Fast-acting insulin aspart (Fiasp®▼).

The recommendation of this subgroup is as follows:*  

| Drug/Indication | Fast-acting insulin aspart (Fiasp®).  
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<td>Fiasp® is indicated for the treatment of diabetes mellitus (DM) in adults and is intended for use at mealtimes. Fiasp® is administered as a subcutaneous injection and may be given from 2 minutes before up to 20 minutes after starting a meal. Fiasp® is available as a 100 U/mL solution for injection in vials, Penfill® cartridges and FlexTouch® pre-filled pens</td>
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| Recommendation | The GMMMG FMESG does not recommend the use of Fiasp® in Type 2 diabetes patients.  
|-----------------|------------------------------------------------------------------------------------------------------------------|
| The group have however approved the restricted use of fast-acting insulin aspart (Fiasp®) in type 1 patients as follows:  
| • In patients who have diabetes and are planning or actively pregnant  
| • In those who have post prandial glucose readings of >10mmol at 2 hours.  
| The decision of whether Fiasp® is appropriate for use should be made by a diabetologist according to the criteria above. These patients should remain under the care of a specialist in diabetes.  
| According to set criteria the Fiasp® was deemed to be a low priority for funding but may move to a medium priority for funding for the specific group described above. |

| Clinical Trial Data – Efficacy | Insulin aspart is a fast-acting insulin analogue with a short duration of action. It has been licensed in the UK since 1999 as NovoRapid® (Novo Nordisk). Fiasp®▼ (Novo Nordisk) is a newly licensed formulation of insulin aspart with a more rapid onset of action than NovoRapid. The active substance is identical to that in NovoRapid; however nicotinamide (vitamin B3) has been added to allow faster insulin absorption. Pharmacokinetic studies found that Fiasp® reaches a maximum serum concentration approximately 7 minutes more quickly than NovoRapid, but that total insulin exposure is similar. Three pivotal trials assessed the effectiveness of Fiasp® as part of a basal-bolus regimen for management of diabetes mellitus. The primary efficacy outcome in each trial was change in HbA1c from baseline. Clinical trials showed it to be non-inferior to standard insulin aspart (NovoRapid®) when used in a basal-bolus regimen in patients with T1DM or T2DM, and superior to basal insulin alone in |
patients with T2DM. Fiasp® taken 20 minutes after the start of a meal was non-inferior to NovoRapid taken 0-2 minutes before eating. There was no apparent difference in bolus insulin requirements between Fiasp® and NovoRapid. The trials assessed several secondary endpoints and demonstrated that Fiasp® was superior to NovoRapid for change in post-prandial glucose in one trial (-0.44 mol/L vs. 0.49 mol/L, treatment difference -0.67, 95% CI -1.29 to -0.04), but there was no significant difference in the other trial. Neither trial found any difference in effect on mean body weight.

Clinical Trial Data – Safety
The EMA presented pooled safety data from the trials discussed above, totalling 1,244 patients exposed to Fiasp® and 853 who received comparators. There were no significant differences in the rate of overall adverse events (AEs) or serious AEs between Fiasp® and NovoRapid®. The overall rate of AEs was also higher in patients with T1DM (73%) than T2DM (53%), but there was no difference between Fiasp® and NovoRapid®.

Almost all patients (>90%) experienced at least one hypoglycaemic event, although most were mild or moderate. There were no differences in the number of patients with severe or plasma glucose-confirmed hypoglycaemia within one hour of administering post-meal Fiasp® (22.5%) or mealtime NovoRapid (28.4%). When Fiasp® was administered at mealtimes, severe or confirmed hypoglycaemia was more common than in the other groups (33.9%). Injection site reactions were slightly more common with Fiasp® than NovoRapid® (3.8 events per 100 patient-years of exposure [PYE] vs. 2.4 events per 100 PYE), but this difference is only apparent in patients with T1DM.

Safety data are currently limited to 26 weeks exposure, although data from the 26 week extension of trial 3852 are expected to be available at a later date.

Cost Effectiveness/Affordability
Fiasp® supplied in a FlexTouch® pen device has the same acquisition cost as NovoRapid® supplied in a FlexPen® (£30.60 for 5 x 3mL devices), vials (£14.08 for 10mL) or Penfill® cartridges (£28.31 for 5 x 3mL cartridges). NovoRapid® is also supplied in the FlexTouch® pen, but at a slightly higher cost (£32.13 for 5 x 3mL).

The pivotal trials found no difference in insulin requirements between Fiasp® and NovoRapid® therefore, depending on choice of device, little or no cost impact would be anticipated if switching between these products. There may be some cost impact if patients switch from other rapid acting insulins to Fiasp®.

The group noted that patent for NovoRapid® was due to expire in 2017 however generics and biosimilars will not be available till 2019.

Patient perspective
There are no apparent differences between Fiasp® and NovoRapid. However the FlexTouch device may offer some advantages in terms of patient acceptability.

* * This recommendation is valid unless it is has been superseded by a NICE TA or national guidance. The recommendation will only be reviewed when there is substantial new data that may change the initial recommendation. For recommendations that are >24 months old please note that there may be new data available and this should be checked prior to prescribing.

▼ Newly marketed drugs and vaccines are intensively monitored for a minimum of two years, in order to confirm the risk / benefit profile of the product. Healthcare professionals are encouraged to report all suspected adverse drug reactions regardless of the severity of the reaction.

References available on request.