Innovation Observatory

NHS National Institute for Health Research

HEALTH TECHNOLOGY BRIEFING FEBRUARY 2019

LY-900014 (ultra-rapid lispro) for adults with type 1 diabetes mellitus

NIHRIO ID	14861	**NICE ID**	9730
Developer/Company	Eli Lilly and Company Ltd	**UKPS ID**	Not available

Licensing and market availability plans	Currently in phase III clinical trials

SUMMARY

LY-900014 (ultra-rapid lispro) is in development for the treatment of adult patients with type 1 diabetes mellitus. Type 1 diabetes mellitus is a condition which usually starts early in life and occurs as a result of the pancreas not producing enough (or sometimes any) insulin. This results in elevated blood sugar levels which can damage many organs in the body. Type 1 diabetes usually runs in families. While type 1 diabetes cannot be cured, having regular, at least daily, injections of insulin can keep blood sugar levels stable. However some people, despite having regular injections of insulin, still do not have stable blood sugar levels.

LY-900014 is a new formulation of insulin lispro that contains certain ingredients designed to increase the speed of insulin lispro absorption. Insulin lispro acts by copying the way naturally produced insulin works in people without diabetes. LY-900014 is administered by insulin pump and early studies have demonstrated rapid absorption of insulin lispro and improved glucose control after meals. If licensed, LY-900014 will offer a new option in insulin therapy for type 1 diabetes with the potential to help to keep blood sugar in range after eating.

PROPOSED INDICATION

Treatment of type 1 diabetes mellitus in adults[1]

TECHNOLOGY

DESCRIPTION

LY-900014 (ultra-rapid lispro) is a novel formulation containing locally-acting excipients (citrate and treprostinil) to accelerate insulin lispro absorption.[2,3] Insulin lispro, is produced by a method known as 'recombinant DNA technology': it is made by bacteria into which a gene (DNA) has been introduced, which makes them able to produce insulin lispro. Insulin lispro is very slightly different from human insulin. The difference means that insulin lispro is absorbed faster by the body than human regular insulin, and can therefore act faster but still the same way as naturally produced insulin and helps glucose enter cells from the blood. By controlling the level of blood glucose, the symptoms and complications of diabetes are reduced.[4]

LY-900014 is in clinical development for the treatment of adults with type 1 diabetes. In the phase III clinical trial (NCT03433677), LY-900014 was administered by continuous subcutaneous insulin infusion at a dose of 100 unit(s)/millilitre (U/ml). No further details about the treatment schedule are reported.[5,6]

INNOVATION AND/OR ADVANTAGES

Ineffective and inconsistent control of postprandial hyperglycaemia has been described as one of the greatest challenges and unmet needs in diabetes management.[7] LY-900014 is a meal time insulin formulation that accelerates the absorption of insulin lispro to help better control blood glucose levels after meals by closely mirroring the way insulin works in people without diabetes[2,8].

Results from phase I clinical trial (NCT03056456) has shown that LY-900014 demonstrated accelerated absorption and a trend toward improved postprandial glucose control in subjects with type 1 diabetes using continuous subcutaneous insulin infusion.[3] If approved, LY-900014 will offer an additional option in mealtime insulin therapy designed to help keep blood sugar in range after eating.[8]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

LY-900014 does not currently have Marketing Authorisation in the EU/UK for any indication.

LY-900014 is in phase III clinical development for children and adolescents with type 1 diabetes, and adults with type 2 diabetes.[9,10]

PATIENT GROUP

DISEASE BACKGROUND

Diabetes mellitus is a lifelong condition where the body's glucose (blood sugar) levels become too high. There are two types of diabetes, type 1 and 2 diabetes. In type 1 diabetes, the pancreas does not produce insulin and this is why it is sometimes called insulin-dependent diabetes. In type 2 diabetes, either the pancreas does not produce enough insulin or the body's cells do not react to insulin.[11,12] Type 1 diabetes is less common than type 2, accounting for approximately 10% of all diabetes cases.[11]

Type 1 diabetes describes an absolute insulin deficiency in which there is little or no endogenous insulin secretory capacity due to destruction of insulin-producing beta-cells in the pancreatic islets of Langerhans. This form of the disease has an auto-immune basis in most cases, and it can occur at any age, but most commonly before adulthood. Loss of insulin secretion results in hyperglycaemia and other metabolic abnormalities. If poorly managed, the resulting tissue damage has both short-term and long-term adverse effects on health; this can result in retinopathy, nephropathy, neuropathy, premature cardiovascular disease, and peripheral arterial disease.[13]

