East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG
Evidence review for Prescribing Clinical Network

Medicine details	
Name, brand name	Fast acting insulin aspart (**Fiasp®**)
Manufacturer	Novo Nordisk
Proposed indication	Treatment of diabetes mellitus in adults.
Requested by	Secondary care. Fast-acting insulin aspart (Fiasp®) use in adult patients for: • Treatment of type 1 diabetes mellitus (T1DM) in adults who require mealtime insulin to control blood glucose levels • Treatment of type 2 diabetes mellitus (T2DM) in adults who require a mealtime insulin to control blood glucose levels • Treatment of T1DM in adults who require a bolus insulin administered via an external continuous subcutaneous insulin infusion (CSII) system

SUMMARY

Clinical Effectiveness

Scottish Medicines Consortium (SMC) *10th April 2017, SMC advice no. 1227/17*
Following an abbreviated submission insulin aspart (Fiasp®) is accepted for use within NHS Scotland for the treatment of diabetes mellitus in adults.[10] The advice further states that insulin aspart (Fiasp®) is a new formulation with a faster onset of action than another formulation of insulin aspart and is available at an equivalent cost[10]

All Wales Medicines Strategy Group (AWMSG) *30th Nov 2016, (published February 2017)*
Insulin aspart (Fiasp®) for the treatment of diabetes mellitus in adults in Wales is granted HTA exemption by the AWMSG based on exclusion criterion no. 6: Product is an alternative formulation of an established medicine which costs the same or less than the existing established medicine[46]

Clinical Effectiveness
A high proportion of patients in the UK fail to achieve nationally recommended glycaemic targets. In 2015, 70.1% of patients with type 1 diabetes mellitus (T1DM), and 33.9% of patients with type 2 diabetes mellitus (T2DM) failed to achieve a glycated haemoglobin level (HbA1c) of ≤7.5%[1-4] HbA1c levels are the result of the combination of fasting plasma glucose (FPG) and postprandial glucose (PPG) levels, and therefore effective management of both components is essential for optimal glycaemic control[5]

Fiasp® is insulin aspart (NovoRapid®), the most widely prescribed rapid-acting insulin analogue in the UK[6], in a new formulation for the treatment of patients with diabetes requiring mealtime (bolus) insulin[7]. Fiasp® has a faster onset of action than NovoRapid®, which improves efficacy by more closely matching the physiological response of endogenous insulin in healthy individuals[8].

Current clinical guidelines recommend the use of a basal-bolus regimen for adults with T1DM and adults with T2DM who do not meet glycaemic targets on basal insulin alone [3, 4, 9]. Fiasp® is an option for patients with T1DM and T2DM who require treatment with a mealtime (bolus) insulin. This includes insulin pump use where necessary. Fiasp® is a mealtime insulin for subcutaneous administration just before (0-2 minutes) the start of the meal, with the option to administer within 20 minutes of starting the meal[7]. Fiasp® has been approved by the Scottish Medicines Consortium (SMC) for the treatment of diabetes mellitus in adults[10] and also the All Wales Medicines Strategy Group (AWMSG).

Efficacy of Fiasp®
Fiasp® effectively improved glycaemic control in patients with T1DM, with a statistically significantly greater reduction in HbA1c and superior PPG control when dosed with a meal vs NovoRapid®, and without an increased risk of hypoglycaemia or weight gain [11, 44]
Fiasp® effectively improved glycaemic control in patients with T2DM, showing non-inferiority to NovoRapid® regarding change in HbA1c and a statistically significant benefit in 1-hour PPG control vs NovoRapid®, without an increased risk of hypoglycaemia or weight change [12, 44]

The clinical value of Fiasp® was investigated in four phase 3 clinical trials as part of the onset® programme. The core efficacy and safety evidence for Fiasp® is provided by onset® 1[11] and onset® 2.[12]

Patients with T1DM (onset® 1)[11, 63]
Fiasp® effectively improved glycaemic control in patients with T1DM, with a statistically significantly larger reduction in HbA1c and superior PPG control when dosed with a meal vs NovoRapid®, without an increased risk of hypoglycaemic or weight gain.[11, 44] Fiasp® effectively improved glycaemic control. Non-inferiority to NovoRapid® regarding HbA1c change from baseline was confirmed for both mealtime and post-meal administration.

- Estimated treatment difference in HbA1c change from baseline: Mealtime Fiasp® vs NovoRapid®: –0.15% point [95% CI: –0.23; –0.07]; p<0.0001 and Post-meal Fiasp® vs NovoRapid®: 0.04% point [95% CI: –0.04; 0.12]; p<0.0001
- The reduction in HbA1c with mealtime Fiasp® was statistically significantly larger than with NovoRapid® Mealtime Fiasp® provided superior PPG control compared with NovoRapid® based on 2-hour PPG increment during a meal test (estimated treatment difference –0.67 mmol/L [95% CI: –1.29; –0.04]; p=0.0187).
- There was no significant difference for post-meal Fiasp® compared with NovoRapid® in 2-hour PPG increment (estimated treatment difference 0.30 mmol/L [95% CI: –0.34; 0.93])
- A statistically significant difference was demonstrated for 1-hour PPG increment (meal test) in favour of mealtime Fiasp®: Mealtime Fiasp® vs NovoRapid®: estimated treatment difference –1.18 mmol/L [95 % CI: –1.65; –0.71]; p-value not reported. The increase in 1-hour PPG increment was significantly greater for post-meal Fiasp® vs NovoRapid®: estimated treatment difference 0.93 mmol/L [95% CI: 0.46; 1.40]; p-value not reported.
- No statistically significant difference was seen in body weight between mealtime Fiasp® and NovoRapid® (estimated difference 0.12 kg [95% CI; –0.30, 0.55]) or between post-meal Fiasp® and NovoRapid® (estimated treatment difference 0.16 kg [95 % CI; –0.27, 0.58])
- Mean total (basal + bolus) daily insulin dose was similar across treatment arms at 26 weeks: mealtime Fiasp® 72.9 units vs post-meal Fiasp® 76.6 units vs NovoRapid® 76.2 units

Patients with T2DM (onset® 2)[12, 64]
Fiasp® effectively improved glycaemic control in patients with T2DM, showing non-inferiority to NovoRapid® regarding change in HbA1c and a statistically significant benefit in 1-hour PPG control vs NovoRapid®, without an increased risk of hypoglycaemia or weight change:12, 44 Fiasp® effectively improved glycaemic control in subjects with T2DM; Non-inferiority to NovoRapid® regarding HbA1c change from baseline was confirmed and HbA1c was reduced by 1.38% point for Fiasp® vs 1.36% point for NovoRapid® from baseline at Week 26: estimated treatment difference –0.02% point [95% CI: –0.15; 0.10]

