JBDS-IP Joint British Diabetes Societies for inpatient care

The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus

Revised March 2022

ABCD Association of British Clinical Diabetologists

Royal College of Physicians

DISN UK GROUP

Royal College of Nursing

UKCPA CLINICAL PHARMACY ASSOCIATION

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This document is coded JBDS 01 in the series of JBDS documents:

Other JBDS documents:

The hospital management of hypoglycaemia in adults with diabetes mellitus	*JBDS 01*
The management of diabetic ketoacidosis in adults	*JBDS 02*
Management of adults with diabetes undergoing surgery and elective procedures: improving standards	*JBDS 03*
Self-management of diabetes in hospital	*JBDS 04*
Glycaemic management during the inpatient enteral feeding of stroke patients with diabetes	*JBDS 05*
The management of the hyperosmolar hyperglycaemic state (HHS) in adults with diabetes	*JBDS 06*
Admissions avoidance and diabetes: guidance for clinical commissioning groups and clinical teams	*JBDS 07*
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COncise adVice on Inpatient Diabetes (COVID:Diabetes)	*JBDS 18*

These documents are available to download from the ABCD website at https://abcd.care/joint-british-diabetes-societies-jbds-inpatient-care-group and the Diabetes UK website at www.diabetes.org.uk/joint-british-diabetes-society

These guidelines can also be accessed via the Diabetologists (ABCD) app (need ABCD membership to access the app)

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To enable the guideline to stay relevant, it is envisaged that all of the JBDS guidelines will be updated or reviewed each year. As such these are 'living' documents – designed to be updated based on recently published evidence or experience. Thus, feedback on any of the guidelines is welcomed. Please email christine.jones@nnuh.nhs.uk with any comments, suggestions or queries.

Conflict of interest statement

The authors declare no conflicts of interest

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Foreword

Hypoglycaemia continues to be one of the most feared short-term complications of diabetes mellitus amongst people with diabetes, healthcare professionals and lay carers alike. Despite advances in therapeutics and technology, for people receiving insulin or sulfonylurea therapy as treatment for their diabetes, evidence would suggest that achieving good glycaemic control while avoiding hypoglycaemia remains very difficult. Intercurrent illness and the hospital setting compounds this situation, with often disrupted access to medications, meals and snacks compared with the home environment.

Often people with diabetes are admitted to hospital with an issue unrelated to their diabetes. They can be under the care of many different medical or surgical specialties; this can result in them being treated by staff without specialist diabetes knowledge.

In response to these issues this guideline was produced by the Joint British Diabetes Societies (JBDS) for Inpatient Care to offer clear guidance for the effective management of hypoglycaemia in hospital. It appears clear that Trusts in England have welcomed this with over 90% reporting that they use it to guide hypoglycaemia management within their hospital(s).

The guideline is reviewed regularly and updated in response to new evidence, national changes and comments received. The authors would like to thank all involved for their comments and would encourage people to contact us with any further suggestions.

This is the fifth iteration of this guideline (original March 2010 with revisions September 2013, April 2018 and January 2020).

We hope that all healthcare professionals involved in the care of people with diabetes in hospital will find this a useful document. By adopting the principles and adapting where necessary, these guidelines should help ensure good quality, timely and effective treatment for people with diabetes in hospital.

