glycosade®

The initiation of **Glycosade®** in Hepatic Glycogen Storage Disease

Vitaflo in Association With You

Supporting education in the dietary management of rare diseases

Purpose

This resource supports the use of **Glycosade®** in the dietary management of children and adults with hepatic glycogen storage disease where the use of a long acting starch is indicated. Hepatic glycogen storage disease will be referred to as glycogen storage disease (GSD) hereafter.

Intended users

This resource is:

- for use by **health care professionals** working with children and adults diagnosed with GSD.
- **not** for use by parents/caregivers of children or adults with GSD or patients themselves.
- for **general information** only and must not be used as a substitute for professional medical advice.

Target population

This resource is for use in children and adults with diagnosed/proven GSD.

Product information

Glycosade is a food for special medical purposes (FSMP).

Any product information contained in this resource, although accurate at the time of publication, is subject to change. The most current product information may be obtained by referring to product labels and www.vitafloweb.com. Please refer to these sources for information regarding ingredients and specific age indications.

Introducing and adjusting **Glycosade** is dependent on the individual patient. Practical advice is given in this resource, however, it is the responsibility of the managing health care professional to use clinical judgement to introduce and adjust **Glycosade** in the most appropriate way for individual patients and it may not always be appropriate to use this resource.

Important notice

Glycosade must only be given to patients with proven GSD under strict medical supervision.

Not for use as a sole source of nutrition.

For enteral use only.

Disclaimer

The information contained in this resource is for general information purposes only and does not constitute medical advice. The resource is not a substitute for medical care provided by a licensed and qualified health care professional and Vitaflo™ International Limited does not accept any responsibility for any loss arising from reliance on information contained in this resource. This resource does not establish or specify particular standards of medical care for the treatment of any conditions referred to in this resource. Vitaflo does not recommend or endorse any specific tests, procedures, opinions, clinicians or other information that may be included or referenced in this resource.

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Contents

1.0 An introduction to Glycosade

1.1 The use of cornstarch in hepatic GSD

GSD is a collection of disorders of inborn errors of carbohydrate metabolism. There are two main categories of GSD — hepatic GSD and muscle GSD. In hepatic GSD, there is abnormal synthesis or degradation of glycogen, and this results in severe, potentially life threatening hypoglycaemia. Hepatic GSD includes types 0, I, III, IV, VI, IX and XI.

Cornstarch therapy or uncooked cornstarch (UCCS) was a major breakthrough in the management of GSD I and has become a standard treatment since the 1980's[1, 2]. Methodology and guidelines for establishing the amount of UCCS in GSD have been documented[3]. Since its success in GSD I, UCCS has also been used in the management of GSD 0, III, VI and IX[4-6].

Although UCCS dramatically improves quality of life for patients with GSD I in particular, it has a limited duration of action. To achieve optimal metabolic control, individuals must take regular and frequent cornstarch therapy, and one study suggests UCCS therapy only prevents hypoglycaemia for a median time of 4.25 hours in children[7]. When used overnight, children and their caregivers must interrupt sleep for nightime intakes as delayed administration can cause hypoglycaemia, seizures, and neurological injury. Even as adults, individuals may still require starch therapy during the night to achieve optimal metabolic control[3, 8].

Vitaflo has carefully researched and developed **Glycosade** - a long acting starch for day and night time use in GSD. **Glycosade** provides a further breakthrough in the management of GSD because it offers a slower release of glucose than UCCS, and therefore the potential for an extended period of euglycaemia[9-13]. When used overnight, a longer period of sleep without the need for waking for additional doses of UCCS may improve quality of life and safety[10] since there is a lower risk for missed overnight therapy.

Vitaflo has developed this resource to support the introduction of **Glycosade** and help achieve good metabolic control.

1.2 What is Glycosade?

Glycosade is a heat and moisture modified corn (maize) starch. This patented process gives **Glycosade** slow-release properties, valuable to the management of GSD.

Glycosade has been developed as an alternative to UCCS for the dietary management of GSD.

1.3 Who can take Glycosade?

Glycosade is for individuals with GSD :

- who experience periods of hypoglycaemia
- who have difficulty maintaining metabolic control
- who need a longer duration of safe fasting than they get with UCCS[10, 12] with greater spacing between therapies.

A re-cap on starch

Starch is the main storage polysaccharide in plants found most abundantly in cereals, roots, tubers, legumes and immature fruits[14] and is the main carbohydrate in the human diet.