- A statistically significant benefit in 2-hour PPG increment (meal test) could not be confirmed for Fiasp® compared with NovoRapid® (estimated treatment difference –0.36 mmol/L [95% CI: –0.81; 0.08]; p=0.0531)
- A statistically significant change from baseline in 1 hour PPG increment was observed for Fiasp® vs NovoRapid®; estimated treatment difference –0.59 mmol/L [95% CI: –1.09; –0.09]; p-value not reported
- No statistically significant difference was seen in body weight increase between Fiasp® and NovoRapid® (estimated treatment difference 0.00 kg [95% CI: –0.60; 0.61])
- Total mean daily insulin dose (basal + bolus) was similar across treatment arms at 26 weeks: Fiasp® 114.5 units vs NovoRapid® 108.6 units

Safety

The safety of Fiasp® has been investigated as part of the onset® programme, involving more than 2,100 people with T1DM or T2DM. The safety profile of Fiasp® is similar to that of NovoRapid®. The NovoRapid® molecule has a well-known tolerability profile based on more than 17 years of clinical experience.[49]

Patients with T1DM

In onset® 1, the overall safety profile of Fiasp® (mealtime and post-meal) and NovoRapid® was similar during 26 weeks of treatment:[44] There were no clinically relevant differences in the adverse event (AE) profiles across treatment groups.

- The overall AE rate per 100 patient years of exposure (PYE) was similar with mealtime Fiasp® (478.6), post-meal Fiasp® (441.0) and NovoRapid® (458.5)
- The proportion of subjects reporting AEs was also similar with mealtime Fiasp® (73.6%), post-meal Fiasp® (70.0%) and NovoRapid® (75.0%)
- Three events were confirmed as major adverse cardiovascular events (MACE) after adjudication: one cardiovascular death (post-meal Fiasp®), one non-ST-elevation myocardial infarction (post-meal Fiasp®) and one stroke (NovoRapid®). All three events were judged as unlikely related to trial product by the investigator
- A similar proportion of subjects reported severe or BG confirmed hypoglycaemic episodes in the mealtime Fiasp® group (92.7% of subjects), post-meal Fiasp® group (95.0% of subjects) and NovoRapid® group (97.4% of subjects)
- The observed rate of severe or BG confirmed hypoglycaemic episodes per 100 PYE was: 5,899, 5,443 and 5,865 for mealtime Fiasp®, post-meal Fiasp® and NovoRapid®, respectively, and there were no statistically significant differences between the treatment groups after 26 weeks of treatment
- There were no clinically significant differences between treatment groups in terms of vital signs, physical examinations, safety laboratory assessments, and electrocardiogram assessments

Patients with T2DM

In onset® 2, the overall safety profile of Fiasp® and NovoRapid® was similar during 26 weeks of treatment:[44]

- The proportion of subjects reporting treatment-emergent adverse events (TEAEs) as well as the rate of TEAEs were similar in the two treatment groups
- The event rate and proportion of subjects reporting AEs were 302.9 events per 100 PYE and 51.0% of subjects in the Fiasp® group, and 292.1 events per 100 PYE and 54.5% of subjects in the NovoRapid® group
- Twelve AEs (five in the Fiasp® group and seven in the NovoRapid® group) were confirmed as cardiovascular events. Of these, six AEs were identified as MACE)
- Six events were confirmed as MACE after adjudication: two in the Fiasp® group (cardiovascular death and non-ST-elevation myocardial infarction) and four in the NovoRapid® group (two cardiovascular death, non-ST-elevation myocardial infarction, and stroke)
- A similar proportion of subjects reported severe or BG confirmed hypoglycaemic episodes in the Fiasp® group (76.8% subjects) and NovoRapid® group (73.3% subjects)
- The observed rate of episodes of severe or BG confirmed hypoglycaemia was 1,788 episodes per 100 PYE in the Fiasp® group and 1,659 episodes per 100 PYE in the NovoRapid® group, and there were no statistically significant differences between the treatment groups after 26 weeks of treatment
- There were no clinically significant differences between treatment groups in terms of vital signs, physical examinations, safety laboratory assessments, and electrocardiogram assessments

Compatibility and tolerability of Fiasp® administered via insulin pump

The compatibility and tolerability of NovoRapid® and Fiasp® administered via an external CSII system in subjects with T1DM was evaluated in onset 4®:[50]

- The results of onset® 4 demonstrated the compatibility and tolerability of both Fiasp® and NovoRapid® when administered via external CSII system in adult subjects with T1DM

- There were no episodes of microscopically confirmed infusion set occlusions (the primary endpoint) in either the Fiasp® or the NovoRapid® treatment groups
- Fiasp® and NovoRapid® each provided effective glycaemic control in a CSII setting. The estimated mean change in HbA1c from baseline to Week 6 favoured Fiasp® (−0.22%), but was not statistically significantly different from NovoRapid® (−0.07%); estimated treatment difference: –0.14% [95% CI: –0.40; 0.11]
- There were no episodes of severe hypoglycaemia and no serious adverse events in either the Fiasp® or the NovoRapid® treatment groups

Patient factors

Fiasp® will be available in the FlexTouch® pen at the same price as the NovoRapid® FlexPen® i.e. £30.60, and thus offers improved efficacy at no additional cost. FlexTouch® is preferred by patients and healthcare professionals [47, 48] and is provided at no extra cost to conventional NovoRapid® FlexPen®. Studies have shown that the FlexTouch® pen is preferred by patients and healthcare professionals over KwikPen® and SoloStar®[47, 48] The FlexTouch® pen device delivers insulin accurately and consistently, and with a reduced injection force compared with FlexPen®, which makes it easier to inject insulin.[56, 57]

Cost implications

Cost of treatment

Fiasp® is the same price as NovoRapid® in a vial or Penfill® cartridge. Fiasp® will be available in the FlexTouch® pen at the same price as the NovoRapid® FlexPen® i.e. £30.60, and thus offers improved efficacy at no additional cost. FlexTouch® is preferred by patients and healthcare professionals [47, 48] and is provided at no extra cost to conventional NovoRapid® FlexPen® (Table 1).