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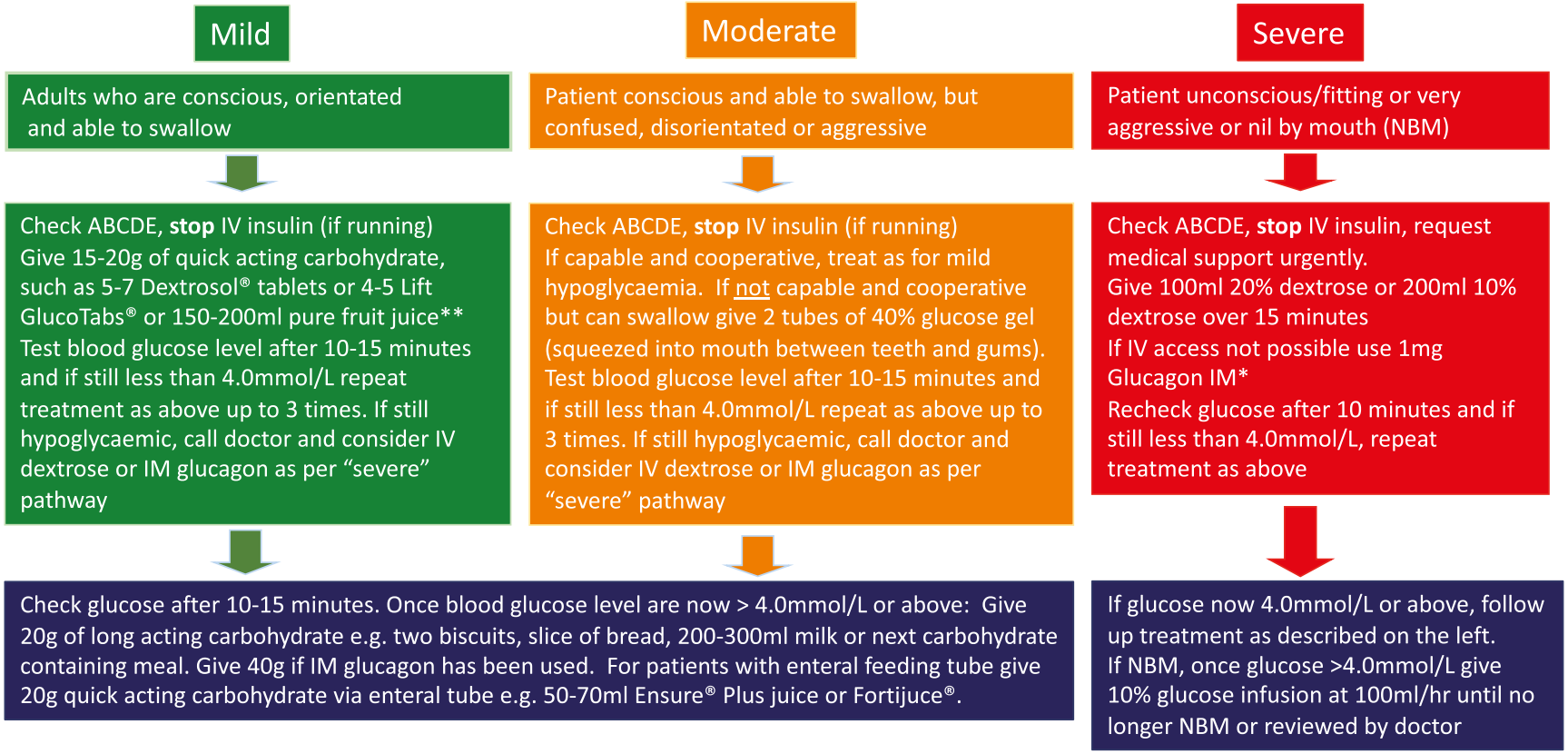
What has changed since the previous guideline?

- The major change has been to move the management section and management algorithm to the front of the document. This is to make it easier for people to access the most frequently used sections of the guideline.
- The potential of "looming" hypoglycaemia in people with diabetes in hospital is discussed when blood glucose levels are in the range 4.0-6.0mmol/L. The importance of proactive adjustment of diabetes treatment and individualised targets for glycaemic control has been emphasised for people with diabetes in hospital.
- The introduction clarifies the treatment of 16-18 year old people with diabetes.
- The term glucose has been consistently applied to glucose containing preparations suitable for intravenous administration.
- The amount of intravenous glucose administered has been specified rather than a suggested range, this is to simplify treatment in an emergency situation.
- We have used the term "people/person with diabetes in hospital (PWDiH)" rather than "patients" or "inpatients" where possible.

