University Hospitals of North Midlands NHS Trust | North Staffordshire Combined Healthcare NHS Trust | Staffordshire and Stoke on Trent Partnership NHS Trust | North Staffordshire Clinical Commissioning Group | Stoke-on-Trent Clinical Commissioning Group

New Medicines Committee Briefing

January 2018

Fiasp® 100 units/mL solution for injection in vial, cartridge (Penfill) and pre-filled pen (FlexTouch)

Fiasp® is to be reviewed for use within:

Primary Care	√
Secondary Care	√

Summary:

- Fiasp is a new formulation of insulin aspart, a rapid-acting insulin analogue, for the treatment of patients with diabetes requiring mealtime (bolus) insulin.[1]
- Fiasp® has a faster onset of action, that closely mimics the physiological response of endogenous insulin compared with insulin aspart (Novorapid®)[2]
- Fiasp® is licensed for administration 2 minutes before a meal and up to 20 minutes after starting meal without compromising HbA_{1c}.
- Fiasp® has been investigated in 4 phase III trials with both type I and Type II diabetic (T1DM and T2DM) patients.[3,4,5]
- Fiasp® was found to be non-inferiority to Novorapid® with regard to HbA_{1c} change from baseline in T1DM and T2DM patients as part of a basal-bolus regimen.[3,6]
- Fiasp in the vial, penfill cartrides and FlexTouch device is the same price as NovoRapid in the vial, Penfill cartridge and FlexPen device respectively.
- No Cost Implications if changing to Fiasp® from NovoRapid®.
- Fiasp® was well tolerated and associated with a statistically significant greater glucose-lowering effect following a meal test compared to NovoRapid® when administered via Continuous Subcutaneous Infusion.[7]
- Scottish Medicines Consortium (SMC) has accepted Fiasp® for use within NHS Scotland.[8]
- Fiasp® is a black triangle drug (▼) and is monitored intensively by the CHM and MHRA.[1]

Formulary application

Consultants submitting application:	Dr Mahesh Sathiavageeswaran Consultant Endocrinologist & Acute Physician
Clinical Director supporting application:	Dr George Varughese Consultant in Diabetes and Endocrinology

Dr Mahesh Sathiavageeswaran has requested Fiasp® to be considered for inclusion into the Joint North Staffordshire Formulary as a treatment option for T1DM and T2DM in adults and pregnancy. He states that it would provide greater flexibility for patients taking mealtime insulin as it can be taken up to 20 minutes after a meal without compromising HbA_{1c}. He also suggested that Insulin Lispro (Humalog®) may be removed from the North Staffordshire Joint Formulary due to its lower market share and narrower indications. Dr Sathiavageeswaran noted on the application form that Fiasp® would be primarily initiated by clinicians and specialist nurses in secondary care and primary care He also stated that the advantage of including Fiasp® on the formulary is its time action profile that is closer to that of the normal human response as well as ability to improve post prandial glucose (PPG) results.
Dr Mahesh Sathiavageeswaran anticipates FIASP® use in up to 10 – 15 patients/year.

Background [1,3,6]

Basal-bolus insulin therapy in patients with T1DM is an essential component for meeting HbA_{1c} target levels of 6.5 – 7% (48 – 53 mmol/mol) recommended by several guidelines to reduce incidence and slow the progression of diabetes related complications, and is one of the recommended steps in T2DM treatment intensification when oral ant-diabetic drugs become less effective.

In T1DM and T2DM, the aim is to replace physiological insulin. Fast acting insulin was developed to control (post-prandial plasma glucose) PPG excursions more effectively than regular human insulin by offering a faster action and shorter duration. These first generation rapid-action insulin analogues were a major step forward.

Fiasp® is mealtime insulin for controlling PPG excursions. It is a new formulation of NovoRapid® whereby 2 new excipients (niacinamide [Vitamin B3] and L-Arginine) have been added to ensure early and fast absorption. These additions have enhanced Fiasp® in achieving better PPG control than NovoRapid®.

Current formulary status

There are currently no Faster Acting Insulin analogues on the North Staffordshire Joint formulary.