Table 1: Pack cost and annual cost per patient for NovoRapid® and Fiasp®

Presentation and strength	Pack size	No. units	Pack cost	Cost/ unit	Dose (units)	Cost per year (£)†
NovoRapid®						
Vial 100 units/mL	10 mL	1000	£14.08	£0.0141		£205.71
Penfill® cartridge 100 units/mL	5 x 3 mL	1500	£28.31	£0.0189		£275.74
PumpCart® cartridges, 100 units/ml	5 x 1.6 mL	800	£15.10	£0.0189	40	£275.76
FlexPen® pen 100 units/mL	5 x 3 mL	1500	£30.60	£0.0204		£298.04
FlexTouch® pen 100 units/mL	5 x 3 mL	1500	£32.13	£0.0214		£312.95
Fiasp®						
Vial 100 units/mL	10 mL	1000	£14.08	£0.0141		£205.71
Penfill® cartridge 100 units/mL	5 x 3 mL	1500	£28.31	£0.0189	40	£275.74
FlexTouch® pen 100 units/mL	5 x 3 mL	1500	£30.60	£0.0204		£298.04

†Calculation of annual treatment cost: unit cost (pack cost/number of units) x daily dose (DDD 40 units) x 365.25. Resource use associated with NovoRapid® and Fiasp®, for example insulin needles for injection, are assumed to be identical, therefore these costs are not considered. It is assumed that other costs of treatment (e.g. use of concomitant medication) or other costs resulting from treatment (e.g. long-term outcomes) are equivalent in both treatment groups.

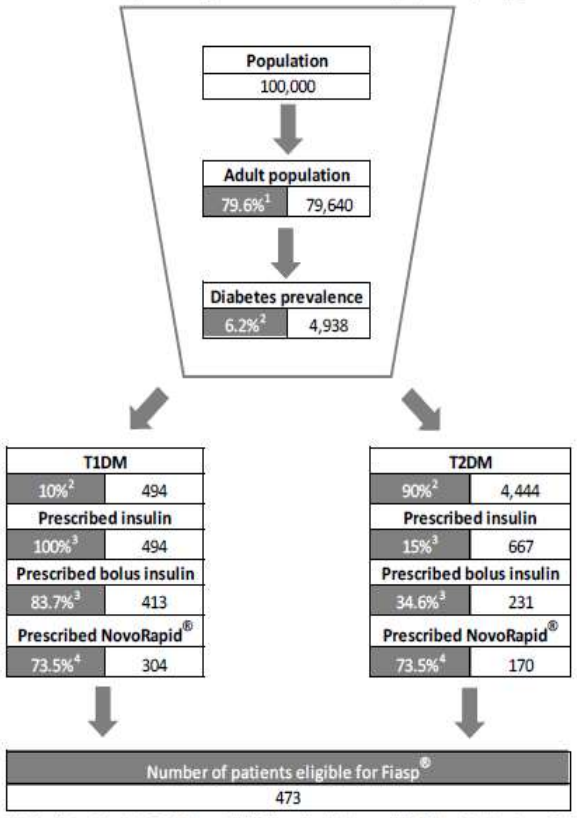
For comparison of insulins the World Health Organization recommends using the daily defined dose (DDD) of 40 units, as insulin dosing is variable and based on individual requirements. Since there is no change in insulin dose observed between Fiasp® and NovoRapid® in the clinical trials it is appropriate to use the WHO DDD for cost comparison purposes. The actual annual cost will depend on an individual's daily dose of insulin. The anticipated annual cost for a patient with T1DM in clinical practice is lower than estimated in Table 1 as they commonly have lower daily doses. There were no statistically significant differences between Fiasp® and NovoRapid® in terms of mean total insulin dose in onset® 1 or onset® 2.

Budget impact

It is assumed that Fiasp® will replace NovoRapid® in a proportion of patients. According to market share data, NovoRapid® is the most widely prescribed bolus insulin in the UK.[51]

Eligible patients Based on a 100,000 population in the UK, there are 304 adults with T1DM and 170 adults with T2DM who are treated with NovoRapid® and eligible for treatment with Fiasp® (Figure 1)h

Figure 1: Estimated number of patients eligible for treatment with Fiasp®, in a 100,000 population in the UK



References: 1. Office for National Statistics;[51]; 2. Diabetes UK[15]; 3. Novo Nordisk, data on file[52]; 4. Novo Nordisk, data on file[51]

Table 2: Estimated number of patients eligible for treatment with Fiasp®, in a 100,000 population in the four UK nations

Nation	Diabetes prevalence	Prescribed NovoRapid®[†]	Patients eligible for Fiasp®
Scotland	5.9%	74.4%	456
Northern Ireland	5.3%	77.3%	425
Wales	6.9%	84.0%	602
England	6.2%	77.4%	498

[†]Market share; [‡]Based on internal company estimates for annual uptake

England Considering a 100,000 local population and a diabetes prevalence in England of 6.2%, and based on the number of patients currently prescribed NovoRapid® (77.4%) – the number of patients eligible for treatment with Fiasp® is 498

Budget impact Fiasp® compared with NovoRapid® has a neutral budget impact. Budget impact calculations assume that patients using the NovoRapid® vial, Penfill® cartridge, and FlexTouch® pen would upgrade to the Fiasp® vial, Penfill® cartridge, and FlexTouch® pen, respectively. Fiasp® Penfill® cartridges are designed for use in the same Novo Nordisk pen devices as NovoRapid® Penfill® cartridges. Patients using the NovoRapid® PumpCart® cartridge are not expected to transition to Fiasp® as it is unavailable in this presentation.

Patients currently using NovoRapid® FlexPen® can upgrade to Fiasp® FlexTouch® at no additional cost. Studies have shown that the FlexTouch® pen is preferred by patients and healthcare professionals over KwikPen® and SoloStar®[47, 48] The FlexTouch® pen device delivers insulin accurately and consistently, and with a reduced injection force compared with FlexPen®, which makes it easier to inject insulin.[56, 57] Currently NovoRapid® FlexPen® is priced at £30.60 and the FlexTouch® at £32.13, hence a potential saving of £1.53 per pack can be expected with these patients switching to Fiasp®.

