## HERTFORDSHIRE AND WEST ESSEX AREA PRESCRIBING COMMITTEE (APC)

### Insulin aspart (Fiasp®) for the treatment of diabetes mellitus

### RECOMMENDED FOR RESTRICTED USE (AMBER INITIATION)

| Name: generic (trade) | What it is | Indication | Decision last revised | Decision Status | NICE / SMC Guidance |
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| Insulin aspart (Fiasp®) | Rapid-acting insulin analogue | Treatment of diabetes mellitus in adults. | December 2017 HMMC | Final | NICE - No Guidance<br>SMC – accepted for use in diabetes mellitus in adults only |

**APC Recommendation (in line with Bedfordshire and Luton Joint Prescribing Committee recommendation):**

- **Insulin Aspart (Fiasp®)** is **RECOMMENDED FOR RESTRICTED USE in defined patient groups who are not well controlled with current mealtime (bolus) insulin FOLLOWING INITIATION BY A SPECIALIST:**

  1. **Type 1 diabetes** on continuous subcutaneous insulin infusion (CSII) pump
  2. **Type 1 diabetes** on basal bolus needing tight control or has rapid post-meal blood glucose (BG) rise
  3. **Pregnant women with diabetes mellitus (Type 1 diabetes; Type 2 diabetes including gestational diabetes Mellitus (GDM))**

- **Recommendations to be reviewed when a biosimilar insulin aspart is available**
- **Prescribe BY BRAND to ensure brand/product continuity and minimise risk of substitution**

Initiation, titration and stabilisation must be undertaken by consultants or consultant led specialist team. Once stabilised for continuation in primary care with patient specific information provided by the hospital specialist

Future audit of outcomes to be reported by hospital specialists to APC

#### EFFICACY

- 2 double blind RCTs (26 weeks) in type 1 diabetes (T1DM) and type 2 diabetes (T2DM) indicate that Fiasp® is non-inferior to NovoRapid® in terms of $HbA_{1c}$ reduction.
- 1 double blind RCT (18 weeks) in T2DM to indicate that Fiasp® plus basal insulin is superior to basal insulin alone in terms of $HbA_{1c}$ reduction.
- 1 double blind RCT (6 weeks) in T1DM to indicate the compatibility and safety with the use of Fiasp® in CSII by external pump.
- Limited comparative evidence with other short acting insulins
- Limited long-term efficacy data

#### SAFETY

- Limited long term safety data
- Fiasp® can be used in pregnancy.
- Fiasp® is a new 'black triangle' (▼) product. It is therefore subject to additional monitoring.
- SPC states that Fiasp® has the same contraindications, adverse effects & interactions as NovoRapid®
- Prescribe by brand name so that products cannot be automatically substituted at the point of dispensing.

#### COST

- Fiasp® is available at a cost of £30.60 for 5x3mL prefilled FlexTouch® pens. Equivalent pack of NovoRapid® FlexTouch® pens: £32.13. & NovoRapid® FlexPens: £30.60.
- At a dose of 40 units daily costs per year are same for: NovoRapid® FlexPen device (£297.02)

#### PATIENT FACTORS

- Patients need to understand the differences between Fiasp® and NovoRapid® to minimise the risk of medication error.
- Patients must be able to use the available insulin pen i.e. FlexTouch® pen

## Background Information

- Fiasp® is licensed for the management of type 1 and 2 diabetes in adults. It is a fast acting mealtime insulin aspart formulation including nicotinamide (vitamin B3), which results in a faster initial absorption of insulin compared to NovoRapid® (which only contains insulin aspart).
- It is for subcutaneous administration up to 2 minutes before the start of the meal, with the option to administer up to 20 minutes after starting the meal
- Each ml contains 100 units insulin aspart which is the same active ingredient as in NovoRapid®. It is available in a cartridge (for penfill), pre-filled pen (FlexTouch® pen), 10mL vial.
- The summary of product characteristics states that onset of action is 5 minutes earlier with Fiasp® compared to NovoRapid®. It has a half-life of 57 minutes which is comparable to NovoRapid®.
- Dm&d have included Fiasp® in the same entry as NovoRapid®, despite the different release profiles. All insulin should be prescribed by brand on prescriptions in all care settings to avoid dispensing and administration errors. Fiasp®, insulin aspart is not interchangeable with Novorapid® insulin aspart because of different absorption profiles and patients should be advised of non-interchangeability and to routinely check labels prior to injecting
- The shelf-life is 30 months at 2-8°C, including an in-use period of up to 28 days up to 30°C.
  Note the shelf life for other short acting insulins is longer (for e.g. 3 years for insulin lispro) while the in-use period information is similar.

## Assessment against Ethical Framework

### Evidence of Clinical Effectiveness

- Refer to efficacy and safety boxes.
- The European Medicines Agency (EMA) efficacy evaluation of Fiasp® as part of a basal-bolus regimen (in the final formulation intended for the market) was based on three therapeutic confirmatory trials evaluating the efficacy and safety of Fiasp® in adult subjects (≥18 years old) with type 1 and type 2 diabetes mellitus
  - Fiasp® was non-inferior to NovoRapid® in T1DM (Onset 1) - change in HbA1c from baseline to 26 weeks (non-inferiority limit of HbA1c set at 0.4%). Primary outcome HbA1c reduction, non-inferiority demonstrated, treatment difference (TD): -0.15% (95% CI -0.23 to -0.07).
  - Fiasp® was non-inferior to NovoRapid ® in T2DM (Onset 2) - change in HbA1c from baseline to 26 weeks (non-inferiority limit of HbA1c set at 0.4%). Primary outcome HbA1c reduction, non-inferiority demonstrated, TD: -0.02% [95% CI -0.15 to 0.10]
  - Fiasp® plus basal insulin was superior to basal insulin alone in T2DM - change in HbA1c from baseline to 18 weeks (non-inferiority limit of HbA1c set at 0.4%),superiority demonstrated, TD: -0.94% [95% CI -1.17 to -0.72])
- Onset 4 supported compatibility and safety with the use of Fiasp® in CSII by external pump, Fiasp® was non-inferior to NovoRapid® in T1DM as no microscopically confirmed episodes of infusion set occlusions with treatment were reported.