6.1.1.1 Rapid-acting insulins			
Insulin aspart ■ NovoRapid®		**Restriction:** For use only by practitioners experienced in the use of insulins	
Insulin glulisine ■ Apidra®		**Restriction:** For use only by practitioners experienced in the use of insulins	
Insulin lispro ■ Humalog®		**Restriction:** For use only by practitioners experienced in the use of insulins	☑ MTRAC
Insulin lispro HIGH STRENGTH ■ Humalog® KwikPen		Not approved for inclusion in the North Staffordshire Joint Formulary	Medicines Review Verdict Sheet

Therapeutic class and mode of action[1]

The primary activity of Fiasp® is the regulation of glucose metabolism. The addition of nicotinamide (vitamin B_3) results in a faster initial absorption of insulin compared to NovoRapid®.
The onset of action was 5 minutes earlier and time to maximum glucose infusion rate was 11 minutes earlier with Fiasp® than with NovoRapid®. The maximum glucose-lowering effect of Fiasp® occurred between 1 and 3 hours after injection. The duration of action was shorter for Fiasp® compared to that of NovoRapid® and lasts for 3–5 hours.

Licensed indications[1]

Treatment of diabetes mellitus in adults

Dosage and administration[1]

Fiasp® is a mealtime insulin 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.

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. In a basal-bolus treatment regimen approximately 50% of this requirement may be provided by Fiasp® and the remaining by intermediate-acting or long-acting insulin.
The individual total daily insulin requirement in adults may vary and is usually between 0.5 and 1.0 unit/kg/day.
The duration of action will vary according to the dose, injection site, blood flow, temperature and level of physical activity.
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.

Safety and adverse effects[1]

Contraindications:

Hypersensitivity to the active substance or to any of the excipients

Special warnings and precautions for use:

Hypoglycaemia

Omission of a meal or unplanned, strenuous physical exercise may lead to hypoglycaemia.

Hypoglycaemia may occur if the insulin dose is too high in relation to the insulin requirement.

The timing of hypoglycaemia usually reflects the time-action profile of the administered insulin formulation. Hypoglycaemia may occur earlier after an injection/infusion when compared to other mealtime insulins due to the earlier onset of action of Fiasp®.

Since Fiasp® should be administered up to 2 minutes before the start of the meal with the option to administer up to 20 minutes after starting the meal, the time to onset of action must be taken into account when prescribing to patients with concomitant diseases or treatment where a delayed absorption of food might be expected.

Combination of thiazolidinediones and insulin medicinal products

Cases of congestive heart failure have been reported when thiazolidinediones were used in combination with insulin, If the combination is used, patients should be observed for signs and symptoms of congestive heart failure, weight gain and oedema. Thiazolidinediones should be discontinued if any deterioration in cardiac symptoms occurs.

Drug Interactions[1]

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.

Presentation[1]

Clear, colourless, aqueous solution for injection
Fiasp 100 units/mL solution for injection in **pre-filled pen** (FlexTouch®)
Fiasp 100 units/mL solution for injection in **cartridge** (Penfill)
Fiasp 100 units/mL solution for injection in **vial**

Patent Status [1]

Date of first authorisation: 09 January 2017

NB: Patent for NovoRapid® expired: June 2017

Guidance and Evidence Summary

NICE Guidance [9,10]	**Yes**

NICE recommends multiple daily injection basal–bolus insulin regimens as the insulin regimen of choice for all adults with T1DM and the use of a basal-bolus regimen for patients with T2DM who do not meet glycaemic targets on basal insulin alone.

Scottish Medicines Consortium (SMC)[8]	**Yes**

SMC accepted Fiasp® to be used within NHS Scotland for treatment of diabetes mellitus in adults. SMC indicated that Fiasp® is a new formulation of insulin aspart with a faster onset of action than Novo

Rapid at an equivalent cost.

All Wales Medicines Strategy Group (AWMSG)[11]	Yes

FIASP® excluded by AWMSG and for health board consideration of local formulary inclusion (February 2017) because:
''The product is an alternative formulation of an established medicine which costs the same or less than the existing medicine''

Regional Drug and Therapeutic Centre (RDTC)[12]	Yes

Fiasp® is a new formulation of insulin aspart with the added nicotinamide to produce a more rapid onset of action. Clinical trials found it non-inferior to NovoRapid when used in a basal-bolus regimen in patients with T1DM and T2DM. There were no overall differences in adverse events or hypoglycaemia but there was difference in the timing of hypoglycaemia. There are no apparent differences or clinical advantages between Fiasp® and NovoRapid®.