Clinical value leading to potential economic value The impact of Fiasp® vs NovoRapid® on long-term clinical outcomes and costs of complications in patients with T1DM in the UK setting has been assessed using the IMS CORE Diabetes Model.54 Improved glycaemic control with Fiasp® results in reduced cumulative incidence of diabetes-related complications over patient lifetimes. Long-term projections suggest that, in the UK setting, treatment of patients with T1DM with Fiasp® is likely to be associated with improved clinical outcomes and reduced costs of treating diabetes-related complications compared with treatment with NovoRapid®.[55] Studies have shown that the negative health and functioning impacts associated with PPH among people with T1DM and T2DM lead to an increase in healthcare resource use and loss of work-related productivity.[22, 37] An internet survey of 906 adults with T1DM and T2DM in Europe and the USA showed that compared with individuals without PPH, those with PPH measure their blood glucose more frequently, and report greater contact with healthcare professionals related to diabetes.[22]

Relevant guidance / reviews

Scottish Medicines Consortium (SMC) *10th April 2017, SMC advice no. 1227/17*
Following an abbreviated submission insulin aspart (Fiasp®) is accepted for use within NHS Scotland for the treatment of diabetes mellitus in adults.[10] The advice further states that insulin aspart (Fiasp®) is a new formulation with a faster onset of action than another formulation of insulin aspart and is available at an equivalent cost[10]

All Wales Medicines Strategy Group (AWMSG) *30th November 2016, (published February 2017)*
Insulin aspart (Fiasp®) for the treatment of diabetes mellitus in adults in Wales is granted HTA exemption by the AWMSG based on exclusion criterion no. 6: Product is an alternative formulation of an established medicine which costs the same or less than the existing established medicine[46]

Guidelines and recommendations The clinical goal in the treatment of diabetes is to achieve good glycaemic control. Current clinical guidelines recommend the use of a basal-bolus regimen for adults with T1DM and adults with T2DM who do not meet glycaemic targets on basal insulin alone [3, 4, 9] CSII therapy is recommended as an option for adults and children >12 years with T1DM45 Fiasp® has been approved by the SMC for the treatment of diabetes mellitus in adults[10]

Current statement on insulin Aspart from Surrey Prescribing Advisory Database.
Insulin Aspart - Drug has been agreed as appropriate for initiation in Primary Care and / or continued in Primary Care following a recommendation from specialists in other health care sectors. Following consideration by the PCN, it has been assigned a GREEN traffic light status.

Likely place in therapy relative to current treatments

Fiasp® is an alternative treatment option for adults with T1DM, and adults with T2DM who require treatment with a mealtime (bolus) insulin, particularly a rapid-acting insulin analogue such as NovoRapid®. Fiasp® provides flexibility in its use as a post-meal option when needed, without compromising efficacy vs NovoRapid® dose at mealtime. Patients can administer:[7] just before (0-2 minutes) the start of the meal for better PPG results vs NovoRapid®, or when needed, up to 20 minutes after the start of a meal without compromising HbA1c control vs NovoRapid® dosed at mealtime.

Fiasp® can also be used for CSII in pumps suitable for insulin infusion and will cover both the bolus insulin requirement (approximately 50%) and basal insulin[7]. Fiasp® offers the option of delivery in a variety of devices including FlexTouch®, which is preferred by patients over KwikPen® and SoloStar® [47, 48].

Current statement on insulin aspart from Surrey Prescribing Advisory Database states that insulin aspart has been agreed as appropriate for initiation in Primary Care and / or continued in Primary Care following a recommendation from specialists in other health care sectors. Following consideration by the PCN, it has been assigned a GREEN traffic light status.

Recommendation to PCN

Fiasp® offers value in terms of clinical and device benefits at no additional cost. Fiasp® is at price parity to NovoRapid® in terms of the vial and Penfill® cartridge, and its FlexTouch® pen is priced the same as the NovoRapid® FlexPen®.

Clinical benefit Fiasp® effectively improves glycaemic control in patients with T1DM, with a statistically significantly larger reduction in HbA1c and superior PPG control when dosed with a meal vs NovoRapid®, without an increased risk of hypoglycaemia or weight change [11, 44]. Fiasp® effectively improves glycaemic control in patients with T2DM, showing non-inferiority to NovoRapid® regarding change in HbA1c and a statistically significant benefit in 1-hour PPG control vs NovoRapid®, without an increased risk of hypoglycaemia or weight change [12, 44]. Many people with diabetes do not follow the recommended guidelines for dosing of bolus insulin at mealtimes. Fiasp® can be administered just before (0-2 minutes) the start of the meal, with the option to administer within 20 minutes of starting the meal, improving insulin requirement accuracy and flexibility without compromising efficacy and safety vs NovoRapid® dosed 0–2 minutes before the start of a meal7. The overall tolerability profile for Fiasp® is similar to that of NovoRapid® [13]

Place in therapy Fiasp® compared with NovoRapid® has a neutral budget impact. It is assumed that Fiasp® will replace NovoRapid® in a proportion of patients. Fiasp® is proposed as a treatment choice as a rapid-acting mealtime insulin for adults with T1DM and T2DM, for subcutaneous administration just before (0-2 minutes) the start of the meal[7] Fiasp® provides flexibility with the option to administer within 20 minutes of starting the meal, without compromising efficacy and safety vs NovoRapid® dosed at mealtime[7] Fiasp® can be used for CSII in pumps suitable for insulin infusion[7] Fiasp® is licensed for the treatment of diabetes in adults[6] and Fiasp® is suitable for prescribing by any clinician competent in the initiation and maintenance of insulin therapy[6], for use in insulin pumps and for use in pregnant women[6]

Request to be positioned as an inclusion to insulin Aspart on Surrey Prescribing Advisory Database as product is an alternative formulation of an established medicine which costs the same or less than the existing established medicine. Current Insulin Aspart recommendation - Insulin Aspart - Drug has been agreed as appropriate for initiation in Primary Care and / or continued in Primary Care following a recommendation from specialists in other health care sectors. Following consideration by the PCN, it has been assigned a GREEN traffic light status.

Medicine details	
Name and brand name	Fast-acting insulin aspart (rINN insulin aspart) Brand name: Fiasp® Manufacturer: Novo Nordisk
Licensed indication, formulation and usual dosage	Licensed for Treatment of diabetes mellitus in adults (launched in UK on 10th April 2017) Fiasp® is a new formulation of the rapid-acting insulin analogue, insulin aspart (NovoRapid®). Fiasp® is a clear, colourless solution for subcutaneous injection. It is available in three delivery methods: ❑ Fiasp® vial 100 units/mL, solution for injection in vial 10 mL ❑ Fiasp® Penfill® 100 units/mL, solution for injection in cartridge 5 x 3 mL ❑ Fiasp® FlexTouch® 100 units/mL, solution for injection in pre-filled pen 5 x 3 mL 1 mL of the solution contains 100 units of insulin aspart (equivalent to 3.5 mg). Fiasp® is recommended to be administered subcutaneously in the abdominal wall or the upper arm. Fiasp® can be used for CSII in pumps suitable for insulin infusion and will cover both the bolus insulin requirement and basal insulin. Dosing with Fiasp® is individual and determined in accordance with the needs of the patient. Fiasp® given by subcutaneous injection should be used in combination with intermediate-acting or long-acting insulin given at least once a day. Moreover, it can be used for continuous subcutaneous insulin infusion (CSII) in pumps or be administered intravenously by healthcare professionals. Blood glucose monitoring and insulin dose adjustment are recommended to achieve optimal glycaemic control.