### Safety

- Refer to safety and patient factors box.
- Reduction in 2-hour PPG increment (mmol/L), Fiasp® was superior to NovoRapid® in Onset 1 (-0.3 vs. 0.4 mmol/L, treatment difference -0.67, 95% CI -1.29 to -0.04, p=0.04), ), but there was no significant difference in Onset 2
- Incidence of severe or plasma glucose-confirmed hypoglycaemia within one hour of administration was significantly higher with mealtime Fiasp® than NovoRapid® in Onset 1 (33.9% vs. 28.4%).
- Observed rate of severe or BG confirmed hypoglycaemic episodes (2-24 hours post administration), no significant difference in hypoglycaemia observed between Fiasp® and NovoRapid®, in Onset 1 (92.7% vs 97.4%) and Onset 2 (76.8% vs 73.3%)
- EMA's pooled analysis of Onset 1,2 and 3 concluded that the rates of injection site reactions were higher for Fiasp® (23 events) than for the comparators (10 events) (3.8 and 2.4 events per 100 PYE, respectively).None of these injection site reactions were serious or severe.

### Cost of treatment and Cost Effectiveness

- Refer to cost box.
- The acquisition cost of Fiasp® is comparable to NovoRapid®, so little to no cost impact would be expected.
- At a dose of 40 units daily costs per year are lower for: insulin lispro [Humalog®] (£285.96); insulin glulisine [Apidra®] (£274.70).

### The needs of the population

- The needs of the population may be low as there are alternative bolus insulins available.
- It appears to offer no particular clinical benefits over NovoRapid®, however would be an option for a cohort of patients with sub-optimal control who may benefit from treatment with a rapid acting bolus insulin, Fiasp® as highlighted by the specialists.

### The needs of the community

- The needs of the community may be low as the estimated patient numbers for treatment are low.
- There would currently be no increased costs if patients prescribed Fiasp® instead of NovoRapid®

### Equity

- No impact anticipated

### Policy Drivers

- NICE guidelines on T1DM, T2DM, Diabetes in pregnancy and technology appraisal guidance 151 for CSII in diabetes
- Scottish Medicines Consortium has accepted Fiasp® for use within NHS Scotland for the treatment of diabetes mellitus in adults
- RDTC New Drug Evaluation concluded that Fiasp® is non-inferior to NovoRapid® when used in a basal-bolus regimen in T1DM and T2DM patients and appears to be an option for people with diabetes who require a rapid-acting bolus insulin analogue
- EoE CCG decisions:
- Bedfordshire and Luton Joint Prescribing Committee (June 2017): Support the use of Fiasp® for the treatment of the following patient groups o T1 on CSII pump
  o T1 on basal bolus needing tight control or has rapid post-meal BG rise
  o Pregnant DM (T1 and also T2 or GDM) on insulin as in this group typically they have very rapid post-meal BG rise especially after breakfast
  with high peaks 1hr post-meal BG, not well captured even by Novorapid taken 30min before meal
- Aylesbury Vale CCG & Chiltern CCG (Buckinghamshire): Support the use of Fiasp® for the treatment of the following patient groups:-
  o For treatment of type 1 diabetics of 16 years or over who may or may not be receiving insulin via an insulin pump who :
    - Have consistently failed to take insulin twenty minutes before a meal and/or
    - Have poor diabetes control due to post prandial glucose (PPG) being off target
  o For treatment of pregnant women with diabetes and in gestational diabetes not meeting 1 hour post prandial glucose target of 7.8 mmol/L

### Implementability

- See above safety and patient factor concerns and issues (with recommendations to mitigate risk)

**References**


- European Public Assessment Report. Fiasp. 10 November 2016. Procedure No. EMEA/H/C/004046/0000. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/004046/WC500220940.pdf
- Bedfordshire and Luton Joint Prescribing Committee (Accessed 01.11.2017) http://www.gpref.bedfordshire.nhs.uk/media/159811/advguid_fiaspformulationinsulinaspart_bulletin255.pdf
- Regional Drug and Therapeutics Centre RDTC: Fast-acting insulin aspart for treatment of diabetes mellitus (July 2017) http://rdtc.nhs.uk/sites/default/files/publications/nde-152-fast-acting-insulin-aspart-01.pdf
- Scottish Medicines Consortium (Advice April 2017) https://www.scottishmedicines.org.uk/SMC_Advice/Advice/1227_17_insulin_aspart_Fiasp/insulin_aspart_Fiasp
- NICE guideline NG17. Type 1 diabetes in adults: diagnosis and management (Updated July 2016). https://www.nice.org.uk/guidance/ng17 .
- NICE guideline NG28. Type 2 diabetes in adult (December 2015). https://www.nice.org.uk/guidance/ng28

- NICE TA151 Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus
  https://www.nice.org.uk/guidance/ta151/resources/continuous-subcutaneous-insulin-infusion-for-the-treatment-of-diabetes-mellitus-pdf-82598309704645

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| Version | 1.1 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include:<br>• Rebadging with HWE ICB and removal of ENHCCG and HVCCG headers<br>• Review date removed and replaced with standard statement. |
| Developed by | ENHCCG and HVCCH PMOT |
| Approved by | HMMC |
| Date approved/updated | December 2017 |
| Review date: | The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available. |
| Superseded version | 1.0 |