Algorithm for the Management of Hypoglycaemia in Adults with Diabetes in Hospital

Hypoglycaemia is a serious condition and should be treated as an emergency regardless of level of conciousness. Hypoglycaemia is defined as blood sugar glucose of <4.0mmol/L (if not <4.0mmol/L but symptomatic give a small carbohydrate snack for symptom relief) See full guideline "The Hospital Management of Hypoglycaemia in Adults with Diabetes Mellitus" at www.diabetes.org.uk/joint-british-diabetes-society



DO NOT omit subsequent insulin doses. Continue regular capillary blood glucose monitoring for 24-48 hours. Review insulin and/or oral hypoglycaemic doses. If previously on IV insulin, would generally consider restarting insulin once blood glucose >4.0 but may require review of regimen. Give hypoglycaemia education and refer to inpatient diabetes team if required.

*Glucagon may take up to 15 minutes to work and may be ineffective in treating hypoglycaemia in undernourished patients, in severe liver disease, sulfonylurea induced hypoglycaemia and in repeated hypoglycaemia.

Treatment of hypoglycaemia algorithms

All non-pregnant, adults with diabetes in hospital with a blood glucose level less than 4.0mmol/L (with or without symptoms of hypoglycaemia) should be treated as outlined in this guideline; remember "4.0 is the floor".

Promote the prescription of hypoglycaemia "rescue" treatment for all people with diabetes in hospital (PWDiH) on insulin or sulfonylurea therapy. This could involve a "PRN (pro re nata)" or "as needed" prescription of intravenous (IV) glucose and/or intramuscular (IM) glucagon. The advent of electronic prescribing allowing the use of an "order set" should make this process easier.

In PWDiH who are conscious and able to swallow, 15-20g of rapid-acting carbohydrate is the treatment of choice (see algorithm A). If the person is fasting for a procedure or operation, then consider using intravenous glucose to avoid the operation or procedure being postponed due to oral carbohydrate consumption. Subsequent treatment algorithms discuss treatment options for those unable to consume oral carbohydrate for a variety of reasons (see algorithms B, C, D & E). These five algorithms are summarised in the "traffic light" algorithm on the preceding page.

Adults who have poorer glycaemic control may start to experience symptoms of hypoglycaemia above 4.0mmol/L. There is no evidence the thresholds for cognitive dysfunction are reset upwards. Adults who are experiencing hypoglycaemia symptoms but have a blood glucose level greater than 4.0mmol/L should be given a carbohydrate containing snack (e.g. banana, a slice of bread or normal meal if due).

The risk of looming hypoglycaemia should be considered in PWDiH who have a blood glucose level of 4.0-6.0mmol/L while in hospital. For the majority of PWDiH on any insulin preparation and/or any insulin secretagogues, consider intervening at a capillary blood glucose (CBG) of <6.0mmol/L to prevent hypoglycaemia. This may require oral or intravenous carbohydrate depending on the clinical situation. An individualised approach is always needed and advice should be sought from the inpatient diabetes team if unsure.

For some PWDiH, especially those using insulin pumps and/or wearable glucose sensors, a range of 4-6mmol/L may be their normal when they are not eating. For these PWDiH it is important to have a discussion with them about the need to avoid severe hypoglycaemia, they may need to aim for higher glucose levels than they are used to. The decision as to whether to intervene at a blood glucose of <6.0 or <5.0mmol/L should ideally be a joint decision between the PWDiH and inpatient diabetes team.

Please consider how best to communicate with colleagues in primary care if there have been significant treatment changes. This would be particularly important if treatment changes were temporary and required review (e.g. withholding a sulfonylurea and metformin after hypoglycaemia during a period of acute kidney injury).

We are aware that different NHS trusts use difference intravenous glucose preparations. A powerpoint version of the algorithm will be available that can be modified to suit local circumstances and treatment availability.