Hyperglycaemia can lead to diabetic ketoacidosis if left untreated where fats and muscles being used by the body as an alternative source of energy. Symptoms of type 1 diabetes include feeling very thirsty, passing urine more often than usual (especially at night), feeling tired, weight loss and loss of muscle mass .[12]

Diabetes can cause a significant amount of disability, distress and increases the risk of developing several severe complications. These can include short term complications, such as hypoglycaemia diabetic ketoacidosis and hyperosmolar hyperglycaemia state, and long term complications such as renal disease, retinopathy, cardiovascular disease such as heart disease and stroke, neuropathy (nerve damage) and foot complications such as foot ulcers and infections which may lead to amputations.[14]

CLINICAL NEED AND BURDEN OF DISEASE

In 2015, 3.8 million people in England were estimated to have both types of diabetes, with approximately 10% having type 1 diabetes[15] Using Office for National Statistics projections, and assuming that there is no change in the way in which diabetes is treated, it is estimated that the number of people with type 1 diabetes will rise from approximately 400,000 to 650,000 people by 2035/2036.[16]

Hospital admissions data for England in 2017-2018 recorded 42,389 finished consultant episodes (FCE) for insulin-dependent diabetes mellitus (ICD 10: E10), 27,791 hospital admissions and 1,731 day cases.[17]

Poor glycaemic control is common in type 1 diabetes. A target HbA1c concentration of 48 mmol/mol (6.5%) or lower is recommended in patients with type 1 diabetes.[13] In the 2014 UK type 1 diabetes population cohort estimates, despite the use of insulin, less than 30% of the 330,236 patients had their HbA1c level less than 59 mmol/mol (7.5%) and greater than 30% had HbA1c levels above75 mmol/mol (9%).[18] Improvement of glycaemic control has clearly been demonstrated to reduce the risk of microvascular complications. [18]

The direct cost (estimated from data on diagnosis, lifestyle interventions, ongoing treatment, management and complications) and indirect cost (estimated from data on mortality, sickness, loss of productivity and informal care) for type 1 diabetes is high at an estimated £1 billion and £0.9 billion respectively in the UK in 2010/2011. Approximately 37,000 working years were lost from deaths and the cost of mortality was estimated at £0.6 billion in 2010/2011.[16]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

The management of type 1 diabetes involves setting up an individual plan jointly agreed with the adult with type 1 diabetes, which is reviewed annually and modified taking into account changes in person's wishes, circumstances and medical findings. This plan includes aspects of :[19]

- Diabetes education, including nutritional advice
- Insulin therapy, including dose adjustment
- Self-monitoring
- Avoiding hypoglycaemia and maintaining awareness of hypoglycaemia
- Family planning, contraception and pregnancy planning for women of childbearing potential.
- Cardiovascular risk factor monitoring and management
- Complications monitoring and management
- Means and frequency of communication with the diabetes professional team
- Frequency and content of follow-up consultations, including review of haemoglobin A1c (HbA1c) levels and experience of hypoglycaemia.

CURRENT TREATMENT OPTIONS

NICE recommends the following pharmacological treatments in the management and treatment of type 1 diabetes in adults:[20]

Insulin regimens

- Offer multiple daily injection basal–bolus insulin regimens, rather than twice‑daily mixed insulin regimens, as the insulin injection regimen of choice for all adults with type 1 diabetes. Provide the person with guidance on using multiple daily injection basal–bolus insulin regimens.
- Do not offer adults newly diagnosed with type 1 diabetes non‑basal–bolus insulin regimens (that is, twice‑daily mixed, basal only or bolus only).

Long-acting insulin

- Offer twice‑daily insulin detemir as basal insulin therapy for adults with type 1 diabetes.
- Consider, as an alternative basal insulin therapy for adults with type 1 diabetes:
    - an existing insulin regimen being used by the person that is achieving their agreed targets
    - Once-daily insulin glargine or insulin detemir if twice‑daily basal insulin injection is not acceptable to the person, or once‑daily insulin glargine if insulin detemir is not tolerated.
- Consider other basal insulin regimens for adults with type 1 diabetes only if insulin determir and alternative basal insulin therapy do not deliver agreed targets. When choosing an alternative insulin regimen, take account of the person's preferences and acquisition cost.

