Surrey Heartlands Integrated Care System (ICS) Area Prescribing Committee

Situation, Background, Assessment and Recommendations (SBAR) Briefing Paper for APC

Commissioning of Continuous Glucose Monitoring (CGM) for patients with Congenital Hyperinsulinism (CHI)

Situation

- An Individual Funding Request (IFR) was received from SASH in August 2022 for a patient born during COVID pandemic, and who was put onto CGM as part of a clinical trial. The trial funding now having stopped, SASH (at the direction of GOSH) submitted the IFR.
- This original IFR was rejected as the application itself identified a cohort of patients that CGM would be suitable for, and therefore a service development was to be written in due course. This service development was due to be written once policies for the much bigger cohorts of CGM for Type 1 and T2 diabetes patients were commissioned.
- However, the commissioning of CGM for these 2 cohorts has taken much longer than anticipated and unfortunately in the interim there has been a patient death in the CHI service which has prompted the centres (and the ICB) to reconsider the urgency of the service development.
- The CHI centres of which one is GOSH, are commissioned by NHS England (NHSE), but CGM is commissioned by ICBs. To prevent further delay the ICB is to make an interim decision with regards to commissioning CGM for a limited cohort of CHI patients whilst awaiting a NHSE national commissioning policy.
- Due to the complex nature of CHI and also associated co-morbidities, including brain damage and neurodevelopmental delay, the extreme young age of the patient as well as the need to supply enteral glucose through a gastrostomy pump, the use of CGM in these patients is considered as a patient safety risk mitigation mechanism in case of gastrostomy pump failure (especially if an alarmed CGM system is used).
- CGM in Type 1 diabetes is commissioned locally as follows:

Date	Committee Name	Narrative	Traffic Light Status
05 April 2023	Surrey Heartlands Integrated Care System Area Prescribing Committee (APC)	The Surrey Heartlands Integrated Care System Area Prescribing Committee have agreed that Continuous Glucose Monitoring (real time and intermittently scanned) is offered to adults and children and young people with TYPE I DIABETES in line with NICE guidance The following CGM devices have been recommended by APC: RED traffic light status • Freestyle Libre 3 (rtCGM) • Dexcom G7 (rtCGM) • Dexcom G6 (rtCGM) • Medtronic Guardian 3 (rtCGM) • Medtronic Guardian 4 (rtCGM) Initiation and continued supplies will be through the specialist diabetes service. BLUE traffic light status (with an information sheet) • Freestyle Libre 2 (isCGM) • Dexcom One (rtCGM) Initiation will be by the diabetes specialist service, who will provide the first 28 days of treatment (and capillary test strips if required), prior to transfer of care to primary care. Use the flow charts below to ensure the most appropriate and cost-effective CGM devices are used to meet patient need	Red

- CGM in Type 2 diabetes has yet to be commissioned.
- Pregnant patients with non-Type 1 diabetes can access funding for the Freestyle Libre 3 and Dexcom 1 CGM systems only.
- CGM systems are included in the list of high cost devices and are therefore commissioned by the ICB and managed by the trust's high cost drugs team and local trust specialists. Patients would be treated under a shared care agreement between tertiary (GOSH) and local providers, it is not expected that GPs would be prescribing for this very

specialist cohort.

Background

Congenital hyperinsulinism (from Great Ormond Street Hospital (GOSH) website)

What is congenital hyperinsulinism (CHI)?

Congenital hyperinsulinism is characterised by inappropriate and unregulated insulin secretion from the beta-cells of the pancreas. In CHI, the beta-cells release insulin inappropriately all the time and insulin secretion is not regulated by the blood glucose level (as occurs normally). The action of insulin causes hyperinsulinaemic hypoglycaemia.

High insulin levels prevent ketone bodies being made. This means that the brain is not only deprived of its most important fuel (glucose), but also ketone bodies which are used as alternative fuels.

What is a normal blood glucose level in CHI?

For the purpose of CHI, hypoglycaemia is agreed to be less than 3.5mmol/litre. In the absence of ketone bodies, infants with CHI are constantly reliant on the circulating blood glucose as the fuel for normal neurological functioning, hence the importance of maintaining the blood glucose concentration above 3.5mmol/litre.

How common is CHI and whom does it affect?

Hypoglycaemia, due to CHI, is a relatively rare but potentially serious condition occurring soon after birth.

The estimated incidence of CHI is one in every 30,000. It is much more common in communities where marriage between blood relatives occurs, possibly as frequently as one in every 2,500 children.

What are the symptoms of CHI?

As CHI is a congenital condition, a child usually starts to show symptoms within the first few days of life, although very occasionally symptoms may appear later in infancy. Symptoms of hypoglycaemia can include floppiness, shakiness, poor feeding and sleepiness, all of which are due to the low blood glucose levels.

