NHS Herts Valleys Clinical Commissioning Group

NHS East and North Hertfordshire Clinical Commissioning Group

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

HIGH STRENGTH INSULIN LISPRO (200UNITS/ML) (HUMALOG® 200) FOR DIABETES MELLITUS

RECOMMENDED FOR RESTRICTED USE

Name: generic (trade)	What it is	Indication	Date Decision last revised	Decision Status	NICE / SMC Guidance
insulin lispro (200units/ml) (Humalog® 200)	High strength rapid-acting insulin analogue	diabetes mellitus - type 1 & 2 (T1 & T2DM)	June 2016	Final	NICE - none SMC – none

High strength insulin lispro (200units/ml) (Humalog® 200) is RECOMMENDED FOR RESTRICTED USE for patients requiring >30 units/dose of Humalog® 100 (insulin lispro 100units/ml) but where pain and bruising are causing poor adherence with therapy.

- Prescribe BY BRAND to ensure brand/product continuity and minimise risk of substitution
- MHRA has issued guidance on commencing treatment with high strength insulins (see LINK). Healthcare professionals & patients need to understand the insulin strength of Humalog® 200 & how to use it correctly to minimise the risk of errors such as the wrong insulin dose being administered.

EFFICACY

- European Public Assessment report (EPAR) states:
  - Based on presented bioequivalence study, Humalog® 200 may be considered bioequivalent with Humalog® 100.
  - Changes to the formulation of the established product are: increasing the lispro concentration from 100units/ml to 200units/ml; changing the buffering agent & increasing the zinc concentration.
  - On the basis of bioequivalence between the insulin lispro 100units/ml & 200units/ml formulation, the positive benefit-risk balance of the 100units/ml may also be claimed for the 200units/ml

SAFETY

- Humalog® 200 has the same contraindications, cautions, adverse effects & interactions as Humalog® 100 (apart from additional safety warnings about higher strength insulin)

COST

- Humalog® 200 costs £58.92 for 5 x 3ml KwikPen – the same cost/unit as Humalog® 100 KwikPen.
- No increased costs if patients prescribed Humalog® 100 KwikPen were prescribed Humalog® 200 KwikPen instead.
- Higher cost than human soluble insulin.
- Slightly higher cost than Humalog® 100 cartridges.
- Lower cost than insulin aspart (NovoRapid®) prefilled pens, slightly higher cost than cartridges.
- Slightly higher cost than insulin glulisine (Apidra®) prefilled pens and cartridges.
- There are proposed savings from a reduction in insulin waste due to less pen transitions. There are no trial/real world data to verify this.

PATIENT FACTORS

- Humalog® 200 is a high-strength insulin. Humalog pre-filled pens (KwikPen) are available in two strengths. The needed dose is dialled in units. Both, the Humalog® 100units/ml & the Humalog® 200units/ml deliver 1 – 60 units in steps of 1 unit in a single injection. The number of units is shown in the dose window of the pen regardless of strength & no dose conversion should be done when transferring patient to a new strength.
- Patients need to read & understand the patient leaflet, education material & have training on correct use.
- Potential benefits of reduced injection volume are uncertain.

Background Information

- Humalog® 200 is the only high strength rapid-acting insulin analogue available in the UK.
- Humalog® 200 is licensed for the treatment of adults with diabetes mellitus who require insulin for the maintenance of normal glucose homeostasis & is also indicated for the initial stabilisation of DM.
- Humalog® 200 is available in a disposable pen injector, called the “KwikPen”. 3 ml cartridges which are sealed within the KwikPen contain 600 units insulin lispro (200 units/ml).
- The shelf-life is 3 years at 2-8°C, including an in-use period of up to 28 days up to 30°C.
- The insulin lispro should not be withdrawn from the pre-filled pen (KwikPen) or mixed with any other insulin.

This HMMC recommendation is based upon the evidence available at the time of publication. The recommendation will be reviewed upon request in the light of new evidence becoming available.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness and Safety

- Refer to efficacy, safety and patient factors box.

Cost of Treatment and Cost Effectiveness

- Refer to cost box

The needs of the population (with the condition)

- Refer to patient factors box.
- The needs of the population may be low as there are alternative insulins available.
- High strength insulin products have been developed to reduce the number & volume of injections. One of the proposed benefits is a reduction in injection site problems, because of the smaller injection volumes which may be less painful. There are no trial/real world data to confirm lower injection site reactions or pain with Humalog® 200 vs Humalog® 100.
- As an example patients injecting 20 units would be injecting 0.2ml of Humalog® 100 or 0.1ml of Humalog® 200.
- Patients requiring >60 unit doses of Humalog® 100 or 200 would require more than 1 injection in one go.
- Patients will be injecting a basal insulin in addition to Humalog® 100 or 200 before meals.

The needs of the community (overall local population)

- There would currently be no increased costs if patients prescribed Humalog® 100 KwikPen were prescribed Humalog® 200 KwikPen instead.
- Humalog® 200 is slightly higher cost than Humalog® 100 cartridges, insulin glulisine (Apidra®) prefilled pen devices/cartridges and insulin aspart (NovoRapid®) cartridges but lower cost than NovoRapid® prefilled pen devices. NovoRapid® is the highest prescribing cost short acting insulin for both CCGs.
- Overall, potential cost impact of the availability of Humalog® 200 is uncertain but the possible cost pressure, if any, would not appear to be substantial.
- Although the patent has expired for insulin aspart and insulin lispro there are currently no biosimilar products available and future availability is uncertain.

Policy Drivers (national guidance & directions and decisions of other local CCGs)

- Use of insulin in diabetes guided by recommendations in the NICE guidelines NG 17, 18 and 28 http://www.nice.org.uk/Search?q=diabetes .
- Cambridgeshire and Peterborough CCG formulary: recommended for patients requiring greater than 40 units of Humalog® per dose.
- No recommendations/not considered by any other neighbouring CCGs

Equity

- No impact anticipated.

Implementability

- See above safety and patient factor concerns regarding high strength insulin (with recommendations to mitigate risk).

Selected References (full reference list available in HMMC evaluation)

- Humalog® 200 units/ml KwikPen Summary of Product Characteristics http://www.medicines.org.uk/emc/
- European Public Assessment Report for Humalog 200 (July 2014) http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Assessment_Report_-_Variation/human/000088/WC500176634.pdf