Continuous subcutaneous insulin infusion (CSII or insulin pump) therapy

CSII or 'insulin pump' therapy is recommended as a treatment provided that:

- Attempts to achieve target HbA1c levels with multiple daily injections (MDIs) result in the person experiencing disabling hypoglycaemia. For the purpose of this guidance, disabling hypoglycaemia is defined as the repeated and unpredictable occurrence of hypoglycaemia that results in persistent anxiety about recurrence and is associated with a significant adverse effect on quality of life

or

- HbA1c levels have remained high (that is, at 8.5% [69 mmol/mol] or above) on MDI therapy (including, if appropriate, the use of long-acting insulin analogues) despite a high level of care.

Rapid-acting insulin

- Offer rapid-acting insulin analogues injected before meals, rather than rapid-acting soluble human or animal insulins, for mealtime insulin replacement for adults with type 1 diabetes.
- Do not advise routine use of rapid-acting insulin analogues after meals for adults with type 1 diabetes.
- If an adult with type 1 diabetes has a strong preference for an alternative mealtime insulin, respect their wishes and offer the preferred insulin.

Mixed insulin

- Consider a twice-daily human mixed insulin regimen for adults with type 1 diabetes if a multiple daily injection basal–bolus insulin regimen is not possible and a twice-daily mixed insulin regimen is chosen.
- Consider a trial of a twice-daily analogue mixed insulin regimen if an adult using a twice-daily human mixed insulin regimen has hypoglycaemia that affects their quality of life.

Optimising insulin therapy

For adults with erratic and unpredictable blood glucose control (hyperglycaemia and hypoglycaemia at no consistent times), rather than a change in a previously optimised insulin regimen, the following should be considered: injection technique, injection sites, self-monitoring skills, knowledge and self-management skills, nature of lifestyle, psychological and psychosocial difficulties, possible organic causes such as gastroparesis.

Adjuncts

Consider adding metformin to insulin therapy if an adult with type 1 diabetes and a Body Mass Index (BMI) of 25 kg/m2 (23 kg/m2 for people from South Asian and related minority ethnic groups) or above wants to improve their blood glucose control while minimising their effective insulin dose.

PLACE OF TECHNOLOGY

If licensed, LY-900014 will offer an additional treatment option as a mealtime insulin therapy for adults with type 1 diabetes with a potential to help keep blood sugar in range after eating.

CLINICAL TRIAL INFORMATION

Trial	PRONTO-Pump, NCT03433677, EudraCT 2017-002374-39, LY-900014 vs insulin lispro; phase III
Sponsor	Eli Lilly and Company
Status	Complete but unpublished
Source of Information	Trial registry[5,6]
Location	Spain and USA
Design	Randomised, crossover assignment, double blinded
Participants	N=48; aged 18 years and older; diagnosed with type 1 diabetes and have been using insulin continuously for at least 12 months; using an insulin pump with 'rapid-acting insulin' for at least 6 months and using the same rapid-acting insulin for at least the past 30 days; have experience using Continuous Glucose Monitoring (CGM) or Flash Glucose Monitoring (FGM) for at least 60 days during the past 12 months; have HbA1c values ≤8.5%, as determined by the central laboratory at screening; have a body mass index (BMI) of ≤35 kilograms per meter squared at screening; have been

	using the MiniMed 530G or 630G (US) or the MiniMed 640G (EU) insulin pump for at least the past 30 days.
Schedule	Randomised to: • LY-900014 administered by CSII at a dose of 100 unit(s)/millilitre (U/ml). • Insulin lispro administered by CSII at a dose of 100 unit(s)/millilitre (U/ml).
Follow-up	6 weeks
Primary Outcomes	Rate of infusion set failures [Time frame: 6 weeks]
Secondary Outcomes	• Percent of participants with at least 1 event of infusion set failure [time frame: 6 weeks] • Rate of premature infusion set changes [time frame: 6 weeks] • Time interval until infusion set change [time frame: 6 weeks] • Bolus/total insulin dose ratio [time frame: 6 weeks] • Interstitial glucose reduction rate from hyperglycaemia following a non-meal-related correction bolus delivered via the pump [time frame: 6 weeks] • Rate of severe hypoglycaemic events [time frame: 6 weeks]
Key Results	Not reported
Adverse effects (AEs)	Not reported
Expected reporting date	Previously reported as September 2018.