Seizures (fits or convulsions) can also occur, again due to low blood glucose levels. If the child's blood glucose level is not corrected, it can lead to loss of consciousness and potential brain injury.

Ideally, children with suspected CHI should be transferred to a specialist centre. There are two centres in the UK that have the expertise to carry out the detailed repeated blood glucose monitoring needed to deliver treatment. Great Ormond Street Hospital (GOSH) is one centre and the other is shared between Manchester Children's Hospital and Alder Hey Hospital in Liverpool.

During the transfer to the specialist centre, children are monitored closely and regularly to keep the blood glucose level as near normal as possible. If the level drops, the nurse and/or doctor in charge will be able to give glucose, either as a drip or an injection.

Medical management

This aims to keep a child's blood glucose level stable at 3.5mmol/litre to 10mmol/litre. This can be managed by regular high carbohydrate feeds alongside medicines to reduce insulin secretion.

There are various drugs and each one will be tried in turn until the one that offers the best

result is found. Drugs used to reduce insulin secretion include: diazoxide, chlorothiazide, nifedipine (this is rarely used as it is not as effective as the other medications), glucagon and octreotide.

Children with CHI often appear to have feeding problems, particularly affecting the movement of food through the digestive system and gastro-oesophageal reflux. This can be treated with medicines, however a naso-gastric tube can be inserted to deliver continuous feeds, although this is rarely needed. If tube feeding is required long term, a gastrostomy is often needed.

Surgical treatment

This may be an option if medical management does not keep a child's blood glucose levels at an acceptable level. If a child has been diagnosed with focal CHI, usually following a PET scan, the area of the pancreas containing the defective beta cells can be removed in an operation under general anaesthetic.

Surgery for focal lesions now often offers a cure to CHI. Surgery to remove all or most of the pancreas is only an option for diffuse disease if medical management fails, but has a greater risk of long-term effects, such as diabetes or pancreatic insufficiency. However, hypoglycaemia can still happen after surgery for diffuse disease, and it can be in a milder form which is then more responsive to medical management. However, hypoglycaemia can also be severe following surgery.

What is the outlook for children with CHI?

Sometimes the management of CHI can be complicated. However, once CHI is stable, a degree of normal life can be achieved. Children and young people can have issues with brain development causing problems with memory and processing information so may need additional support in school and the workplace.

When babies and young children are fed through an NG tube, there is a chance that they will 'forget' how to feed so it is important to continue feeding small amounts by mouth in addition to NG feeds. Assessment and support from speech and language specialists can help a child to regain the desire to eat and drink by mouth.

In children who have had some or the majority of their pancreas removed, there is a chance of developing insulin dependent diabetes. This is a condition where the remaining portion of the pancreas does not make enough insulin, so insulin has to be injected several times a day.

Many children with this type of diabetes cope well with treatment and have a near normal childhood. Pancreatic insufficiency, where the pancreas cannot release the enzymes needed to break down fats, can also occur, but oral enzyme replacement therapy with meals is an option. With increased knowledge and research, the outcomes for these children are continually improving.

Self-monitoring of blood glucose (SMBG) by capillary blood glucose devices

Self-monitoring of blood glucose is an integral part of therapy in diabetes treated with insulin, it involves the measurement of blood glucose concentration by people with diabetes or their carer using self-monitoring devices such as test strips. Capillary blood glucose monitoring involves pricking the finger with a lancet device to obtain a small blood sample at certain times of the day. The drop of blood is then applied to a test strip which is inserted into a blood glucose meter for automated determination of the glucose concentration in the blood sample at the time of the test.
This method of measuring blood glucose control of diabetes is inexpensive compared to newer technologies, but is more inconvenient for the user, and provides limited information on blood glucose levels providing "fixed" data points during the day, and frequency is

dependent on the person.

Real time Continuous glucose monitoring (rtCGM)

This involves measuring interstitial fluid glucose levels throughout the day and night. A continuous glucose monitor typically comprises a disposable sensor with a tiny cannula inserted into the skin to measure glucose levels, and a transmitter connected to the sensor that sends real time readings wirelessly to a receiver or a smart device that displays results. The user can obtain real-time data as well as trends, they can then analyse data and respond to changes in real-time or can make changes to insulin delivery, dose or timing based on retrospective data or trends. Some systems allow sharing of the data with their family/carers and health care professionals. Calibration is required for some continuous glucose monitors; hence they are used in conjunction with capillary blood testing. Most monitors can send alerts for high or low glucose levels and rapid rate of change of glucose levels.

Continuous glucose monitoring provides the user access to hundreds to thousands of data points per day, together with data trends and analysis and glucose level predictions. It also allows the user access to glucose level 'alerts' for out-or-range low a high glucose level.
Until recently rtCGM devices were only available on the NHS through hospital specialist teams.