	Patients with T1DM The recommended starting dose of Fiasp® in insulin naïve patients with T1DM is approx 50% of the total daily insulin dose (i.e. both basal and bolus insulin) and should be divided between the meals based on the size and composition of the meals. The remainder of the total daily insulin dose should be administered as intermediate-acting or long-acting insulin. As a general rule, 0.2 to 0.4 units of insulin per kilogram of body weight can be used to calculate the initial total daily insulin dose in insulin naïve patients with T1DM. ***Patients with T2DM*** Suggested initial dose is 4 units at one or more meals. Number of injections and subsequent titration will depend on individual glycaemic target and the size and composition of the meals. **Transfer from other insulin medicinal products** Converting from another mealtime insulin can be done on a unit-to-unit basis. Due to the earlier onset of insulin action, Fiasp® should be injected just before (0-2 minutes) the start of the meal, with the option to administer within 20 minutes after starting the meal. Transferring a patient from another type, brand or manufacturer of insulin to Fiasp® must be done under medical supervision and may require a change in dosage
Summary of mechanism of action, and relevant pharmacokinetics	Mealtime (bolus) insulins, which include rapid-acting insulin analogues and short-acting insulins, are usually taken before or with a meal and act to minimise the rise in PPG that follows eating. Fiasp® has been developed to have a faster onset of action and a profile that more closely matches the endogenous physiological insulin profile of healthy individuals without diabetes.[8] In Fiasp® the addition of nicotinamide (vitamin B3) results in a faster initial absorption of insulin, leading to an earlier onset of action and greater early glucose-lowering effect compared with NovoRapid®. When compared with NovoRapid®, Fiasp® has[8]: 2 x faster onset of appearance in the bloodstream 2 x higher insulin concentration within 30 minutes of injection 74% greater insulin action within 30 minutes of injection
Important drug interactions	The following substances may reduce insulin requirement: Oral antidiabetics, monoamine oxidase inhibitors (MAOIs), beta-blockers, angiotensin converting enzyme (ACE) inhibitors, salicylates, anabolic steroids, sulphonamides and GLP-1 receptor agonist. The following substances may increase insulin requirement:Oral contraceptives, thiazides, glucocorticoids, thyroid hormones, sympathomimetics, growth hormone and danazol. Beta-blocking agents may mask the symptoms of hypoglycaemia. Octreotide/lanreotide may either increase or decrease the insulin requirement. Alcohol may intensify or reduce the hypoglycaemic effect of insulin.
Monitoring requirements	Blood glucose monitoring and insulin dose adjustment are recommended to achieve optimal glycaemic control. Adjustment of dose may be necessary if patients undertake increased physical activity, change their usual diet or during concomitant illness. Blood glucose levels should be monitored adequately under these conditions. Patients on basal-bolus treatment who forget a mealtime dose are advised to monitor their blood glucose level to decide if an insulin dose is needed. Patients should resume their usual dosing schedule at the next meal.
Prescribing considerations	Green as current Insulin Aspart. Current statement on insulin Aspart from Surrey Prescribing Advisory Database. Insulin Aspart - Drug has been agreed as appropriate for initiation in Primary Care and / or continued in Primary Care following a recommendation from specialists in other health care sectors. Following consideration by the PCN, it has been assigned a GREEN traffic light status.

Other considerations	Fiasp® is a familiar product in a new formulation: insulin aspart is the most prescribed rapid-acting insulin with 17 years of clinical use and an established tolerability profile[49]

Potential patient group (if appropriate to include)	
Brief description of disease	Diabetes mellitus is a chronic metabolic disorder characterised by elevated blood glucose[26]. It is estimated that more than 1 in 16 people in the UK has diabetes[15] A high proportion of patients in the UK fail to achieve nationally recommended glycaemic targets. In 2015, 70.1% of patients with type 1 diabetes mellitus (T1DM), and 33.9% of patients with type 2 diabetes mellitus (T2DM) failed to achieve a glycated haemoglobin level (HbA1c) of ≤7.5%[1-4] HbA1c levels are the result of the combination of fasting plasma glucose (FPG) and postprandial glucose (PPG) levels, and therefore effective management of both components is essential for optimal glycaemic control[5]
Potential patient numbers per 100,000	Considering a 100,000 local population and a diabetes prevalence in England of 6.2%, and based on the number of patients currently prescribed NovoRapid® (77.4%) – the number of patients eligible for treatment with Fiasp® is 498 It is likely Fiasp will become the preferred rapid acting analogue for patients with type 1 diabetes and those on pumps. We will start by using it in patients with type 1 and type 2 diabetes who fail to control their post prandial glucose excursions who are already on rapid acting insulin anlogues. In the first year 50-100 patients per acute trust will be started on this insulin.
Outcomes required	Fiasp® has a faster onset of action than NovoRapid®, which improves efficacy by more closely matching the physiological response of endogenous insulin in healthy individuals[8] Clinical value of Fiasp®. Fiasp® effectively improves glycaemic control in patients with T1DM, with a statistically significantly greater reduction in HbA1c and superior PPG control when dosed with a meal vs NovoRapid®, and without an increased risk of hypoglycaemia or weight change[11] Fiasp® effectively improves glycaemic control in patients with T2DM, showing non-inferiority to NovoRapid® regarding change in HbA1c and a statistically significant benefit in 1-hour PPG control vs NovoRapid®, without an increased risk of hypoglycaemia or weight change[12] The overall tolerability profile for Fiasp® is similar to that of NovoRapid® [11-13]

Summary of current treatment pathway
National Institute for Health and Care Excellence (NICE) **NICE guideline NG17: Type 1 diabetes in adults – diagnosis and management[3]** -Offer rapid-acting insulin analogues injected before meals, rather than rapid-acting soluble human or animal insulins, for mealtime insulin replacement for adults with T1DM -Do not advise routine use of rapid-acting insulin analogues after meals for adults with T1DM -If an adult with T1DM has a strong preference for an alternative mealtime insulin, respect their wishes and offer the preferred insulin

NICE guideline NG28: Type 2 diabetes in adults – management[4]

-Start insulin therapy for adults with T2DM from a choice of insulin types and regimens:
-Offer NPH insulin injected once or twice daily according to need
-Consider starting both NPH and short-acting insulin (particularly if the person's HbA1c is 75 mmol/mol [9.0%] or higher), administered either: separately **or** as a pre-mixed (biphasic) human insulin preparation
-Monitor adults with T2DM who are on a basal insulin regimen (NPH insulin, insulin detemir or insulin glargine) for the need for short-acting insulin before meals (or a pre-mixed [biphasic] insulin preparation)
-Monitor adults with T2DM who are on pre-mixed (biphasic) insulin for the need for a further injection of short-acting insulin before meals or for a change to a basal bolus regimen with NPH insulin or insulin detemir or insulin glargine, if blood glucose control remains inadequate.