Starches vary considerably in their composition and structure. They are composed of two types of polysaccharide - amylose and amylopectin - and consist of one or both types. Variation in the ratio between amylose and amylopectin gives the starch individual properties.

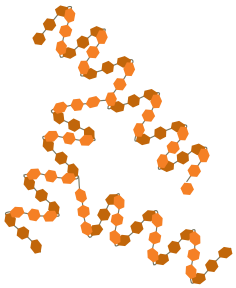
The structure of starch

Amylose and amylopectin combine to form a complex, semi-crystalline structure.

Amylose

A mainly linear chain consisting of around 50 to 500 glucose units. The chain has limited branching points and composed of α-1,4-linked glucose polymers. Amylose constitutes around 15-30% of the polysaccharides in common starch[14].

Amylopectin



A complex chain consisting of up to 100,000 glucose units. It is highly branched by small glucose chains and composed of α-1,4-linked glucose polymers branched by α-1,6-linkages. Amylopectin constitutes around 70-85% of the polysaccharides in common starch[17].

Properties of uncooked starch

In its uncooked state, starch generally shows slower digestibility than cooked starch because the complex crystalline structure reduces the accessibility of the digestive enzyme. Uncooked, amylose tends to be more resistant to digestion than amylopectin[18] meaning that it may not be fully absorbed and digested.

Some types of starch are referred to as waxy starch because they are derived from the waxy-looking endosperm tissue. These are very low amylose, high amylopectin starches. Glycosade is a high amylopectin, waxy starch treated with heat and moisture giving extended release properties, offering a longer period of euglycaemia compared to cornstarch[9-13].

1.4 How does Glycosade differ from uncooked cornstarch?

	UCCS	Glycosade
Structure 	Derived from naturally occurring maize starch. Composed of amylose and amylopectin with a high amylose content around 25%[14].	Derived from naturally occurring waxy maize starch and treated with heat and moisture to enhance slow release properties. Composed almost entirely of amylopectin >99%[10].
Process 	Used in its natural form and does not undergo any treatment after milling.	Undergoes a patented heat and moisture treatment process to slow down digestion and increase utilisation.
Influence on absorption and digestion 	Behaves as a slow-release carbohydrate releasing glucose slowly, as it is gradually degraded by digestive enzymes. May not be completely absorbed in some individuals[9, 15].	Behaves as a slow release carbohydrate releasing glucose slowly and with a more gradual decline in blood glucose levels in individuals with GSD[9, 10, 16]. Following heat and moisture treatment, is designed to be *slowly* and more *completely* digested.
Product quality and consistency 	Used in its natural form, shows variation between brand, batch, geographical origin and season.	A patented process produces a product of consistent quality allowing a more predictable outcome.

ALWAYS check the label for carbohydrate content

Due to the variable characteristics of starch, there may be a difference in carbohydrate content and behaviour when comparing UCCS and Glycosade. Additionally, there may be differences between brands of cornstarch and you should ALWAYS check labels. This variation has implications in the management of GSD and is an important consideration when initiating and transitioning between starches.

1.5 The evidence base for Glycosade so far – main findings

Glycosade is the product of many years of research and has been studied for day and night time use. This is a summary of evidence so far:

2007

A novel starch for the treatment of glycogen storage disease Bhattacharya et al 2007[9]

A study of starch load

Double-blind, cross-over design of **Glycosade** and UCCS in patients with GSD I and III

- Longer duration of euglycaemia and slower glucose decline with **Glycosade**
- Better short-term metabolic control with **Glycosade** in the majority of patients

2013

Comparison of Glycosade and uncooked cornstarch for the treatment of glycogen storage disease type I Hubert-Buron et al 2013[19]

A study of starch load

Poster presentation of a comparison between **Glycosade** and UCCS in patients with GSD Ia and Ib

- Fasting times significantly increased in 9 of 12 patients
- No significant difference in glucose or lactate concentration between **Glycosade** and UCCS

2008

Use of modified cornstarch therapy to extend fasting in GSD Ia and Ib Correia et al 2008[10]

A study of starch load

Double-blind, cross-over design of **Glycosade** and UCCS in patients with GSD Ia and Ib

- Slower rise and fall in blood glucose observed with **Glycosade** meaning more participants stayed normoglycaemic for longer
- Enhanced safety seen with **Glycosade** and potential for patients with hepatic GSD to sleep longer through the night without the need for additional starch dosing

2015

A pilot longitudinal study of the use of waxy maize heat modified starch in the treatment of adults with GSD type I – a randomized double-blind cross-over design Bhattacharya et al 2015[13]