Midlands Therapeutics Review and Advisory Committee (MTRAC)	No

Efficacy

The clinical efficacy of Fiasp® has been investigated in 4 phase III trials (onset ®, 1 onset®2, onset®3 and onset®4).[3,4,6,13] The efficacy and safety of Fiasp® was assessed against NovoRapid for T1DM and T2DM in RCTs onset® 1 and 2 respectively[6,3] while onset®3 and 4 were supporting evidence to ® 1 and 2.

Onset 1 in patients with T1DM[6]

Russell-Jones D. *et al.* in a 26 weeks, multicentre, multinational, double-blind, active controlled, 3-arm parallel trial compared the efficacy of Fiasp® in terms of glycemic control with NovoRapid® with an 8 week run in period. The three arm involved mealtime Fiasp® and mealtime NovoRapid in combination with insulin detemir in a basal-bolus regimen as well as open-label post meal Fiasp® in combination with insulin detemir.

A total of 1,143 patients age ≥ 18years with T1DM (HbA_{1c} 7-9.5%) were randomized to mealtime Fiasp® (n=381), mealtime NovoRapid® (n=380) or post meal Fiasp® (20 minutes post meal) (n=282) across 9 countries across Europe, Canada and USA. Inclusive criteria included patients with body mass index $\leq$35kg/m^2 who had been treated with 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. Baseline characteristics were similar between the three groups.

The primary end point was to compare the change in HbA_{1c} from baseline after 26 weeks. In T1DM, the reduction in HbA_{1c} was non-inferior with regard to HbA_{1c} change from baseline as part of a basal-bolus regimen (estimated treatment difference (ETD) -0.15%, 95%CI: -0.23 to -0.07, p<0.0001). Mealtime Fiasp® was non-inferior to mealtime NovoRapid®. Post-meal Fiasp® was also non-inferior to mealtime

NovoRapid® (ETD 0.04%, 85% CI -0.04 to 0.12). The reduction in HbA_{1c} was statistically significantly greater with mealtime FA than with mealtime NovoRapid®. *P*=0.0405).

The secondary endpoints included confirming the superiority of mealtime Fiasp® over NovoRapid® in relation to post prandial plasma glucose (PPG), regulation, number of hypoglycaemic events and body weight regulation.

Change from baseline after 26 weeks in the 2 hour (meal test) showed mealtime Fiasp® provided superior PPG control compared with NovoRapid® (ETD -0.67, 95% CI -1.29 to -0.04, p=0.0187). The estimated change from baseline in 1 hour PPG was 1.3mmol/l (22.9mg.dl) with post meal Fiasp®. At 2 hours, there was no statistically significant difference. Body weight and number of treatment emergent events or hypoglycaemic episodes as confirmed by blood glucose were comparable between Fiasp® and NovoRapid®.

Safety: There was similarity in the overall adverse event rate with all 3 study arms (mealtime Fiasp® n=478.6, post-meal Fiasp® =441 and mealtime NovoRapid®= 458.5). Proportion of subjects reporting adverse events were similar. No significant differences in severe or blood glucose confirmed hypoglycaemia.

Conclusion:

In patients with T1DM, onset® 1 confirmed non-inferiority of Fiasp® to NovoRapid® in HbA_{1c} change from baseline for both mealtime and post-meal administration. There was a statistically significantly greater reduction in HbA_{1c} with mealtime Fiasp® vs. NovoRapid® after 26 weeks of treatment (ETD -0.15%, 95% CI: -0.23 to -0.07, p-value <0.0001). Mealtime Fiasp® was associated with statistically significantly improved control of PPG increment vs. NovoRapid® as demonstrated in both the 1- and 2-hour meal tests (ETD at 1 hour -1.18 mmol/L, [95% CI -1.65 to -0.71], p-value not reported and at 2 hour -0.67 mmol/L, [95%CI -1.29 to -0.04] respectively, p=0.0187).

Limitations:
The meal test protocol: All subjects received the same 0.1 units/kg body weight bolus dose and no adjustment was made for insulin – carbohydrate ratios: therefore for all subjects, the insulin dose was an approximation of their usual dose.