A. Adults who are conscious, orientated and able to swallow

1. Quickly check the following. Don't spend too much time on this, particularly if the person is otherwise well, before moving on to step 2:
    a. Airway
    b. Breathing
    c. Circulation
    d. Disability (including Glasgow Coma Scale (GCS) and blood glucose)
    e. Exposure (including temperature)
2. If the person with diabetes in hospital (PWDiH) has an insulin infusion in situ, **stop immediately. Continue to follow the guidance below. Restart the insulin infusion once the hypo has been fully treated. Consider reviewing insulin infusion requirement and dosing**
3. Give 15-20g rapid-acting carbohydrate of the person with diabetes in hospital's PWDiH's choice where possible. Some examples are:
    a. 5-7 Dextrosol® tablets (or 4-5 Lift GlucoTabs™)
    b. 1 bottle (60ml) Lift juice shots
    c. 150-200ml pure fruit juice (e.g. orange juice), do not use if following a low potassium diet (e.g. to treat chronic kidney disease) in view of its potassium content
    d. 3-4 heaped teaspoons of sugar dissolved in water (sugar dissolved in water is not an effective treatment for PWDiH taking acarbose as it prevents the breakdown of sucrose to glucose)
4. Repeat capillary blood glucose measurement 10-15 minutes later. If it is still less than 4.0mmol/L, repeat step 1 (no more than 3 treatments in total). If it is above 4.0mmol/L then go to step 5.
5. If blood glucose remains less than 4.0mmol/L after 30-45 minutes or 3 treatment cycles, **call for medical assistance**. If agreed locally, glucagon (and IV glucose) may be given without prescription in an emergency for the purpose of saving a life or via a Patient Group Directive. Consider:
    a. 1mg of glucagon IM (only licensed for insulin induced hypoglycaemia, may be less effective when administered repeatedly, in PWDiH prescribed sulfonylurea therapy or PWDiH with a history of alcohol abuse or chronic liver disease)
    b. 100ml of 20% glucose (at 400ml/hour over 15 minutes) or 200ml of 10% glucose (at 800ml/hour over 15 minutes). Care should be taken with infusion pump settings if larger volume bags are used to ensure the whole bag is not inadvertently administered. Consider smallest possible volume in renal and/or cardiac failure
6. Repeat capillary blood glucose measurement 10 minutes later. If it is still less than 4.0mmol/L, repeat step 3.
7. Once blood glucose is above 4.0mmol/L and the PWDiH has recovered, give a long-acting carbohydrate snack (20g) of the PWDiH's choice where possible, taking into consideration any specific dietary requirements. PWDiH given glucagon require a larger portion of long-acting carbohydrate (40g) to replenish glycogen stores (double the suggested amounts below) although nausea associated with glucagon injections may be an issue. Examples include:

a. Two biscuits

b. One slice of bread/toast

c. 200-300ml glass of milk (not soya or other forms of 'alternative milk, e.g. almond or coconut)

d. Normal meal if due (must contain carbohydrate)

8. PWDiH who self-manage their insulin pumps (CSII) may not need a long-acting carbohydrate, but should take initial treatment as outlined and adjust their pump settings appropriately. Many PWDiH will have a locally devised hypoglycaemia protocol that should be checked to ensure it remains appropriate for use in the inpatient setting.

9. **DO NOT omit insulin injection if due**. The insulin injection about to be given is unlikely to be the insulin dose that was active at the time of the hypoglycaemia episode and so should not be omitted. However, consideration will have to be given as to which insulin dose was active at the time of the hypoglycaemic episode and so a review of their insulin regimen is likely to be required.

10. If the hypoglycaemia was caused by sulfonylurea or long-acting insulin therapy then be aware the risk of hypoglycaemia may persist for up to 24-36 hours following the last dose, especially if there is concurrent renal impairment.

11. Document event in PWDiH's clinical record. Ensure regular capillary blood glucose monitoring is continued for at least 24 to 48 hours. Ask the PWDiH to continue this at home if they are to be discharged. Give hypoglycaemia education or refer to local Diabetes Inpatient Team. An education leaflet is available from the Trend Diabetes website (https://trenddiabetes.online/) (log in required).