Longitudinal randomised study

Double-blind, longitudinal, cross-over study of **Glycosade** and UCCS in patients with GSD I

- Safe introduction of **Glycosade** in to dietary plans
- Longer median duration of starch loads with **Glycosade**
- Reduced insulin release in some patients when using **Glycosade**

LONG-TERM STUDY

2015

Safety and efficacy of long-term use of extended release cornstarch therapy for glycogen storage disease types 0, III, VI and IX Ross et al 2015[11]

Safety and efficacy study

Open-label trial of **Glycosade** followed by a long-term observational phase (12 months) in patients with GSD 0, III, VI and IX

- **Glycosade** efficacious in 100% of patients
- **Glycosade** extended overnight fasting times
- All markers of metabolic control remained stable in the long-term phase

LONG-TERM STUDY

2016

Safety and efficacy of chronic extended release cornstarch therapy for glycogen storage disease types I Ross et al 2016[12]

Safety and efficacy study

Open-label trial of **Glycosade** followed by a long-term observational phase (12 months) in patients with GSD Ia and Ib

- **Glycosade** efficacious in 88% of patients with GSD Ia and 77% with GSD Ib
- **Glycosade** extended overnight fasting times in 95% of females and 78% of males

All markers of metabolic control remained stable in the long-term phase

LONG-TERM STUDY

2019

Use of waxy maize heat modified starch in the treatment of children between 2 and 5 years with glycogen storage disease type I: A retrospective study Hijazi et al 2019[20]

Safety and efficacy study

- stable glucose and lactate levels in children who transitioned to **Glycosade**
- fasting periods of 6.5-8 hours observed
- fewer reported hypoglycaemias than with a continuous nocturnal pump feed

2024

2024

Glyde study[16]

Studies prior to the Glyde study use varied starch loads, variable dosing methodology and did not always account for different carbohydrate loads and characteristics between UCCS and **Glycosade**. The Glyde study standardises this procedure and adds to the body of existing evidence by reporting on starch requirements based on carbohydrate per kilogram ideal body weight in a broader age range from 2 years old across GSD types

2.0 Initiating Glycosade

2.1 Starting Glycosade

A starch load test measures an individual's response to **Glycosade**.

For all starches, a starch load test is recommended to establish initial requirements[21, 22]. It is important to remember that the starch load test is a **starting point** only and adjustment is necessary depending on activity level and food intake of the individual, for example.

The information below refers to establishing starch requirement based on carbohydrate content per kilogram ideal body weight and considers glucose production rates where appropriate[23].

Both the requirement and response to **Glycosade** varies between individuals. Determinant factors include GSD type, age, weight, disorder phenotype, residual activity of the affected enzyme, pubertal growth spurts, general health, and metabolic condition, which will vary from one individual to another. The amount of **Glycosade** required needs to be established for every individual and requires ongoing reassessment according to clinical need.

Aims of the starch load test

GSD Ia and Ib

- determine initial **amount** of **Glycosade** required to prevent hypoglycaemia and prevent associated hyperlactataemia
- determine **duration** of euglycaemia and safe period of fasting

GSD 0, III, VI and IX

- determine initial **amount** of **Glycosade** required to prevent hypoglycaemia and associated ketosis
- determine **duration** of euglycaemia and safe period of fasting
- determine the delay in onset of ketosis

Before starting the test

It is important that the individual is able to tolerate the amount of **Glycosade** needed for the starch load test. While **Glycosade** is indicated in most countries from 2 years of age, it may not be tolerated in all young children. Intolerance is primarily manifested by development of diarrhoea or hypoglycaemia. If this occurs, tolerance may be established by introducing small amounts and increasing weekly up to the required amount[20]. Close monitoring of glucose values is recommended when starting **Glycosade** in younger children (please note age indications for **Glycosade** in your country).

When tolerance is established, ensure the individual is in optimal metabolic control and general good health.