Onset® 2 Trial in patients with T2DM[3]

This was a 26 weeks (with an 8 week run in), multicenter, multinational, 1:1 randomised, double-blind, active controlled, treat to target, parallel group trial that compared the efficacy and safety of Fiasp® with NovoRapid®, both in combination with once daily (OD) insulin glargine (Apidra®) and Metformin (M) in a basal-bolus regimen. 682 adults (>18 yrs and body mass ≤40kg/m^2) with T2DM treated with basal insulin for at least 6 months, were randomized (after run in) 1:1 to mealtime Fiasp® (n= 341) or NovoRapid® (n=341) along with insulin glargine and metformin. Subjects recorded self-monitored blood glucose.

The outcome of the trial was to confirm the efficacy of treatment with mealtime Fiasp® in T2DM patients in comparison to mealtime NovoRapid® in relations to glycaemic control measured by HbA_{1c} after 26 weeks 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.

Fiasp® was non-inferior to NovoRapid with regards to HbA_{1c} from baseline (ETD -0.02%; 95% CI -0.15 to 0.10, p<0.0001). Mean HbA_{1c} before the 6 week run in were similar 8.2% (65.6mmol/mol) for Fiasp® patients and 8.1% (65.2mmol/mol) for NovoRapid® patients. Fiasp® was statistical superior to NovoRapid® in estimated change from baseline in 1hr PPG (meal test) (ETD -0.59 mmol/l 95% CI -0.1.09 to -0.09, p value not reported). The increment associated with Fiasp at 2-hour PPG were nom-significant compared to NovoRaapid® (ETD -0.36mmol/L, 95% CI -0.81 to 0.08, p=0.0531).

Safety:

Adverse event rate was similar to that seen in the Onset 1 trial between the two groups. Six major adverse cardiac events were identified (Fiasp® n=2, NovoRapid® group n=4). All were judges unlikely to be related to trial product. In terms of severe or blood glucose confirmed hypoglycaemia no significant differences were recorded (Estimated rate ratio 1.09 [95% CI 0.88 to 1.36]. All other outcomes (vital signs, physical examinations etc. showed no clinically significant differences.

Conclusion:
In patients with T2DM, onset® 2 confirmed non-inferiority of Fiasp® to NovoRapid® regarding HbA_{1c} change from baseline (ETD -0.02%, 95% CI -0.15 to 0.10, p<0.0001). Treatment with Fiasp® resulted in better control in 1-hour PPG increment (ETD -0.59 mmol/L, 95% CI -1.09 to -0.09, p-value not reported), and a similar control of 2-hour PPG increment when compared with NovoRapid® (ETD-0.36 mmol/L, 95% CI -0.81 to 0.08, p=0.0531).

Limitations:
Use of continuous glucose monitoring has shown that existing approaches for calculating basal-bolus doses may overestimate total insulin dose required and underestimate meal-time insulin requirements.
Patients required to perform finger-prick tests to record blood glucose. In 'real life' many patients are unwilling to do this (non-compliance)
Inclusion of subjects with relatively good glycemic control, not representative of patients usually encountered in clinical practice.
Initiation of 3 bolus doses simultaneously and the liquid meal test – not fully representative of 'real life'

Onset® 3 trial in patients T2DM[4]
This was an 18 weeks, multicentre, multinational, randomised, open-label, active controlled, parallel trial comparing the efficacy and safety of mealtime Fiasp® in a basal-bolus regimen with OD insulin in combination with metformin (n=116) against basal OD insulin in combination with metformin (n=120) in adults with T2DM. Eligible patients were >18 years with T2DM inadequately controlled on basal insulin and oral anti-diabetics (mean HbA_{1c} 7.9%). The primary endpoint of the study was change from baseline in HbA_{1c} after 18 weeks. Secondary endpoints included 2-hour PPG, plasma glucose change from baseline, hypoglycaemic rate and weight gain.

Mean HbA_{1c} at baseline was 7.9% in both group but was statistically significantly reduced in Fiasp® (6.8%) than in basal insulin (7.7%) (ETD -0.94% 95% CI; -1.17, -0.72). HbA_{1c} <7% was achieved by 60.3% of Fiasp® group compared to 18.3% patients in basal group. 2-hour PPG was reduced significant in Fiasp® group. There was no significant difference between the groups in fasting glucose change from baseline (ETD -0.12 mmol/L (95% CI -0.66; 0.42). Both hypoglycaemia rate and weight gain were greater in the Fiasp® group than basal insulin group.

Conclusion:
Fiasp® + basal insulin effectively improved long-term glycaemic control measured by HbA_{1c} and were superior to basal insulin + metformin in the lowering of HbA_{1c}.