All hospital provided rtCGM are listed as excluded (from National Tariff) devices in the NHS Payment System.

Intermittently scanned glucose monitoring (isCGM)

Intermittently scanned continuous glucose monitoring, also known as flash glucose monitoring, involves wearing a sensor just under the skin (usually in the upper arm) that automatically monitors interstitial fluid glucose levels. A sensor can be used for up to 2 weeks. A reader or a mobile device with the appropriate app installed can be used to scan the sensor to obtain real-time data as well as trends by scanning the sensor with a reader device (including smart phones). The information provided gives a glucose level and information regarding the rate of change of glucose levels glucose readings. A reader or smart phone with the appropriate app installed can be used to scan the sensor to obtain real time data as well as glucose trends. The information provided gives a sensor glucose level and information regarding direction of glucose level including its rate of change. This rate is indicated as an upward, downward or oblique arrow.

The Freestyle Libre 2 does not have a predictive low or high alarm (unless it is used in conjunction with a smartphone and app), but it can be set to alert on high or low glucose settings. So if used with a smartphone it is classed as rtCGM, but if with a reader it is isCGM.

The only currently available isCGM is Freestyle Libre 2 and costs £912 per patient per year on FP10 prescription.

Role of SMBG in patients on CGM

Historically, CGM was used as an adjunct to fingerstick blood glucose testing. Now, most systems (intermittent and real-time) are more accurate and "non-adjunctive," enabling treatment decisions without finger stick blood glucose confirmation if symptoms match glucose levels. However, patients still need access to blood glucose meters and test strips during CGM start-up (the first 30-120 minutes when glucose data are not available) and for when symptoms do not match CGM-reported glucose levels, so competency in managing symptoms, and access to finger stick test strips and a blood glucose meter is still advised.

Please note: there is no NICE guidance with regards to using CGM in the identified cohort of patients (CHI or non-diabetes indications)
Assessment

Outcomes

- Prevent hypos while reducing the carbohydrates in daytime feeds and encourage oral intake.
- Assist parents to better manage hypoglycaemic episodes and avoid brain injury by prompt management and optimising treatment.
- Improve quality of life by reducing the number of hypoglycaemic episodes
- Prevent severe hypoglycaemia and its fatal impacts.
- Reduce patient and carer anxiety.
- To decide treatment changes at home and avoid hospitals' admissions.
- Inform ongoing monitoring of care.
- Improve the quality of remote video and telephone clinical consultations and enable ongoing monitoring of patients, thereby enhancing outcomes of care.

Standard care

- Standard care in the UK would include frequent capillary blood glucose sampling via heel prick blood tests pre-feed, if symptomatic or more frequently during illness. However, frequently patients with hyperinsulinism present with asymptomatic hypos which may not be detected and treated and this might harm brain development.

Advantages of CGM

1. Reduce frequency of severe hypoglycaemia episodes
2. Reduce % time spent in hypoglycaemia (derived from CGM)
3. Reduce out-patient and emergency visits.
4. Improved neurodevelopmental prognosis and growth.
5. Reduce patient and carer anxiety.
6. Reduce capillary blood glucose strip usage and associated pain/discomfort.
7. Reduction of carbohydrates in her daytime feeds in a safe manner
8. Improve quality of life
9. Attendance at nursery / normalised neurodevelopment and social skills

The standard intervention is known to be ineffective in recognition of asymptomatic hypoglycaemia - continuing with this approach will result in neurological and growth compromise.

The use of a CGM allows for trends and alert settings to be made. This is compared to the current snapshot blood glucose levels that are currently being taken by capillary blood glucose levels pre feed, pre-exercise and pre overnight feeds.

Risk of patient harm

Since 2022, there has been a death of a child within the Highly Specialist CHI service, which has prompted the 3 centres to take urgent action for CHI patients who have continuous overnight enteral glucose delivered via a gastrostomy feed pump.

The centres have taken this issue up with their commissioners (NHS England), but it is likely to take a long time before a national policy will be forthcoming, so in the meantime the ICB Is asked to make an interim decision with regards to funding CGM for this tightly defined cohort of patients, defined as follows:

"All patients with Congenital Hyperinsulinism (CHI) who are under the care of one of the 3 nationally commissioned centres (GOSH, Manchester University NHS Foundation Trust and Alder Hey Children's NHS Foundation Trust) who require overnight continuous enteral

glucose delivery via a gastrostomy feed pump, should be on a CGM which will be an additional alert in case of (gastrostomy) feed pump failure."

Financial implications/risks

- GOSH is one of 3 hospitals commissioned by NHS England for treating Hyperinsulinism via a highly specialist service.
- This means GOSH has a catchment area of approximately 1/3rd of the population of England (around 19million people).
- Out of this 19 million, GOSH have 318 patients in the service, of which 33 require CGM.
- Patient numbers for Surrey Heartlands ICB are unknown and unable to be extrapolated due to genetic variability. To date, only one patient locally is known to fulfil the proposed criteria.
- Cost analysis from recent NICE guidance costs: isCGM at £912 and rtCGM at £2000 per annum.
- Versus costs of non-use, poor control, and long-term implications for patient / patient death, vastly outweigh the cost of the CGM.