It is **not** advisable to evaluate **Glycosade** therapy in the following situations:

- ketotic GSD when protein provision is being altered
- GSD type Ib when experiencing an acute episode of inflammatory bowel disease. Consideration should be taken when using **Glycosade** in type Ib GSD due to the associated increased risk of malabsorption which can be difficult to predict
- individuals who are unwell (e.g. fever, diarrhoea, vomiting)
- teenagers during pubertal growth spurts
- pregnancy

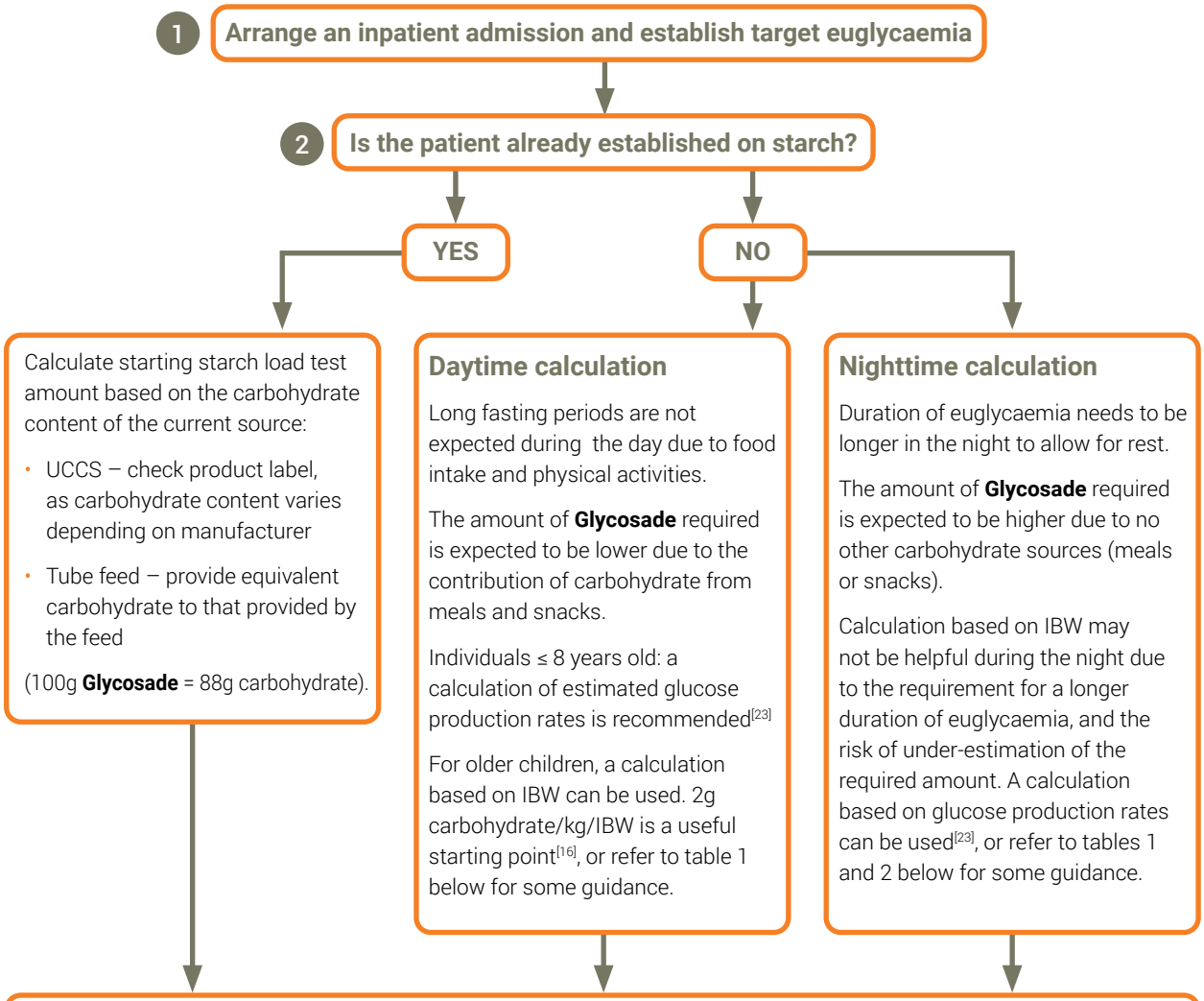
2.2 Completing the test in individuals with GSD I

To maintain euglycaemia, individuals with GSD I depend on a regular supply of exogenous carbohydrate, often above recommendations for the general population[3, 20] . The amount of **Glycosade** required by an individual is based on their glucose requirement and hence, the carbohydrate content of **Glycosade**.

The following information shows how to determine a starting amount of **Glycosade** and perform a starch load test for day and nighttime use. Prepare **Glycosade** according to instructions found on the packaging and consume straight away.

Note that a lower amount of **Glycosade** will be required when used during the day due to the contribution of carbohydrate from food.