Onset® 4 trial in patients with T1DM[13]
This is a 6 weeks, multicentre, multinational, randomised, double-blind parallel group trial that evaluated the compatibility, efficacy and safety of Fiasp® (n=25) and NovoRapid® (n=12) administered via external continuous subcutaneous insulin (CSII) system in adults with T1DM. The primary endpoint of the study was the number of microscopically confirmed episodes of infusion set occlusion. Eligible patients were ≥18 years with T1DM for more than 12 months; HbA_{1c} <9.0%; BMI 20.0-35.0kg/m^2; using an external CSII system for at least 6 months.

There were no microscopically confirmed episodes of infusion set occlusions in both treatment groups. 7 possible infusion-set occlusions were reported by 5 patients on Fiasp® with none confirmed. Both

macroscopic and microscopic evaluation showed no colour change or particle formation in the infusion sets. The mean HbA_{1c} decreased from baseline in both Fiasp® group (7.34% to 7.14%) and NovoRapid® group (7.74% to 7.63%). This change in baseline HbA_{1c} over 6 weeks of treatment was not significant (ETD -0.14% 95% CI 0.40-0.11).
Conclusion:

Improved PostPrandial Glycemic Control with Faster-Acting Fiasp® in patients with T1DM via CSII[7]

Bode BW at al. in a double-blind, randomised, crossover, active-controlled trial compared 2-hour PPG response following 2 weeks of CII with Fiasp® or NovoRapid®. The primary endpoint of the study was to evaluate the mean change (increment) in PG 2 hours after a standardised meal test after 2 weeks of CII treatment. Secondary endpoints relating to the meal test included change in PG concentration 1 hour and mean fructosamine levels after 2 weeks of treatment. The 43 patients had masked continuous glucose monitoring throughout.
Fiasp® delivered a statistically significant glucose lowering effect following meal versus NovoRapid (3.03mmol/L vs 4.02mmol/L [54.68mg/dL vs 72.52mg/dL] *p*=0.044). 1-hour PPG level were -1.64mmol/L (-2.9.47mg/dL) lower with Fiasp® compared to NovoRapid® (p=0.006). Duration of lower interstitial glucose levels was statistically significantly shorter for Fiasp® vs NovoRapid® (2.03 hours vs 2.45 hours; ETD -0.42 95% CI -0.72 to -0.11; p = 0.008).

Safety:
No new safety or tolerability issues were identified. There were slightly hiher rate of treatment emergent adverse events in Fiasp® compared to NovoRapid® (38 (88.4%) vs 33(78.6%). The rate of overall treatment-emergent hypoglycemic events (<3.9mmol/L [70mg/dL]) per exposure day was 0.87 with Fiasp® and 0.97 with NovoRapid®. Changes in measurements related to vital signs, physical examination were similar between the two groups.

Conclusion:
CII delivery of Fiasp® delivered a statistically significantly greater glucose-lowering effect than NovoRapid® after a standardised meal test with mean reduction in PG concentration in the first 2 hours 25% greater with Fiasp®.

Limitations: Short duration of study and small number of participants.

Cost Analysis

Current UHNM prices table for NMC review

Medicine Description	Brand	Pack size	UHNS (incl. VAT)	Primary Care (exl. VAT
FIASP 100units/1mL INJECTION (10mL)	INSULIN ASPART	1		£14.08
FIASP FLEXTOUCH 300units/3mL PREFILLED PEN	INSULIN ASPART	5		£30.60
FIASP PENFILL 300units/3mL CARTRIDGE	INSULIN ASPART	5		£28.31
NovoRAPID 100units/mL INJECTION (10mL)	INSULIN ASPART	1		£14.08
NovoRAPID FLEXPEN 300units/3mL PREFILLED PEN	INSULIN ASPART	5		£30.60
NovoRAPID FLEXTOUCH 300units/3mL PREFILLED PEN	INSULIN ASPART	5		£32.13
NovoRAPID 300units/3mL CARTRIDGE	INSULIN ASPART	5		£28.31
NovoRAPID PUMPCART 160units/1.6mL CARTRIDGE	INSULIN ASPART	5		£15.10
INSULIN HUMALOG 100units/1mL INJECTION (10mL)	INSULIN LISPRO	1		£16.61
INSULIN HUMALOG 300units/3mL CARTRIDGE	INSULIN LISPRO	5		£28.31
INSULIN HUMALOG 300units/3mL KWIK PEN	INSULIN LISPRO	5		£29.46
APIDRA 100units/1mL INJECTION (10mL)	INSULIN GLULISINE	1		£12.50
APIDRA 300units/3mL SOLOSTAR PEN	INSULIN GLULISINE	5		£28.30
APIDRA 300units/3mL CARTRIDGES	INSULIN GLULISINE	5		£22.50