NICE technology appraisal guidance TA151: Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus [45]

-Continuous subcutaneous insulin infusion or insulin pump therapy is recommended as a possible treatment for adults and children 12 years and over with T1DM if:
-attempts to reach target haemoglobin A1c (HbA1c) levels with multiple daily injections result in the person having 'disabling hypoglycaemia', or HbA1c levels have remained high (8.5% or above) with multiple daily injections (including using long-acting insulin analogues if appropriate) despite the person and/or their carer carefully trying to manage their diabetes. CSII therapy is not recommended for the treatment of people with T2DM

Scottish Intercollegiate Guidance Network (SIGN) SIGN guideline 116 – Management of diabetes[9]

For the management of T1DM: An intensified treatment regimen for adults with T1DM should include either regular human or rapid-acting insulin analogues. CSII therapy is associated with modest improvements in glycaemic control and should be considered for patients unable to achieve their glycaemic targets

For the management of T2DM: When commencing insulin therapy, bedtime basal insulin should be initiated and the dose titrated against morning (fasting) glucose. If the HbA1c level does not reach target, then addition of prandial insulin should be considered. Soluble human insulin or rapid-acting insulin analogues can be used when intensifying insulin regimens to improve or maintain glycaemic control

Evidence review

The EPAR review is the only review of the new formulation of faster-acting insulin aspart which has been undertaken so far.[44] It included trials until December, 2015. Its conclusions were as follows:
In order to, not only avoid symptoms of hyperglycaemia, but also avoid long-term complications of diabetes there is consensus that good metabolic control as reflected by HbA1c at least <7% is desirable.

The data from the pivotal clinical trials show a clinically relevant glucose lowering effect associated with treatment with Fiasp as expected considering that the active component is insulin aspart.

The data provided on Fiasp show that, compared to NovoRapid, there is a shift in the PK/PD profile resulting in an earlier onset of the glucose-lowering effect while the total glucose-lowering effect is similar. With respect to results in the pivotal phase III studies, statistically significant lowering of the post-prandial glucose (PPG) increment with Fiasp compared to NovoRapid in patients with T1DM was documented, as well as a modest decrease in HbA1c (mean treatment difference -0.15%) after 26 weeks . The 52 week data indicate that the difference in effect between Fiasp and NovoRapid was less pronounced compared to week 26.

In patients with T2DM, there was no difference in HbA1c at weeks 26, but a statistically significant reduction in 1-hour PPG increment was observed.

There is no consistent data to support that the small differences in HbA1c documented in patients with type 1 diabetes would translate into a reduced risk in diabetic complications. The differences in PPG could possibly be of clinical relevance, but it is uncertain if the effect on PPG is an independent marker of

risk considering the limited effect on HbA1c. Further, the effect decreased over time.

With respect to safety, there was a difference in the pattern of hypoglycaemic episodes with a significantly higher rate of hypoglycaemia within the first 2 hours after the meal for Fiasp compared to Novorapid. However, the overall rate and severity of events was comparable between treatments.

The subsequent ONSET trials[11,12, 58. 62] were also examined to check for any significant updates on the information above. Basically the findings tied in with the EPAR review:

- Faster onset of action of Fiasp compared with NovoRapid (5 minutes compared with 10 minutes).
- Better post-prandial control of blood glucose with Fiasp
- Similar overall bioavailabilty with Fiasp and NovoRapid
- Similar reduction in HbA_{1c} for both Fiasp and NovoRapid
- Similar weight gain overserved over 26 weeks and <1kg for both Fiasp and NovoRapid
- The overall safety profiles are similar for Fiasp and NovoRapid

Clinical Evidence

The clinical efficacy of Fiasp® has been investigated in four phase 3 trials, involving more than 2,100 people[11, 12, 58, 62]

This evidence review is based on the following key phase III clinical studies:

- Trial ID: NN1218-3852 (onset® 1)[11] in patients with T1DM
- Trial ID: NN1218-3853 (onset® 2)[12] in patients with T2DM

Supporting evidence also comes from two phase III clinical studies:

- Trial ID: NN1218-4049 (onset® 3)[58] in patients with T2DM
- Trial ID: NN1218-3931 (onset® 4)[62] in patients with T1DM

onset® 1 [11, 63]

- Design: 26-week, multicentre, multinational, double-blind, active controlled, treat-to-target, three-armed parallel trial with an 8-week run-in period. Mealtime Fiasp® was compared with mealtime NovoRapid®, both in combination with insulin detemir in a basal-bolus regimen[11] The trial also included a 26-week open-label post-meal Fiasp® dosing arm in combination with insulin detemir[11]
- Population: 1,143 adults (age ≥18 years, across nine countries across Europe, Canada and the US) with T1DM (HbA_{1c} 7.0–9.5%) and body mass index ≤35.0 kg/m^2, who had been treated with a basal-bolus insulin regimen for at least 12 months, and any regimen of insulin detemir or insulin glargine for at least 4 months prior to screening
- Intervention: Fiasp® (100 units/mL solution for subcutaneous [SC] injection) was provided in a 3 mL PDS290 pen injector, and was administered 0–2 minutes before a meal in the blinded arm, and 20 minutes after the start of a meal in the open-label arm
- Outcomes: The primary objective was to compare the change from baseline in HbA_{1c} after 26 weeks of randomised treatment to a non-inferiority limit of 0.4% for mealtime Fiasp® vs. mealtime NovoRapid®. Secondary outcomes included confirming the superiority of mealtime Fiasp® compared with mealtime NovoRapid® in terms of PPG regulation, number of hypoglycaemic events and body weight regulation.