In individuals with GSD I, it is likely that a carbohydrate source has already been established at diagnosis to maintain euglycaemia. Therefore, in most cases, the amount of **Glycosade** required for the starch load test can be calculated from the carbohydrate provided by the current treatment (UCCS, tube feeds or modular feeds). However, a guide to calculating **Glycosade** amount based on glucose production rates and ideal body weight (IBW) is provided for exceptions.



Typical intakes of **Glycosade** from studies for GSD I are shown below to help establish an appropriate starting amount. It is important to note that figures provided from these studies suggest a **starting point**, and individual metabolic needs vary, requiring clinical judgment for appropriate adjustment, based on individual biochemistry and clinical guidelines. Frequency will depend on the length of euglycaemia achieved and the individual's food intake and lifestyle.

Table 1: range of intakes in GSD I for daytime

Glyde study[16]	
Age (years)	**Daytime intake range (g)**
7 - 10	30 - 70
11 - 14	50 - 75
15 - 17	75
Adults (18+)	30 - 90

Table 2: range of intakes in GSD I for nighttime

Glyde study[16]		Ross *et al*[12*]	
Age (years)	**Nighttime intake range[16] (g)**	**Age (years)**	**Nighttime intake range[12*] (g)**
7 - 8	105	5 - 6	60 - 75
9 - 10	100 - 115	7 - 8	75 - 90
11 - 14	135 - 145	Pre-pubertal	90 - 120
15 - 17	135 - 145	Pubertal	135 - 150
Adults (18+)	90 - 165	Adults	120 - 150

*additional data provided by authors.

Before starting the test, check blood glucose level is within an acceptable range and the individual is not hypoglycaemic. It is important to note that because **Glycosade** is slow acting, it can take around 30 minutes to influence blood glucose levels. This should be considered when ensuring an acceptable starting blood glucose level. Reference ranges may differ between countries and centres.

4 Start the test

If the individual is transitioning from an overnight enteral tube feed, the individual should eat or be given a bolus feed within 15 minutes of stopping the feed in the morning[21, 22] and **Glycosade** given within 30 minutes[16]. Prepare **Glycosade** according to instructions found on the packaging and consume straight away. When performing the starch load test, do not mix **Glycosade** with food or drink as this may affect the action of the starch. Aim for a consistent level of activity throughout the test. Measure glucose and lactate at regular intervals (for example every 15-60 minutes) for 10-12 hours or until:

- biochemical or clinical hypoglycaemia occurs or is reported by the individual
- the individual wishes to discontinue

The biggest risk of hypoglycaemia generally occurs

- at the start of the test due to the risk of rebound hypoglycaemia
- when blood glucose levels start to decline

More frequent monitoring is beneficial during these times.

5 Review Results

Results from the starch load test provide a starting point to determine the optimal amount of **Glycosade** for the individual. The following gives information on interpreting results and planning next steps.

Starch load test results	Next steps
 Blood glucose levels are sustained for **longer** than usual management and lactate levels remain in acceptable parameters. Two peaks in glucose are observed in optimal dosing. A reduced amount or fewer number of administrations of **Glycosade** compared to usual management are required to maintain euglycaemia. **Glycosade** is the preferred management by the medical team and individual.	Commence **Glycosade**. The amount of **Glycosade** used in the starch load test provides a starting point for management. Consider wider influences on the individual's glycaemic control including: • Activity levels which may increase energy requirements • Intake of food which may reduce the amount of **Glycosade** required • Pubertal stage and growth spurts which may influence energy requirements Clinical judgement and lifestyle of the individual will determine how **Glycosade** is divided and distributed throughout the day.
 Blood glucose levels drop at the **same time**, or **earlier** than with usual management.	End the starch load test and continue the individual on their usual dietary management. If the medical team surmise that the amount of **Glycosade** was too low, consider a further starch load test on a subsequent occasion with a higher amount of **Glycosade**.

Interpreting lactate levels	
Low lactate levels	If lactate levels remain **low** throughout the test, this may indicate that the amount of **Glycosade** used was too high. Make small reductions to the amount and monitor closely.
High lactate levels	If lactate levels remain **high** throughout the test, this may indicate that the amount of **Glycosade** is too low. Make small increments to the amount and monitor closely.

