriate refer to the Diabetes Specialist Nurse or suitably trained Practice Nurse): • On safe injection technique, blood glucose monitoring, the symptoms of hypoglycaemia and treatment. • Dosing instructions – to be injected once a day. • Supply an liraglutide information pack • Discuss driving and the need to inform the DVLA and their insurance company. • Discuss risks of pancreatitis including symptoms and importance of stopping if liraglutide occurs. • Issue monitoring booklet if necessary. • Enable informed consent to therapy
14. Responsibilities of Primary Care	• Prescribe liraglutide as part of the shared care agreement. • To monitor and prescribe according to the monitoring table. • To ensure that the monitoring and dosage record is kept up to date. • If operating under shared care advise the Specialist if the patient does not attend for appropriate monitoring. • Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary. • Monitor the general health of the patient. • Stop treatment on the advice of the specialist. • Ensure no drug interactions with other medicines.
15. Responsibilities of patients	• Monitor blood glucose levels if requested. • To attend hospital and GP clinic appointments, bring monitoring booklet if supplied. • Failure to attend could result in medication being stopped. • To report adverse effects to their specialist or GP.
16. Additional Responsibilities	Responsibilities of all prescribers: Any serious reaction to an established drug should be reported to CHM
17. Supporting documentation	Include patient information leaflet if available
18. Patient monitoring booklet	Include patient information leaflet if available
19.GP letter	Attached below
20.Guideline date.	01 Jan 2011
21. Guideline review date	01 Jan 2013

Shared care agreement – next page

Shared Care Agreement Form if Prescribing Liraglutide under Shared Care

Consultant request

Dear Dr ***IMPORTANT: ACTION NEEDED**

Patient name:
Date of birth:
Diagnosis:

This patient is suitable for treatment with liraglutide for the treatment of
(insert indication)

This drug has been accepted for Shared Care according to the enclosed protocol (as agreed by Trust / LHB / AWMSG). I am therefore requesting your agreement to share the care of this patient.

Treatment was started on (*insert date started*) (*insert dose*)

If you are in agreement, please undertake monitoring and treatment from *(insert date*)
NB: date must be at least 1 month from initiation of treatment).

Baseline tests: *(insert information)*

Next review with this department: *(add date)*
You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice. The patient will not be discharged from out-patient follow-up while taking liraglutide.

Please use the reply slip overleaf and return it as soon as possible.

Thank you.

Yours

Signature

Consultant name

GP Response

Dear Dr

Patient *(Insert Patients name)*

Identifier *(Insert Patient Date of birth/address)*

I have received your request for shared care of this patient who has been advised to start …..

A I am willing to undertake shared care for this patient as set out in the protocol

B I wish to discuss this request with you

C I am unable to undertake shared care of this patient.

GP signature Date

GP address/practice stamp