  Results Fiasp® was non-inferior to NovoRapid® with regard to HbA_{1c} change from baseline in people with T1DM as part of a basal-bolus regimen (estimated treatment difference -0.15, 95% CI -0.23 to -0.07, p <0.0001). The reduction in HbA_{1c} was statistically significantly greater with mealtime Fiasp® than with mealtime NovoRapid®. Mealtime Fiasp® provided superior PPG control compared with mealtime NovoRapid® based on 2-hour PPG increments during a meal test (estimated treatment difference -0.67, 95% CI -1.29 to -0.04, p=0.0187). In onset® 1, Fiasp® resulted in a statistically significant HbA_{1C} estimated treatment difference for mealtime Fiasp® vs. mealtime NovoRapid® of -

0.15%, (95% CI -0.23 to -0.07, p <0.0001).[11]

NOTE TO PCN: Published trial

onset® 2 [12, 64]

- Design: 26-week, multicentre, multinational, 1:1 randomised, double-blind, active controlled, treat-to-target, parallel group trial comparing the efficacy and safety of Fiasp® vs. NovoRapid®, both in combination with once daily (OD) insulin glargine (100 units/mL)and metformin in a basal-bolus regimen
- Population: 689 adults (age ≥18 years, in 10 countries across Europe, Asia and North America) with T2DM (HbA_{1c} 7.0–9.5%) and body mass index ≤40 kg/m^2, who had been treated with basal insulin for at least 6 months prior to screening, and receiving once daily treatment with NPH insulin, insulin detemir or glargine for at least 3 months prior to the screening visit
- Intervention: Fiasp®
- Outcome: To confirm efficacy of treatment with mealtime Fiasp® in terms of glycaemic control measured by HbA_{1c} after 26 weeks of randomised treatment, compared with mealtime NovoRapid®, both in combination with OD insulin glargine and metformin, using a non-inferiority approach. Secondary outcomes included change from baseline in 2-hour PPG increment, number of hypoglycaemic episodes and change in body weight.

  Results Fiasp® was non-inferior to NovoRapid® with regard to HbA_{1c} change from baseline in people with T2DM as part of a basal-bolus regimen (estimated treatment difference -0.02%, 95% CI -0.15 to 0.10, p<0.0001). In T2DM, the 1-hour PPG increments favours Fiasp® compared with NovoRapid® and similar HbA_{1c} control (estimated treatment difference -0.59 mmol/L, 95% CI -1.09 to -0.09, p-value not reported). 2-hour PPG increments associated with Fiasp® were non-significant compared to NovoRapid® (estimated treatment difference -0.36 mmol/L, 95% CI -0.81 to 0.08, p = 0.0531).

In addition to onset® 1 and onset® 2, supportive efficacy and safety evidence was provided by onset® 3 and onset® 4.

NOTE TO PCN: Published trial

NOTE TO PCN: The following trials do not appear to have been published to date.]

onset® 3 [58]

- Design: 18-week, multicentre, multinational, randomised, open-label, active controlled, parallel group trial comparing the efficacy and safety of Fiasp® with basal insulin and metformin vs. basal insulin and metformin in adult patients with T2DM

  Results Fiasp® with basal insulin and metformin effectively improved long-term glycaemic control as measured by HbA_{1c} and was superior to basal insulin and metformin from baseline to Week 18 (estimated treatment difference -0.94%, 95% CI -1.17 to -0.72)

onset® 4 [62]

- Design: 6-week, multicentre, multinational, randomised, double-blind parallel group trial evaluating the compatibility and safety of NovoRapid® (n=12) and Fiasp® (n=25) administered via an external subcutaneous insulin infusion system in adult subjects with T1DM. The primary outcome was the number of microscopically confirmed episodes of infusion set occlusion[25]
- **Results** Both Fiasp® and NovoRapid® provided effective glycaemic control in terms of HbA_{1c} (estimated treatment difference -0.14, 95% CI: 0.4-0.11, p not significant). There were no episodes of microscopically confirmed infusion set occlusions. Rates of hypoglycaemia were similar between treatment groups (BG confirmed hypoglycaemia: 76% with Fiasp® vs. 66.7% in the NovoRapid® group).[62] In conclusion, onset 4® demonstrated compatibility and tolerability of Fiasp® when administered via an insulin pump.

Evidence strengths and limitations

Onset® 1 and 2 were randomised, controlled, parallel, treat-to-target (TTT) trials in subjects with T1DM (onset® 1) and T2DM (onset® 2).[11,12] The TTT approach and very tight visit schedule during the trial was chosen to ensure optimal titration of bolus insulin based on subjects' self-measured plasma glucose values. The rationale behind the TTT design is that the benefits of glycaemic control should be balanced with associated side-effects of a therapy (e.g. risk of hypoglycaemia or weight gain). TTT design is recommended by the European Medicines Agency.[26]

The 8-week run-in period was chosen to optimise the basal insulin treatment; from randomisation and onwards, the focus was on optimising the bolus insulin. The trial duration in both studies was 26 weeks to ensure that stable glycaemic control was maintained for a sufficient period.

The clinical efficacy and safety of Fiasp® was assessed vs. the currently marketed NovoRapid® formulation, NovoRapid® in robust head-to-head comparisons, and so building on the extensive efficacy and safety evidence of NovoRapid® over many years.

Onset® 1 and 2 were multinational trials. In onset® 1, patients were randomised at sites in nine countries across Europe, Canada and the US.[11] In onset® 2, patients were randomised in ten countries, across Europe, Israel, India and the US.[12] Inclusion criteria regarding diabetes duration, current anti-diabetes treatment and HbA_{1c} goals were set to ensure that all subjects reflected the intended diabetes population. In both trials, the treatment groups were well matched with respect to the baseline demographics and characteristics.

Equity / Stakeholder views (if relevant)	
Decisions of local Trusts DTCs and neighbouring APCs	**Kingston Hospital NHS Foundation Trust** • No discussion regarding Fiasp to date **Royal Surrey County Hospital NHS Foundation Trust** • Decision deferred until discussion at PCN **Epsom & St Helier University Hospitals NHS Foundation Trust** • No discussion regarding Fiasp to date **Surrey & Sussex Healthcare NHS Trust** • No discussion regarding Fiasp to date **Frimley Health NHS Foundation Trust** • No discussion regarding Fiasp to date **Ashford & St Peters NHS Foundation Trust** • No discussion regarding Fiasp to date **Royal Sussex County Hospital (Brighton)** • No discussion regarding Fiasp to date **Queen Victoria Hospital NHS Foundation Trust** • No discussion regarding Fiasp to date **South West London Medicines Optimisation Group** • No discussion regarding Fiasp to date
Recommendations from national / regional decision making groups	**Scottish Medicines Consortium (SMC)** *10th April 2017, SMC advice no. 1227/17* Following an abbreviated submission insulin aspart (Fiasp®) is accepted for use within NHS Scotland for the treatment of diabetes mellitus in adults.[10] The advice further states that insulin aspart (Fiasp®) is a new formulation with a faster onset of action than another formulation of insulin aspart and is available at an equivalent cost[10] **All Wales Medicines Strategy Group (AWMSG)** *30th November 2016, (published February 2017)* Insulin aspart (Fiasp®) for the treatment of diabetes mellitus in adults in Wales is granted HTA exemption by the AWMSG based on exclusion criterion no. 6: Product is an alternative formulation of an established medicine which costs the same or less than the existing established medicine[46]