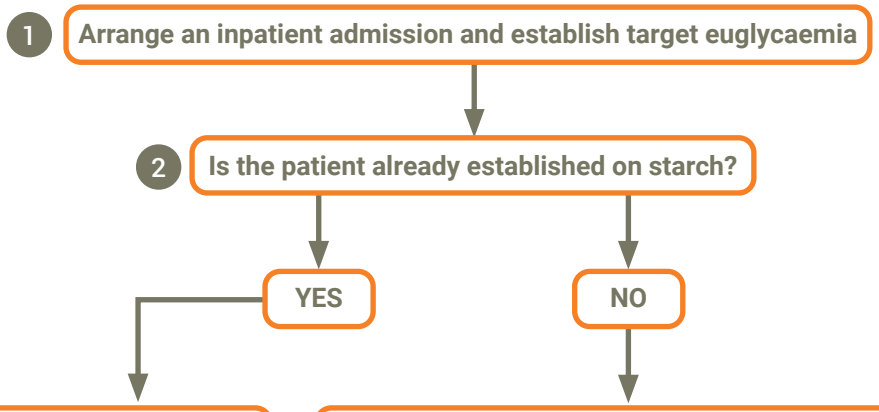
2.3 Completing the test in individuals with GSD 0, III, VI and IX

Glycosade is suitable for individuals with ketotic GSDs who experience morning hypoglycaemia and/or ketosis, requiring starch in the middle of the night. **Glycosade** is also indicated to maintain daytime euglycaemia and where additional carbohydrate may be beneficial prior to exercise or to promote linear growth. It should be noted that because the release of glucose from **Glycosade** is gradual, it may not be appropriate for all types of exercise or individuals.

The ketotic forms of GSD are caused by different enzyme deficiencies in glycogen degradation to those seen in GSD I. Although clinical presentation can be similar, there are distinguishing features requiring alternative management when it comes to starting **Glycosade**. Additional considerations are:

- **Later diagnosis**
  Ketotic GSDs are typically diagnosed later than GSD I and clinical presentation is often less severe[5]. This means that the individual may not already be established on cornstarch therapy or tube feeds at the time of commencing **Glycosade**, so there is no reference point for carbohydrate or starch requirement.
- **Lower requirement for carbohydrate from starch therapy**
  Individuals with ketotic GSDs have some ability to produce endogenous glucose by gluconeogenesis and so dietary protein contributes to the maintenance of euglycaemia. The need for a continuous exogenous supply of carbohydrate remains, although requirements may be less than in GSD I[5].
- **Indication for a loading test**
  A starch load test should be considered for every individual with ketotic GSD although in some cases, may not be deemed necessary. In this case, blood glucose and tolerance are monitored following gradual introduction of starch[4, 5]. Necessity should be a multidisciplinary decision based on the individual and local practice. A consensus regarding the most appropriate setting can also be made by the metabolic team who will consider the severity of the disorder and hypoglycaemic risk.
- **Biochemical parameters**
  Whereas in GSD I, lactate levels increase at the onset of hypoglycaemia, levels typically remain normal in ketotic GSDs, so do not serve as a biochemical marker. In ketotic GSDs, ketones are measured as an indicator of hypoglycaemia.

The following information shows how to determine a starting amount of **Glycosade** and perform a starch load test. Note that a lower amount of **Glycosade** will be required when used in the day time due to the contribution of carbohydrate from food.



Patient is established on a carbohydrate source.

Calculate starting starch load test amount based on current source of carbohydrate.

(100g **Glycosade** = 88g carbohydrate).

Patient is **NOT** established on a carbohydrate source

Calculate based on 1-1.5g carbohydrate/kg IBW[4, 5, 16, 24] depending on day or nighttime use.

(100g **Glycosade** = 88g carbohydrate)

1-1.5g carbohydrate/kg IBW is derived from the Glyde trial and other published guidelines and evidence[4, 5, 16, 24] whereby 1-1.5g/kg IBW was used as a starting point, then adjusted according to individual needs. Tables 3 and 4 show typical intakes observed in these studies[16, 11]. Variation in phenotype and severity means that the amount of **Glycosade** required is very variable amongst individuals.

Calculating the amount of **Glycosade** to perform a starch load test based on 1-1.5g carbohydrate/kg IBW provides a **starting** point. From here, requirements can be adjusted and fine-tuned, and it is important to note that clinical judgment is required for appropriate adjustment based on individual biochemistry. Frequency will depend on the length of euglycaemia achieved and the individual's food intake and lifestyle.

Table 3: Range of intakes in ketotic GSDs for daytime[16]

Glyde study[16]	
Age (years)	**Daytime intake range (g)**
2 - 4	15 - 30
5 - 6	20 - 55
7 - 8	20 - 55
9 - 10	20 - 75
11 - 14	20 - 75
15 - 17	45 - 60
Adults (18+)	60 - 80

Table 4: Range of intakes for ketotic GSDs for nighttime[11*, 16]

Glyde study[16]		Ross *et al* (2015)[11*]
Age (years)	**Nighttime intake range (g)**	**Nighttime intake range(g)**
5 - 6	-	30 - 60
7 - 8	-	
9 - 10	60 - 85	
11 - 14	60 - 90	
15 - 17	60 - 80	
Adults (18+)	60 - 80	

*additional data provided by authors.