Trial	PRONTO-Pump-2, NCT03830281, phase III
Sponsor	Eli Lilly and Company
Status	Not yet recruiting
Source of Information	Trial registry[1]
Location	EU countries(not incl UK), USA, Canada, Israel, Australia and Puerto Rico
Design	Randomised, parallel assignment, double blinded
Participants	N=526 (planned); aged 18 years and older; have been diagnosed with type 1 diabetes and continuously using insulin for at least 1 year; have been using CSII therapy for a minimum of 6 months; currently treated with <100 Units of one of following rapid-acting analog insulin via CSII for at least the past 30 days: insulin lispro U-100, insulin aspart, fast-acting insulin aspart, insulin glulisine; must be using a MiniMed 530G or 630G (US), 640G (EU) insulin pump for at least the past 90 days
Schedule	Randomised to: • LY-900014 administered via CSII • Insulin lispro (Humalog) administered via CSII
Follow-up	Not reported
Primary Outcomes	Change from baseline in HbA1c [time frame: baseline, 16 weeks]
Secondary Outcomes	• 1-hour postprandial glucose (ppg) excursion during mixed-meal tolerance test (mmtt) [time frame: 16 weeks] • 2-hour ppg excursion during mmtt [time frame: 16 weeks] • Rate of severe hypoglycaemia [time frame: baseline through 16 weeks] • Rate of documented symptomatic hypoglycaemia [time frame: baseline through 16 weeks]

	• Change from baseline in 1,5-anhydroglucitol (1,5-ag) [time frame: baseline, 16 weeks] • Change from baseline in 10-point self-monitoring blood glucose (smbg) values [time frame: baseline, 16 weeks] • Change from baseline in bolus/total insulin dose ratio [time frame: baseline, 16 weeks] • Percentage of participants with hba1c <7% and ≤6.5% [time frame: 16 weeks] • Percentage of time with sensor glucose values between 71 and 180 mg/dl [time frame: 16 weeks] • percentage of participants with at least 1 pump occlusion alarm that leads to an unplanned infusion set change [time frame: baseline through 16 weeks] • percentage of participants with at least 1 event of unexplained hyperglycaemia >300 mg/dl confirmed by smbg that leads to an unplanned infusion set change [time frame: baseline through 16 weeks]
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as November 2019

Trial	NCT03760640, phase II
Sponsor	Eli Lilly and Company
Status	Not yet recruiting
Source of Information	Trial registry[21]
Location	USA
Design	Randomised, crossover assignment, double blinded
Participants	N=50 (planned); aged 18 years and older; diagnosed with type 1 diabetes and have been using insulin continuously for at least 12 months; using an insulin pump with 'rapid-acting insulin' for at least 6 months and using the same rapid-acting insulin for at least the past 30 days; have HbA1c values ≥6.0% and ≤8.0%; must have been using the MiniMed 670G insulin pump for at least the past 90 days; must use their Guardian (3) sensor at least an average of 75% of the time and remain in Auto Mode an average of 70% of the time.
Schedule	Randomised to: • LY-900014 administered via CSII by the Medtronic MiniMed 670G System for 4 weeks. • Insulin lispro (Humalog) administered via CSII by the Medtronic MiniMed 670G System for 4 weeks.
Follow-up	The study will consist of two treatment periods of 4 weeks
Primary Outcomes	Percentage of time with sensor glucose values between 70 and 180 milligrams per deciliter (mg/dl) [time frame: week 2 through week 4]
Secondary Outcomes	• Mean sensor glucose value [time frame: week 2 through week 4] • Percentage of time spent in auto mode [time frame: week 2 through week 4] • Percentage of time with sensor glucose values <54 mg/dl [time frame: week 2 through week 4] • Rate of severe hypoglycaemic events [time frame: week 2 through week 4] • Total daily insulin dose [time frame: week 2 through week 4]

Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as September 2019

ESTIMATED COST

The cost of LY-900014 is not yet known.