Stakeholder views	
CCG priorities	Poorly managed diabetes is associated with serious complications, including cardiovascular disease, renal disease, retinopathy, amputation, depression and neuropathy.[15, 16] Diabetes places a major burden on UK healthcare budgets and currently accounts for approximately 10% of the total health resources expenditure in the UK. In 2010/2011 diabetes cost approximately £23.7 billion (£9.8 billion in direct costs and £13.9 billion in indirect costs), with diabetes-related complications accounting for the greatest proportion of direct health costs.[25] Much of the management and monitoring of people with diabetes, especially those with T2DM, is undertaken by the GP and members of the primary care team[59]. By reducing HbA1c, the use of Fiasp® can help GPs achieve the following Quality and Outcomes Framework (QOF) indicators: • DM007. The % of patients with diabetes, on the register, in whom the last IFCC-HbA1c is 59 mmol/mol or less in the preceding 12 months[59] • DM008. The % of patients with diabetes, on the register, in whom the last IFCC-HbA1c is 64 mmol/mol or less in the preceding 12 months[59] • DM009. The % of patients with diabetes, on the register, in whom the last IFCC-HbA1c is 75 mmol/mol or less in the preceding 12 months[59] HbA1c results are now reported across the UK using the IFCC reference measurement procedure of mmol/mol. The values of 59, 64 and 75 mmol/mol are the equivalent of 7.5%, 8.0% & 9.0% respectively The NHS Outcomes Framework aims to improve quality throughout the NHS by focussing on health outcomes.[60] Good glycaemic control will help meet objectives outlined in the Framework: • Domain 1: Preventing people from dying prematurely[60] – 1a. Potential years of life lost from causes amenable to healthcare • Domain 2: Enhancing quality of life for people with long-term conditions[60] – 2.1. Ensuring people feel supported to manage their condition – 2.3. Reducing time spent in hospital by people with long-term conditions

Health economic considerations	
Cost per year per patient	Fiasp® in the FlexTouch® pen is the same price as NovoRapid® in the FlexPen® Cost per pack Fiasp® vial 100 units/mL, solution for injection in vial 10 mL £14.08 Fiasp® Penfill® 100 units/mL, solution for injection in cartridge 5 x 3 mL £28.31 Fiasp® FlexTouch® 100 units/mL, solution for injection in pre-filled pen 5 x 3 mL £30.60

Table 1: Pack cost and annual cost per patient for NovoRapid® and Fiasp®

Presentation and strength	Pack size	No. units	Pack cost	Cost/ unit	Dose (units)	Cost per year (£)†
NovoRapid®						
Vial 100 units/mL	10 mL	1000	£14.08	£0.0141		£205.71
Penfill® cartridge 100 units/mL	5 x 3 mL	1500	£28.31	£0.0189		£275.74
PumpCart® cartridges, 100 units/ml	5 x 1.6 mL	800	£15.10	£0.0189	40	£275.76
FlexPen® pen 100 units/mL	5 x 3 mL	1500	£30.60	£0.0204		£298.04
FlexTouch® pen 100 units/mL	5 x 3 mL	1500	£32.13	£0.0214		£312.95
Fiasp®						
Vial 100 units/mL	10 mL	1000	£14.08	£0.0141		£205.71
Penfill® cartridge 100 units/mL	5 x 3 mL	1500	£28.31	£0.0189	40	£275.74
FlexTouch® pen 100 units/mL	5 x 3 mL	1500	£30.60	£0.0204		£298.04

†Calculation of annual treatment cost: unit cost (pack cost/number of units) x daily dose (DDD 40 units) x 365.25. Resource use associated with NovoRapid® and Fiasp®, for example insulin needles for injection, are assumed to be identical, therefore these costs are not considered. It is assumed that other costs of treatment (e.g. use of concomitant medication) or other costs resulting from treatment (e.g. long-term outcomes) are equivalent in both treatment groups.

Alternative treatments cost per patient per year

Costs of alternative rapid-acting insulin analogues[61]

Rapid acting insulin analogues	10 ml vial	5×3 ml cartridge (100 units/ml solution)	5×3 ml pre-filled pen (100 units/ml solution)
Insulin glulisine (Apidra®)	£16.00	£28.30	SoloSTAR® £28.30
Insulin lispro (Humalog®)	£16.61	£28.31	Kwikpen® £29.46
Insulin aspart (NovoRapid®)	£14.08	Penfill® £28.31	FlexPen® £30.60 FlexTouch® £32.13

Costs are excluding VAT; taken from MIMS (October 2016).

Other financial considerations (if relevant)

It is assumed that Fiasp® will replace NovoRapid® in a proportion of patients. According to market share data, NovoRapid® is the most widely prescribed bolus insulin in the UK[51.] Based on a 100,000 population in the UK, there are 304 adults with T1DM and 170 adults with T2DM who are treated with NovoRapid® and eligible for treatment with Fiasp®

Patients currently using NovoRapid® FlexPen® can upgrade to Fiasp® FlexTouch® at no additional cost. Studies have shown that the FlexTouch® pen is preferred by patients and healthcare professionals over KwikPen® and SoloStar®[47, 48] The FlexTouch® pen device delivers insulin accurately and consistently, and with a reduced injection force compared with FlexPen®, which makes it easier to inject insulin.[56, 57] Currently NovoRapid® FlexPen® is priced at £30.60 and the FlexTouch® at £32.13, hence a potential saving of £1.53 per pack can be expected with these patients switching to Fiasp®.

Health economic data (if available)	**Clinical value leading to potential economic value** The impact of Fiasp® vs NovoRapid® on long-term clinical outcomes and costs of complications in patients with T1DM in the UK setting has been assessed using the IMS CORE Diabetes Model.[54] Improved glycaemic control with Fiasp® results in reduced cumulative incidence of diabetes-related complications over patient lifetimes. Long-term projections suggest that, in the UK setting, treatment of patients with T1DM with Fiasp® is likely to be associated with improved clinical outcomes and reduced costs of treating diabetes-related complications compared with treatment with NovoRapid®.[55] Studies have shown that the negative health and functioning impacts associated with PPH (post-prandial hyperglycaemia) among people with T1DM and T2DM lead to an increase in healthcare resource use and loss of work-related productivity.[22, 37] An internet survey of 906 adults with T1DM and T2DM in Europe and the USA showed that compared with individuals without PPH, those with PPH measure their blood glucose more frequently, and report greater contact with healthcare professionals related to diabetes.[2]

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