Check starting blood glucose and ketone levels are within an acceptable range. It is important to note that because **Glycosade** is slow acting, it can take around 30 minutes to influence blood glucose levels. This should be considered when ensuring an acceptable starting blood glucose level. Ranges may differ between countries, centres and individuals.

4 Start the test

If the individual is transitioning from an overnight enteral tube feed, the individual should be fed or given a bolus within 15 minutes of stopping the feed[21, 22] and **Glycosade** given within 30 minutes[16]. Prepare **Glycosade** according to instructions on the packaging and consume immediately. When performing the starch load test, do not mix **Glycosade** with food or drink as this may affect the action of the starch. When performing the starch load test, do not mix Glycosade with food or drink as this may affect the action of the starch. Aim for a consistent level of activity throughout the test. Measure glucose and ketones at regular intervals (for example every 15-60 minutes) for 10-12 hours or until:

- biochemical or clinical hypoglycaemia occurs or is reported by the individual
- the individual wishes to discontinue
- at the start of the test due to the risk of rebound hypoglycaemia

The biggest risk of hypoglycaemia generally occurs

- at the start of the test due to the risk of rebound hypoglycaemia
- when blood glucose levels start to decline

More frequent monitoring is therefore beneficial during these times.

5 Review Results

Results from the starch load test provide a starting point to determine the optimal amount of **Glycosade** for the individual. The following information gives guidance on interpreting results and planning next steps.

Starch load test results	Next steps
 Blood glucose levels are sustained for **longer** than usual management and ketones (namely, beta-hydroxybutyrate) remain in acceptable ranges. Two peaks in glucose are observed in optimal dosing. A reduced amount or fewer number of administrations of **Glycosade** compared to usual management are required to maintain euglycaemia. **Glycosade** is the preferred management by the medical team and individual.	Commence **Glycosade**. The amount of **Glycosade** used in the starch load test provides a starting point for dietary prescription. Consider wider influences on the individual's glycaemic control including: • usual activity levels which may increase energy requirements • Intake of food which may reduce the amount of **Glycosade** required • Pubertal stage and growth spurts which may influence energy requirements Clinical judgement and lifestyle of the individual will determine how **Glycosade** is divided and distributed throughout the day. The bedtime dose should be given directly before going to sleep.
 Blood glucose levels drop at the **same time**, or **earlier** than with usual management and/or ketones are outside of acceptable range.	End the starch load test and continue the patient on their usual dietary management. If the medical team surmise that the amount of **Glycosade** was too low, consider a further starch load test on a subsequent occasion with a higher amount of **Glycosade**.

Interpreting ketone levels	
Low ketone levels (beta-hydroxybutyrate)	If ketone levels remain **low** throughout the test, this may indicate that the amount of **Glycosade** used was too high. Make small reductions to the amount and monitor closely.
High ketone levels (beta-hydroxybutyrate)	Because the release of glucose from **Glycosade** is gradual, it may be too slow to correct ketones. A starch load test should not be started if ketone levels are **high** (i.e. >0.2mmol/L). Correct glucose and ketone levels before starting the test.

3.0 Ongoing monitoring

Section 2 of this guide provides a guide to initiating **Glycosade** by suggesting a starting point for the starch load test. It is recommended that individuals taking **Glycosade** are monitored throughout the starch load test and on an ongoing basis according to local practice and procedures, or as outlined in the most recent national/international guidelines for management[3-5, 22].

Response to **Glycosade** will be different and vary according to age, growth, type of GSD and activity levels. Periodic adjustment will be required to maintain good metabolic control.

If fewer overall meals or tube-feeds are needed as a result of inclusion of **Glycosade**, the overall diet should be assessed to ensure adequacy of macro- and micronutrients and supplemented as required.

Additional monitoring will be required if illness is suspected, or during illness when adjustment of dose or change of treatment may be considered according to local practice.