ADDITIONAL INFORMATION

Eli Lilly and Company Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE Technology appraisal guidance under development. Empagliflozin for type 1 Diabetes Mellitus, adjunct to insulin ID1275]. Expected publication date TBC
- NICE Technology appraisal guidance under development. Dapagliflozin, in combination with insulin, for treating type 1 diabetes [ID1478]. Expected publication date TBC
- NICE Technology appraisal guidance under development. Dapagliflozin, empagliflozin and sotagliflozin for treating type 1 diabetes [ID1217]. Expected publication date TBC.
- NICE Technology appraisal guidance under development. Diabetes – buccal insulin (ID311). Expected publication date TBC.
- NICE Technology appraisal guidance under development. Sotagliflozin, in combination with insulin, for treating type 1 diabetes [ID1376]. Expected publication date, December 2019.
- NICE Technology appraisal guidance. Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (TA151). July 2008.
- NICE clinical guideline. Type 1 diabetes: diagnosis and management (NG17). August 2015 (Last updated July 2016).
- NICE Quality Standard. Diabetes in adults (QS6). August 2016.
- NICE Interventional Procedures Guidance. Allogeneic pancreatic islet cell transplantation for type 1 diabetes mellitus (IPG257). April 2008.
- NICE Diagnostics Guidelines. Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system) (DG21). February 2016.
- NICE evidence summary. Diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar) (ESNM64). December 2015.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. NHS Diabetes Prevention Programme: Primary Care Toolkit to Support Local Implementation of the NHS DPP. July 2016.
- NHS England. Action for Diabetes. January 2014.
- NHS England. 2013/14 NHS Standard Contract for Islet Transplantation Service. A03/S/c.
- NHS England. 2013/14 NHS Standard Contract for Pancreas transplantation service (adult). A03/S/a.
- • NHS England. 2013/14 NHS Standard Contract for specialised endocrinology services (Adult) A03/S/a.

OTHER GUIDANCE

- Scottish Intercollegiate Guidelines Network. Management of diabetes (SIGN116). 2017.
- British Medical Journal. Diagnosis and management of type 1 diabetes in adults: summary of updated NICE guidance. 2015.[22]
- American Diabetes Association. Type 1 Diabetes through the life span: a position statement of the American diabetes association. 2014.[23]

REFERENCES

1 ClinicalTrials.gov. *A study comparing LY900014 to insulin lispro (humalog) in adults with type 1 diabetes using insulin pump therapy (PRONTO-Pump-2).* 2019. Available from: https://clinicaltrials.gov/ct2/show/NCT03830281?term=LY900014&draw=1&rank=8 [Accessed 05 February 2019].

2 Eli Lilly. *Medicines in development. Ultra-Rapid Lispro.* 2019. Available from: https://www.lilly.com/discovery/pipeline [Accessed 01 February 2019].

3 Kazda CM LJ LR, Hardy T, Reddy S, Chua SPC, et al. *Ultra rapid lispro (URLi) shows faster insulin absorption vs lispro during insulin pump (CSII) use in patients with type 1 diabetes.* 2018. Available from: https://www.easd.org/virtualmeeting/home.html#!resources/ultra-rapid-lispro-urli-shows-faster-insulin-absorption-vs-lispro-during-insulin-pump-csii-use-in-patients-with-type-1-diabetes [Accessed 04 February 2019].

4 European Medicines Agency. *Humalog.* 2015. Available from: https://www.ema.europa.eu/en/medicines/human/EPAR/humalog [Accessed 12 February 2019].

5 ClinicalTrials.gov. *A study of LY900014 and insulin lispro with an external continuous subcutaneous insulin infusion system in adult participants with type 1 diabetes (PRONTO-Pump).* 2018. Available from: https://clinicaltrials.gov/ct2/show/study/NCT03433677 [Accessed 01 February 2019].

6 EU Clinical Trials Register. *Clinical trials.* 2017. Available from: https://www.clinicaltrialsregister.eu/ctr-search/trial/2017-002374-39/ES [Accessed 12 February 2019].

7 Kaan AH, Amanda R, Hal J, Nicole S, K. GS. Possible Ways to Improve Postprandial Glucose Control in Type 1 Diabetes. *Diabetes Technology & Therapeutics*. 2018;20(S2):S2-24-S2-32. Available from: https://www.liebertpub.com/doi/abs/10.1089/dia.2018.0114 10.1089/dia.2018.0114.

