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

1. INDICATIONS

As set out in NICE CG87, MANAGEMENT OF TYPE 2 DIABETES

GLP 1 analogues are licensed to be given in combination with Metformin and/or Sulphonylurea or Glitazone in patients who have not achieved adequate glycaemic control on maximum tolerated doses of oral therapies.

**GLP 1 analogues are not indicated as First Line Therapy**

In combination with Metformin and/or a Sulphonylurea and/or Pioglitazone (only as dual therapy) if blood glucose control remains or becomes inadequate:

- Hba1c more than or equal to 7.5% / 59mmols or other higher level agreed with the individual
  AND
- BMI 35kg/m2 or more in people of European descent (adjust for other ethnic groups) and there are problems associated with high weight
  OR
- BMI less than 35kg/m2 and insulin is unacceptable of occupational implications or if weight loss would benefit other co-morbidities

Liraglutide – can be used in combination with oral antidiabetic medications and as add-on to Insulin. Novo Nordisk recommend to use Levemir once daily, initially at a dose of 10 U or 0.1-0.2 U/kg. The dose of Levemir should be titrated based on individual patients' needs.

Exenatide is currently licensed to use in combination with basal insulin
GLP 1 treatment should only be continued if the patient has a beneficial metabolic response at 6 months (Hba1c reduction by at least 1% AND initial bodyweight reduction by at least 3%)

2. Therapeutic background and use

Naturally:
- GLP-1 is secreted in the intestine mostly in response to food intake. It stimulates the secretion of insulin and reduces hepatic glucose production
- GLP-1 also reduces GI motility and increases the feeling of being full
- GLP-1 agonists lower fasting and post-prandial blood glucose levels and are associated with weight loss
- GLP-1 agonists suppresses glucagon secretions which is inappropriately increased in Type 2 Diabetes

3. Contraindications/Caution
- Hypersensitivity to the active ingredients or any of the excipients
- Type 1 Diabetes
- Moderate to Severe renal impairment (eGFR < 50 ml/min)
- Not recommended in severe inflammatory bowel disease or gastroparesis
- Previous history of pancreatitis
- Pregnancy and breastfeeding (lack of data)
- Paediatric and adolescents < 18yr (lack of data)
LIRAGLUTIDE only
- Hepatic Impairment- mild, moderate and severe– no adequate data
- Personal or any family history of Medullary Thyroid Cancer (MTC) or Multiple Endocrine Neoplasia Syndrome type 2 (MEN 2).

4. Drug Interactions NB: also refer to the BNF
Below applicable to Exenatide and Bydureon
Drugs with narrow therapeutic index and/or which require clinical monitoring:
- GLP 1 slows gastric emptying (amount of medicine absorbed and rate of absorption may be effected). Take other medicines 1hr before or 4hrs after Exenatide

Gastro-resistant Formulations:
- Take 1hr before or 4hrs after

Sulphonylureas:
- Increased risk of hypoglycaemia therefore consider temporary dose reduction by 50% initially then titrate dose back up
- Initial blood glucose monitoring may be required

Warfarin:
- Not known but INR has increased in some patients. Recommendation is to monitor INR more frequently

Oral Contraceptive Pill:
- Recommendation to be taken at least 1hr before or after Exenatide. No dose adjustment required.
5. Adverse Drug Reactions NB: also refer to BNF

Most serious toxicity is seen with long term use therefore patients may present to the GP first

Common side effects
- Nausea/Vomiting – eases with continued use, try short course of anti emetic, lesser extent with Liraglutide and Bydureon
- Diarrhoea/ Constipation/ Abdominal pain/ Dyspepsia
- Headache
- Nasopharyngitis
- Hypoglycaemia – when used in combination with Sulphonylurea or insulin

Less Common side effects
- Pancreatitis – discontinue immediately
- Altered renal function – if significant change review treatment
- Local reaction

Unknown rare
- Thyroid and Parafollicular cell pathology with Liraglutide

If the patient has symptoms of acute pancreatitis, (persistent, severe abdominal pain) they should stop treatment immediately and seek medical attention urgently.

Report any adverse reaction to a black triangle drug to the CHM - MHRA via the yellow card scheme or online: www.yellowcard.gov.uk
6. Baseline Investigations

Prior to commencing GLP-1 the following should be undertaken:

- LFTs / Renal / Glycated Haemoglobin
- Weight/BMI
- Advised to inform DVLA if appropriate - only if taken in combination with other diabetes medications that may cause hypoglycaemia
- TFT for Liraglutide

7. Monitoring

Self Monitoring - If used in combination with Sulphonylurea/Basal insulin as there is a small risk of hypoglycaemia

GLP 1 treatment should only be continued if the patient has a beneficial metabolic response at 6months (Hba1c reduction by at least 1% AND initial bodyweight reduction by at least 3%)

<table>
<thead>
<tr>
<th>MONITORING</th>
<th>FREQUENCY</th>
<th>RESULTS</th>
<th>ACTION</th>
<th>BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hba1c</td>
<td>6 monthly</td>
<td>At 6 months at least 1% reduction</td>
<td>Review treatment</td>
<td>Consultant/GP</td>
</tr>
<tr>
<td>Bodyweight</td>
<td>6 monthly</td>
<td>At 6 months at least 3% reduction</td>
<td>Review treatment</td>
<td>Consultant/GP</td>
</tr>
<tr>
<td>U&amp;E, eGFR</td>
<td>1 monthly then 6 monthly</td>
<td>Significant change</td>
<td>Review treatment</td>
<td>Consultant/GP</td>
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</tbody>
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8. Comparative Table
<table>
<thead>
<tr>
<th></th>
<th>Exenatide</th>
<th>Liraglutide</th>
<th>Prolonged release exenatide (Bydureon)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage</strong></td>
<td>5mcg to 10mcg sc BD ½ to 1 hour before meal</td>
<td>0.6mg to 1.2 mg sc OD, independent of meals</td>
<td>2mg SC once weekly, requires reconstitution</td>
</tr>
<tr>
<td></td>
<td>Start at 5mcg BD increasing to 10mcg after 1 month</td>
<td>Start at 0.6 mg and increase to 1.2mg after at least 1 week</td>
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<tr>
<td></td>
<td>They may need to stay on 5cmg for a further month if nausea persists</td>
<td>(NICE has not approved use of 1.8mg)</td>
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<tr>
<td><strong>Concomitant Anti hyperglycaemic drug</strong></td>
<td>Metformin+/ Sulphonylurea</td>
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<td>Metformin+ glitazone</td>
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<td></td>
<td>Basal insulin</td>
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<tr>
<td><strong>Specific Counselling</strong></td>
<td>Pancreatitis</td>
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<td>Pregnancy/lactation</td>
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<td></td>
<td></td>
<td>Thyroid Tumour</td>
<td></td>
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</tbody>
</table>

**References:**
NICE (2009) CG87 Type 2 diabetes - newer agents (a partial update of CG66): quick reference guide

Dr Shanthi Chandran – MK Diabetes Care Oct 2012