B. Adults who are conscious but confused, disorientated, unable to cooperate or aggressive but are able to swallow

1. Quickly check the following. Don't spend too much time on this before moving on to step 2:
    a. Airway
    b. Breathing
    c. Circulation
    d. Disability (including Glasgow Coma Scale (GCS) and blood glucose)
    e. Exposure (including temperature)
2. If the person with diabetes in hospital (PWDiH) has an insulin infusion in situ, **stop immediately. Continue to follow the guidance below. Restart the insulin infusion once the hypo has been fully treated. Consider reviewing insulin infusion requirement and dosing**
3. If the PWDiH is capable and cooperative, follow **section A** in its entirety.
4. If the PWDiH is not capable and/or uncooperative, but is able to swallow, give 2 tubes 40% glucose gel (e.g. Glucogel®) squeezed into the mouth between the teeth and gums or (if this is ineffective) give glucagon 1mg IM (only licensed for insulin induced hypoglycaemia, glucagon may be less effective in PWDiH prescribed sulfonylurea therapy or PWDiH with a history of alcohol abuse or chronic liver disease).
5. Repeat capillary blood glucose levels after 10-15 minutes. If it is still less than 4.0mmol/L repeat steps 1 and 3 (no more than 3 treatments in total and only give IM glucagon once).
6. If blood glucose remains less than 4.0mmol/L after 30-45 minutes or 3 treatment cycles, **call for medical assistance**. If agreed locally, IV glucose may be given without prescription in an emergency for the purpose of saving a life or via a Patient Group Directive. Give 100ml of 20% glucose at 400ml/hour or 200ml of 10% glucose at 800ml/hour over 15 minutes. Care should be taken with infusion pump settings if larger volume bags are used to ensure the whole bag is not inadvertently administered. Consider smallest possible volume in renal impairment and/or cardiac failure.
7. Repeat capillary blood glucose measurement 10 minutes later. If it is still less than 4.0mmol/L, repeat steps 3 and 4 if required.
8. Once blood glucose is above 4.0mmol/L and the PWDiH has recovered, give a long-acting carbohydrate snack (20g) of the PWDiH's choice where possible, taking into consideration any specific dietary requirements. PWDiH given glucagon require a larger portion of long-acting carbohydrate (40g) to replenish glycogen stores (double the suggested amounts below) although nausea associated with glucagon injections may be an issue. Examples include:
    a. Two biscuits
    b. One slice of bread/toast
    c. 200-300ml glass of milk (not soya or other forms of 'alternative' milk, e.g. almond or coconut)
    d. Normal meal if due (must contain carbohydrate)
9. PWDiH who self-manage their insulin pumps (CSII) may not need a long-acting carbohydrate, but should take initial treatment as outlined and adjust their pump settings appropriately. Many PWDiH will have a locally devised hypoglycaemia protocol that should be checked to ensure it remains appropriate for use in the inpatient setting.

10. **DO NOT omit insulin injection if due**. The insulin injection about to be given is unlikely to be the insulin dose that was active at the time of the hypoglycaemia episode and so should not be omitted. However, consideration will have to be given as to which insulin dose was active at the time of the hypoglycaemic episode and so a review of their insulin regimen is likely to be required.
11. If the hypoglycaemia was caused by sulfonylurea or long-acting insulin therapy then be aware the risk of hypoglycaemia may persist for up to 24-36 hours following the last dose, especially if there is concurrent renal impairment.
12. Document event in PWDiH's clinical record. Ensure regular capillary blood glucose monitoring is continued for at least 24 to 48 hours. Ask the PWDiH to continue this at home if they are to be discharged. Give hypoglycaemia education or refer to local Diabetes Inpatient Team. An education leaflet is available from the Trend Diabetes website (https://trenddiabetes.online/) (log in required).