4.0 References

1. Chen, Y.-T., M. Cornblath, and J.B. Sidbury, Cornstarch therapy in type I Glycogen-Storage Disease. The New England Journal of Medicine, 1984. 310(3): p. 171-175.
2. Chen, Y.-T., *et al.*, Type I glycogen storage disease: nine years of management with cornstarch. European journal of pediatrics, 1993. 152(1): p. 56-59.
3. Kishnani, P.S., *et al.*, Diagnosis and management of glycogen storage disease type I: a practice guideline of the American College of Medical Genetics and Genomics. Genetics in Medicine, 2014.
4. Kishnani, P.S., *et al.*, Diagnosis and management of glycogen storage diseases type VI and IX: a clinical practice resource of the American College of Medical Genetics and Genomics (ACMG). Genetics in Medicine, 2019: p. 1.
5. Kishnani, P.S., *et al.*, Glycogen storage disease type III diagnosis and management guidelines. Genet Med, 2010. 12(7): p. 446-63.
6. Borowitz, S.M. and H.L. Greene, Cornstarch therapy in a patient with type III glycogen storage disease. Journal of pediatric gastroenterology and nutrition, 1987. 6(4): p. 631-634.
7. Lee, P. J. *et al.* Uncooked cornstarch - efficacy in type I glycogenosis Archives of Disease Childhood 1996 74(6) p. 546-7.
8. Wolfsdorf, J.I. and J.F. Crigler Jr, Cornstarch regimens for nocturnal treatment of young adults with type I glycogen storage disease. The American Journal of Clinical Nutrition, 1997. 65: p. 1507-1511.
9. Bhattacharya, K., *et al.*, A novel starch for the treatment of glycogen storage diseases. Journal of inherited metabolic disease, 2007. 30(3): p. 350-7.
10. Correia, C.E., *et al.*, Use of modified cornstarch therapy to extend fasting in glycogen storage disease types Ia and Ib. The American Journal of Clinical Nutrition, 2008. 88: p. 1272-1276.
11. Ross, K.M., *et al.*, Safety and efficacy of long-term use of extended release cornstarch therapy for glycogen storage disease types 0, III, VI, and IX. Journal of Nutritional Therapeutics, 2015. 4(4): p. 137-142.
12. Ross, K.M., *et al.*, Safety and efficacy of chronic extended release cornstarch therapy for glycogen storage disease type I, in JIMD Reports, Volume 26. 2016, Springer. p. 85-90.
13. Bhattacharya, K., *et al.*, A pilot longitudinal study of the use of waxy maize heat modified starch in the treatment of adults with glycogen storage disease type I: a randomized double-blind cross-over study. Orphanet Journal of Rare Diseases, 2015. 10(1): p. 18.
14. Alcázar-Alay, S.C. and M.A.A. Meireles, Physicochemical properties, modifications and applications of starches from different botanical sources. Food Science and Technology, 2015. 35(2): p. 215-236.
15. Bodamera, O.A., *et al.*, Utilization of cornstarch in glycogen storage disease type Ia. European Journal of Gastroenterology & Hepatology, 2002. 14(1251-1256).
16. Glycosade v UCCS in the Dietary Management of Hepatic GSD (Glyde) - data on file 2024.
17. Durrani, C.M. and A.M. Donald, Physical characterisation of amylopectin gels. Polymer gels and networks, 1995. 3(1): p. 1-27.
18. Birt, D.F., *et al.*, Resistant starch: promise for improving human health. Advances in Nutrition, 2013. 4(6): p. 587-601.
19. Hubert-Buron, A., *et al*., Comparison of Glycosade® and uncooked cornstarch (UCCS) for the treatment of glycogen storage disease type I (GSDI). 2013.
20. Hijazi G *et al.* Use of waxy maize heat modified starch in the treatment of children between 2 and 5 years with glycogen storage disease type I: A retrospective study Molecular Genetics and Metabolism Reports 2019 21 p.1-6.
21. MacDonald, A, *et al* Disorders of Carbohydrate Metabolism Clinical Paediatric Dietetics 5th Edition Chapter 29 Wiley 2020.
22. Rake, J.P., *et al.*, Guidelines for management of glycogen storage disease type I - European Study on Glycogen Storage Disease Type I (ESGSD I). Eur J Pediatr, 2002. 161 Suppl 1: p. S112-9.
23. Bier, D.M., *et al.*, Measurement of "true" glucose production rates in infancy and childhood with 6, 6-dideuteroglucose. Diabetes, 1977. 26(11): p. 1016-1023.
24. Schreuder AB, Rossi A, Grünert SC, *et al.* Glycogen Storage Disease Type III. 2010 Mar 9 [Updated 2022 Jan 6]. In: Adam MP, Everman DB, Mirzaa GM, *et al.*, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK26372

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