North Staffordshire and Stoke-on-Trent CCGs – Total Actual Spend of Fast Acting Insulin Nov 2016 – Oct.2017

Sum of Total Act		
Insulin Type	**BNF Name**	**Total**
Insulin Aspart	Ins Aspart_Inj 100u/ml 1.6ml Cart	£224
	Ins Aspart_Inj 100u/ml 10ml Vl	£639
	Ins Aspart_Inj 100u/ml 3ml Cart	£4,485
	Ins Aspart_Inj 100u/ml 3ml Pf Pen	£510
	Ins Fiasp_FlexTouch 100u/ml 3ml Pf Pen	£340
	Ins Fiasp_Inj 100u/ml 10ml Vl	£404
	Ins Fiasp_Penfill 100u/ml 3ml Cart	£341
	Ins NovoRapid_FlexPen 100u/ml 3ml Pf Pen	£322,645
	Ins NovoRapid_FlexTouch 100u/ml 3mlPfPen	£8,196
	Ins NovoRapid_Inj 100u/ml 10ml Vl	£26,033
	Ins NovoRapid_Penfill 100u/ml 3ml Cart	£173,465
	Ins NovoRapid_PumpCart 100u/ml 1.6mlCart	£27,912
Insulin Aspart Total		**£565,194**
Insulin Glulisin	Ins Apidra SoloStar_100u/ml 3ml PF Pen	£50,643
	Ins Apidra_100u/ml 10ml Vl	£4,268
	Ins Apidra_100u/ml 3ml Cart	£7,583
	Ins Glulisine_100u/ml 10ml Vl	£667
	Ins Glulisine_100u/ml 3ml Cart	£26
	Ins Glulisine_100u/ml 3ml Pf Pen	£1,704
Insulin Glulisine Total		**£64,891**
Insulin Lispro	Ins Humalog_100u/ml 10ml Vl	£10,754
	Ins Humalog_100u/ml 3ml Cart	£46,417
	Ins Humalog_100u/ml 3ml Pf Pen	£27
	Ins Humalog_KwikPen 100u/ml 3ml Pf Pen	£93,568
	Ins Humalog_KwikPen 200u/ml 3ml Pf Pen	£14,167
	Ins Lispro_Inj 100u/ml 10ml Vl	£9,909
	Ins Lispro_Inj 100u/ml 3ml Cart	£25,650
	Ins Lispro_Inj 100u/ml 3mlPfPen	£19,956
Insulin Lispro Total		**£220,449**
Grand Total		**£850,534**

Total expenditure table for NMC review

Expenditure for Jul16-Jun17: Medicine Description	UHNM Royal Stoke TOTAL EXPENDITURE (VAT applied as appropriate)	UHNM County Hospital TOTAL EXPENDITURE (VAT applied as appropriate)	UHNM TOTAL EXPENDITURE (VAT applied as appropriate)
FIASP 100units/1mL INJECTION (10mL)	£0.00	£0.00	£0.00
FIASP FLEXTOUCH 300units/3mL PREFILLED PEN	£0.00	£0.00	£0.00
FIASP PENFILL 300units/3mL CARTRIDGE	£0.00	£0.00	£0.00
NovoRAPID 100units/mL INJECTION (10mL)	£2,493.92	£67.59	£2,561.51
NovoRAPID FLEXPEN 300units/3mL PREFILLED PEN	£11,565.09	£756.43	£12,321.52
NovoRAPID FLEXTOUCH 300units/3mL PREFILLED PEN	£33.82	£0.00	£33.82
NovoRAPID 300units/3mL CARTRIDGE	£2,734.69	£156.27	£2,890.96
NovoRAPID PUMPCART 160units/1.6mL CARTRIDGE	£115.97	£0.00	£115.97
INSULIN HUMALOG 100units/1mL INJECTION (10mL)	£1,381.66	£99.66	£1,481.32
INSULIN HUMALOG 300units/3mL CARTRIDGE	£848.35	£149.47	£997.82
INSULIN HUMALOG 300units/3mL KWIK PEN	£3,684.81	£784.79	£4,469.61
APIDRA 100units/1mL INJECTION (10mL)	£0.00	£0.00	£0.00
APIDRA 300units/3mL SOLOSTAR PEN	£718.20	£27.00	£745.20
APIDRA 300units/3mL CARTRIDGES	£27.00	£0.00	£27.00
TOTAL	£23,603.52	£2,041.21	£25,644.73