Recommendations

- All patients with Congenital Hyperinsulinism (CHI) who are under the care of one of the 3 nationally commissioned centres (GOSH, Manchester University NHS Foundation Trust and Alder Hey Children's NHS Foundation Trust) who require overnight continuous enteral glucose delivery via a gastrostomy feed pump, should be on a CGM which will be an additional alert in case of gastrostomy feed pump failure.
- SH ICB to commission CGM (clinicians should choose the product at lowest acquisition cost that will provide the appropriate level of care required clinically), for the patient cohort described above, noting that rtCGM most likely to be required, as an additional alert will be required.
- GOSH will retain clinical responsibility for the patient and will liaise with secondary care providers with regards to prescription and supply so that patient can access treatment closer to home. **It is not expected that primary care will prescribe the CGM for these patients, due to their complex clinical needs.**
- It is suggested that the APC designate a RED - Specialist ONLY traffic light status due to the following criteria (from the APC decision-making criteria to support colour classification):
    1. Specialist assessment to enable patient selection, initiation and continuation of treatment.
    2. Long term specialist monitoring of efficacy and not suitable for shared care
    5. Unlicensed or off-label treatment without acceptance of authoritative body of recommended opinion e.g., BNF, cBNF or Palliative Care Formulary
    6. Primary Care is unable to monitor therapy sufficiently to oversee treatment or adjust the dose where necessary to ensure safety.

References:

The data for prevention of hypoglycaemia in people at highest risk using CGM come from the type 1 diabetes literature and include:

1. Lutz Heinemann, Guido Freckmann, Dominic Ehrmann, Gabriele Faber-Heinemann, Stefania Guerra, Delia Waldenmaier, Norbert Hermanns Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial. Lancet; 2018

2. van Beers CA, DeVries JH, Kleijer SJ, Smits MM, Geelhoed- Duijvestijn PH, Kramer MH et al. Continuous glucose monitoring for patients with Type 1 diabetes and impaired awareness of

hypoglycaemia (IN CONTROL): a randomised, open-label, cross- over trial. Lancet Diabetes Endocrinol 2016; 4: 893–902.

3. NICE Guidelines for managing diabetes with Continuous Glucose Monitoring in children:

https://www.nice.org.uk/guidance/QS125/chapter/Quality-statement-4-Continuous-glucose-monitoring-in-type-1-diabetes

1.2.62 Offer ongoing real-time continuous glucose monitoring with alarms to children and young people with type 1 diabetes who have:

-frequent severe hypoglycaemia or

-impaired awareness of hypoglycaemia associated with adverse consequences (for example, seizures or anxiety) or

-Inability to recognise, or communicate about, symptoms of hypoglycaemia (for example, because of cognitive or neurological disabilities).

There are few published data for the use of CGM in people with hyperinsulinism listed below.

1. Arpana Rayannavar, Okan U Elci , Lauren Mitteer, Diva De León. Affiliations. Continuous Glucose Monitoring Systems: Are They Useful for Evaluating Glycemic Control in Children with Hyperinsulinism? Horm Res Paediatr. 2019;92(5):319-327.

2. Katarina Braune , Mandy Wäldchen, Klemens Raile , Sigrid Hahn , Tebbe Ubben, Susanne Römer , Daniela Hoeber , Nora Johanna Reibel , Michael Launspach , Oliver Blankenstein , Christoph Bührer . Open-Source Technology for Real-Time Continuous Glucose Monitoring in the Neonatal Intensive Care Unit: Case Study in a Neonate with Transient Congenital Hyperinsulinism. J Med Internet Res. 2020 Dec 4;22(12): e21770.

3. Chris Worth, Simon Harper, Maria Salomon-Estebanez, Elaine O'Shea, Paul Nutter, Mark J Dunne, Indraneel Banerjee.Timing of Hypoglycaemia in Patients with Hyperinsulinism (HI): Extension of the Digital Phenotype (approved to be published in The Journal of Medical Internet Research)

4. Abstract presented in European Society of Paediatric Endocrinology 2021

5. Efficacy of Use in Continuous Glucose Monitoring System in patients with Congenital Hyperinsulinism. Yesica Tropeano, Preetha Purushothaman, Clare Gilbert, Kate Morgan, Louise Doodson, Antonia Dastamani. Endocrinology Department, Great Ormond Street Hospital for Children, London, UK

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VERSION CONTROL SHEET

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v.1	*23/08/2023*	*G. Randall*	*Draft*	*Out for consultation*
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