8 PR Newswire. *Results from two phase 3 studies show lilly's ultra rapid lispro (URLi) met primary efficacy endpoint in people with type 1 and type 2 diabetes.* 2018. Available from: https://www.prnewswire.com/news-releases/results-from-two-phase-3-studies-show-lillys-

ultra-rapid-lispro-urli-met-primary-efficacy-endpoint-in-people-with-type-1-and-type-2-diabetes-300722380.html [Accessed 01 February 2019].

9 ClinicalTrials.gov. *A study comparing LY900014 to insulin lispro (humalog) in children and adolescents with type 1 diabetes (PRONTO-Peds).* 2019. Available from: https://clinicaltrials.gov/ct2/show/NCT03740919 [Accessed 12 February 2019].

10 ClinicalTrials.gov. *A study of LY900014 compared to insulin lispro in participants with type 2 diabetes (PRONTO-T2D).* 2019. Available from: https://clinicaltrials.gov/ct2/show/NCT03214380 [Accessed 12 February 2019].

11 National Health Service. *Diabetes.* 2019. Available from: https://www.nhs.uk/conditions/diabetes/ [Accessed 04 February 2019].

12 NHS inform. *Type 1 diabetes.* 2019. Available from: https://www.nhsinform.scot/illnesses-and-conditions/diabetes/type-1-diabetes [Accessed 04 February 2019].

13 British National Formulary. *Type 1 diabetes.* 2019. Available from: https://bnf.nice.org.uk/treatment-summary/type-1-diabetes.html [Accessed 04 February 2019].

14 Diabetes UK. *Complications of diabetes.* 2019. Available from: https://www.diabetes.org.uk/guide-to-diabetes/complications [Accessed 05 February 2019].

15 Public Health England. *3.8 million people in England now have diabetes.* 2016. Available from: https://www.gov.uk/government/news/38-million-people-in-england-now-have-diabetes [Accessed 12 February 2019].

16 Hex N, Bartlett C, Wright D, Taylor M, Varley D. Estimating the current and future costs of Type 1 and Type 2 diabetes in the UK, including direct health costs and indirect societal and productivity costs. *Diabetic Medicine*. 2012;29(7):855-62. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1464-5491.2012.03698.x doi:10.1111/j.1464-5491.2012.03698.x.

17 NHS Digital. *Hospital Admitted Patient Care Activity, 2017-18.* 2017. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2017-18 [Accessed 17 December 2018].

18 Baxter M, Hudson R, Mahon J, Bartlett C, Samyshkin Y, Alexiou D, et al. Estimating the impact of better management of glycaemic control in adults with Type 1 and Type 2 diabetes on the number of clinical complications and the associated financial benefit. *Diabetic Medicine*. 2016;33(11):1575-81. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.13062 doi:10.1111/dme.13062.

19 National Institute of Health and Care Excellence. *Managing type 1 diabetes in adults.* 2016. Available from: https://pathways.nice.org.uk/pathways/type-1-diabetes-in-adults/managing-type-1-diabetes-in-adults#content=view-index&path=view%3A/pathways/type-1-diabetes-in-adults/managing-type-1-diabetes-in-adults.xml [Accessed 05 February 2019].

20 National institute of Health and Care Excellence. *Type 1 diabetes in adults: diagnosis and management.* 2016. Available from: https://www.nice.org.uk/guidance/ng17/chapter/Introduction [Accessed 04 February 2019].

21 ClinicalTrials.gov. *A study of LY900014 in a medtronic pump.* 2019. Available from: https://clinicaltrials.gov/ct2/show/NCT03760640 [Accessed 12 February 2019].

22 Amiel SA, Pursey N, Higgins B, Dawoud D. Diagnosis and management of type 1 diabetes in adults: summary of updated NICE guidance. *BMJ : British Medical Journal*. 2015;351:h4188. Available from: https://www.bmj.com/content/bmj/351/bmj.h4188.full.pdf 10.1136/bmj.h4188.

23 Chiang JL, Kirkman MS, Laffel LM, Peters AL. Type 1 diabetes through the life span: a position statement of the American Diabetes Association. *Diabetes Care*. 2014 Jul;37(7):2034-54. Available from: 10.2337/dc14-1140.

NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.