References

[1] Summary of Product Characteristics FIASP® 100IU/ml solution for injection. Novo Nordiak Ltd 2017. Available at: https://www.medicines.org.uk/emc/product/8109 (Accessed 5th December 2017)

[2] Heise T, Hovelmann U, et al: Faster-Acting insulin aspart: earlier onset of appearance and greater early pharmacokinetic and pharmacodynamic effects than insulin aspart; Diabetes, Obesity and Metabolism., 2015;17 (7): 682 - 688

[3] Bowering K, Case C, et al: Faster Aspart Versus Insulin Aspart As Part of a Basla-Bolus Regimen in Inadequately Controlled Type 2 Diabetes: The Onset 2 Trial: Diabetes Care 2017; 40; 951 - 957

[4] Rodbard H TS, Vidrio-Velaquez M, Tripathy D, Piletic D, Demissie M. Adding faster-acting insulin aspart to basal insulin significantly improved glycemic control: the Onset 3® trial. 76th annual Scientific Sessions of the American Diabetes Association (ADA); New Orleans, US 10-14 Jun 2016

[5] Bode B HL, Tamer S, Ybanez P, Demissie M. 994P Improved Postprandial Glycemic Control with Faster-Acting Insulin Aspart in Subjects with Type 1 Diabetes Using CSII. 75th annual Scientific Sessions of the American Diabetes Association (ADA); Massachusetts, US 5-9 June, 2015

[6] Russell-Jones D, Bode B.E, et al: Fast-Acting Insulin Aspart Improves Glycemic Control in Basal-Bolus Treatment for Type 1 Diabetes (T1DM): Results of a 26 week, Multicentre, Active-Controlled, Treat-to-Target, Randomised, Parallel-Group Trial (Onset 1): Diabetes Care 2017; 40; 943 – 950

[7] Bode BW, Johnson JA, Hyveled, et.al: Improved PostPRANDIAL Glycemic Control with Faster-Acting Insulin Aspart (FA) in patients with Type 1 Diabetes Using Continuous Subcutaneous Insulin Infusion. Diabetes Technology & Therapeutics 2017; 19; (1); 25 - 33

[8] Scottish Medicines Consortium. Insulin aspart (Fiasp®) 100 units/mL solution for injection in vial; solution for injection in cartirdge (Penfill); solution for injection in pre-filled pen (FlexTouch). SMC No 1227/17. 2017. Available at https://www.scottishmedicines.org.uk/. (Accessed 10 December 2017)

[9] National Institute for Health and Care Excellence. NICE Guidance NG17. Type 1 Diabetes in adults: diagnosis and management. 2015. Available at https//www.nice.org.uk/guidance/ng17 (Accessed 11 December 2017)

[10] National Institute for Health and Care Excellence. NICE guidelines NG28. Type 2 diabetes in adults: management. 2015. Available at https//www.nice.org.uk/guidance/ng28. (Accessed 11 December 2017)

[11] All Wales Medicines Strategy Group. Medicines excluded by AWMSG and for health board consideration of local formulary inclusion 2017. Available at http://www.awmsg.org/awmsgonline/app/sitesearch?execution=e1s1. (Accessed on 02/01/2018)

[12] Regional Drug and Therapeutics Centre. New Drug Evaluation. Fast-acting insulin aspart for the treatment of diabetes mellitus. No 152 July 2017 . Available via http://rdtc.nhs.uk/sites/default/files/publications/nde-152-fast-acting-insulin-aspart-01.pdf (accessed 02/01/18)

[13] Zijlstra E., Demissie M. et. Al. Investigation of Pump Compatibility of Fast-Acting Insuin Aspart in Subjects With Type 1 Diabetes. J Diabetes Sci Technol. 2018;12(1):145-151. doi: 10.1177/19322968177303