C. Adults who are unconscious and/or having seizures and/or are very aggressive

1. **Check:**
    a. **Airway (and give oxygen)**
    b. **Breathing**
    c. **Circulation**
    d. **Disability (including Glasgow Coma Scale (GCS) and blood glucose)**
    e. **Exposure (including temperature)**
2. If the person with diabetes in hospital (PWDiH) has an insulin infusion in situ, **stop immediately. Continue to follow the guidance below. Restart the insulin infusion once the hypo has been fully treated. Consider reviewing insulin infusion requirement and dosing**
3. **Request immediate assistance from medical staff**
4. If agreed locally, IV glucose or IM glucagon may be given without prescription in an emergency for the purpose of saving a life or via a Patient Group Directive.
5. If **IV access is available** give 100ml of 20% glucose at 400ml/hour or 200ml of 10% glucose at 800ml/hour over 15 minutes. If an infusion pump is available then use this, but if not available the infusion should not be delayed. Care should be taken with infusion pump settings if larger volume bags are used to ensure the whole bag is not inadvertently administered. The smallest possible volume should be administered in renal and/or cardiac failure.
6. If **no IV access is available** then give 1mg Glucagon IM. Glucagon is only licensed for insulin induced hypoglycaemia and may be less effective in PWDiH prescribed sulfonylurea therapy (may take up to 15 minutes to take effect). Glucagon mobilises glycogen from the liver and will be less effective in those who are chronically malnourished (including those who have had a prolonged period of starvation), abuse alcohol or have chronic liver disease. In this situation IV glucose is the preferred option. If no IV access is available initially, continue trying to achieve IV access as IM glucagon is less likely to be successful if required for a second time.
7. Repeat capillary blood glucose measurement 10 minutes later. If it is still less than 4.0mmol/L, repeat step 5 (or 6 if IV access remains unavailable).
8. Once blood glucose is above 4.0mmol/L and the PWDiH has recovered, give a long-acting carbohydrate snack (20g) of the PWDiH's choice where possible, taking into consideration any specific dietary requirements. PWDiH given glucagon require a larger portion of long-acting carbohydrate (40g) to replenish glycogen stores (double the suggested amounts below) although nausea associated with glucagon injections may be an issue. Examples include:
    a. Two biscuits
    b. One slice of bread/toast
    c. 200-300ml glass of milk (not soya or other forms of 'alternative' milk, e.g. almond or coconut)
    d. Normal meal if due (must contain carbohydrate)
9. If PWDiH remains nil by mouth see algorithm D.

10. PWDiH who self-manage their insulin pumps (CSII) may not need a long-acting carbohydrate, but should take initial treatment as outlined and adjust their pump settings appropriately. Many PWDiH will have a locally devised hypoglycaemia protocol that should be checked to ensure it remains appropriate for use in the inpatient setting.
11. **DO NOT omit insulin injection if due**. The insulin injection about to be given is unlikely to be the insulin dose that was active at the time of the hypoglycaemia episode and so should not be omitted. However, consideration will have to be given as to which insulin dose was active at the time of the hypoglycaemic episode and so a review of their insulin regimen is likely to be required.
12. If the PWDiH was on IV insulin, continue to check blood glucose every 15 minutes until above 4.0mmol/L, then re-start IV insulin after review of dose regimen to try and prevent hypoglycaemia recurrence. Consider concurrent IV 10% glucose infusion at 100ml/hr and/or stepping down the insulin increments on the variable scale if appropriate (check local Trust guidance)
13. If the hypoglycaemia was caused by sulfonylurea or long-acting insulin therapy then be aware the risk of hypoglycaemia may persist for up to 24-36 hours following the last dose, especially if there is concurrent renal impairment.
14. Document event in PWDiH's clinical record. Ensure regular capillary blood glucose monitoring is continued for at least 24 to 48 hours. Ask the PWDiH to continue this at home if they are to be discharged. Give hypoglycaemia education or refer to local Diabetes Inpatient Team. An education leaflet is available from the Trend Diabetes website (https://trenddiabetes.online/) (log in required).

D. Adults who are 'nil by mouth'

1. Quickly check the following. Don't spend too much time on this before moving on to step 2:
    a. Airway
    b. Breathing
    c. Circulation
    d. Disability (including Glasgow Coma Scale (GCS) and blood glucose)
    e. Exposure (including temperature)
2. If the person with diabetes in hospital (PWDiH) has an insulin infusion in situ, **stop immediately. Continue to follow the guidance below. Restart the insulin infusion once the hypo has been fully treated. Consider reviewing insulin infusion requirement and dosing**
3. If the PWDiH has a variable rate intravenous insulin infusion, adjust as per prescribed regimen, and seek medical advice. Most variable rate intravenous insulin infusions should be restarted once blood glucose is above 4.0mmol/L although an infusion rate adjustment may be indicated.
4. Treat with intravenous glucose (algorithm C, section 5).
5. Once blood glucose is greater than 4.0mmol/L and the PWDiH has recovered consider intravenous infusion of 10% glucose at a rate of 100ml/hr until PWDiH is no longer 'Nil by Mouth' or has been reviewed by the medical team.
6. If the hypoglycaemia was caused by sulfonylurea or long-acting insulin therapy then be aware the risk of hypoglycaemia may persist for up to 24-36 hours following the last dose, especially if there is concurrent renal impairment.
7. Document event in PWDiH's clinical record. Ensure regular capillary blood glucose monitoring is continued for at least 24 to 48 hours. Ask the PWDiH to continue this at home if they are to be discharged. Give hypoglycaemia education or refer to local Diabetes Inpatient Team. An education leaflet is available from the Trend Diabetes website (https://trenddiabetes.online/) (log in required).

E. Adults requiring enteral/parenteral feeding

After successful initial treatment, all people with diabetes in hospital (PWDiH) requiring total parenteral nutrition (TPN) and experiencing hypoglycaemia should be referred to a dietitian/ nutrition team and/or inpatient diabetes team.

Risk factors for hypoglycaemia

- Blocked/displaced feeding tube
- Change in feed regimen
- Enteral feed discontinued
- TPN or IV glucose discontinued
- Diabetes medication administered at an inappropriate time to feed
- Changes in medication that cause hyperglycaemia e.g. steroid therapy reduced/stopped
- Feed intolerance
- Vomiting
- Deterioration in renal function
- Severe hepatic dysfunction

Treatment – To be administered via feed tube:

Do not administer these treatments via a TPN line. *In PWDiH receiving TPN, treatment should be administered orally or intravenously as appropriate.*

1. Quickly check the following. Don't spend too much time on this before moving on to step 2:
    i) Airway
    ii) Breathing
    iii) Circulation
    iv) Disability (including Glasgow Coma Scale (GCS) and blood glucose)
    v) Exposure (including temperature)
2. If the person with diabetes in hospital (PWDiH) has an insulin infusion in situ, **stop immediately. Continue to follow the guidance below. Restart the insulin infusion once the hypo has been fully treated. Consider reviewing insulin infusion requirement and dosing**
3. Give 15-20g rapid-acting carbohydrate of the PWDiH's choice where possible. All treatments should be followed by a 40-50ml water flush of the feeding tube to prevent tube blockage (1). Some examples are:
    - 2 tubes 40% glucose gel (e.g. Glucogel®) - not for use with fine bore NGT
    - 1 bottle (60ml) Lift juice shots
    - 150-200ml orange juice
    - 50-70ml Fortijuce® (NOT Fortisip®) to give 15-20g carbohydrate
    - Re-start feed to rapidly deliver 15 – 20g carbohydrate

4. Repeat capillary blood glucose measurement 10 to 15 minutes later. If it is still less than 4.0mmol/L, repeat step 3 (no more than 3 treatments in total).
5. If blood glucose remains less than 4.0mmol/L after 30-45 minutes (or 3 treatment cycles) give 100ml of 20% glucose at 400ml/hour or 200ml of 10% glucose at 800ml/hour over 15 minutes. If an infusion pump is available then use this, but if not available the infusion should not be delayed. Care should be taken with infusion pump settings if larger volume bags are used to ensure the whole bag is not inadvertently administered. The smallest possible volume should be administered in renal and/or cardiac failure.
6. Once blood glucose is above 4.0mmol/L and the PWDiH has recovered:
    - Restart feed
    - If bolus feeding, give additional bolus feed (read nutritional information and calculate amount required to give 20g of carbohydrate)
    - 10% IV glucose at 100ml/hr. Volume should be determined by clinical circumstances (refer to Appendix 5 for administration details)
7. **DO NOT omit insulin injection if due**. The insulin injection about to be given is unlikely to be the insulin dose that was active at the time of the hypoglycaemia episode and so should not be omitted. However, consideration will have to be given as to which insulin dose was active at the time of the hypoglycaemic episode and so a review of their insulin regimen is likely to be required.
8. If the hypoglycaemia was caused by sulfonylurea or long-acting insulin therapy then be aware the risk of hypoglycaemia may persist for up to 24-36 hours following the last dose, especially if there is concurrent renal impairment.
9. Document event in PWDiH's clinical record. Ensure regular capillary blood glucose monitoring is continued for at least 24 to 48 hours. Ask the PWDiH to continue this at home if they are to be discharged. Ensure PWDiH has been referred to a dietitian or inpatient diabetes team for individualised hypoglycaemia treatment advice. An education leaflet is available from the Trend Diabetes website (https://trenddiabetes.online/) (log in required).

When hypoglycaemia has been successfully treated *(after following the initial steps outlined in algorithms A-E)*

- Consider completing an incident form (e.g. DATIX) if appropriate.
- If "hypo boxes" have been used then restock as appropriate.
- Identify the risk factors for hypoglycaemia (see Table 2).
- Take measures to avoid hypoglycaemia in the future. The Inpatient Diabetes Team can be contacted to discuss this.
- Unless the cause is easily identifiable and both the nursing staff and PWDiH are confident steps can be taken to avoid future events, a medical or Diabetes Inpatient Specialist Nurse (DISN) review should be considered. If the hypoglycaemia event was severe or recurrent, or if the PWDiH voices concerns then a review is indicated.
- Please **DO NOT** omit the next insulin injection or start variable rate intravenous insulin infusion to 'stabilise' blood glucose. If unsure of subsequent diabetes treatment, discuss with the inpatient diabetes team (e.g. it may be safe to omit a meal time bolus dose of rapid-acting insulin if the PWDiH has declined food and taken their usual basal insulin).
- Medical team (or DISN if referred) to consider reducing the dose of insulin or sulfonylurea that would have been active at the time of the hypoglycaemic event. This is to prevent further hypoglycaemia episodes occurring.
- Please **DO NOT** treat isolated spikes of hyperglycaemia with 'stat' doses of rapid-acting insulin. Instead maintain regular capillary blood glucose monitoring and adjust normal insulin or sulfonylurea doses only if a particular pattern emerges.
- If the PWDiH's diabetes treatment has changed significantly on discharge, or enhanced monitoring has been recommended, please communicate this to their primary care team in a timely manner.

Supporting Evidence

This guideline is for the management of hypoglycaemia in non-pregnant adults (aged 16 years or older) with diabetes mellitus within the hospital setting. The issue of hypoglycaemia occurring during pregnancy is beyond the scope of these guidelines. Where young people aged 16-18 years are managed by adult teams because of local arrangements, it is considered appropriate for them to be managed using local adult guidelines, the teams are familiar with rather than using potentially unfamiliar paediatric guidelines. Where individuals aged 16-18 are managed by paediatric teams, the paediatric guidelines should be followed (2,3).

This guideline is aimed at all healthcare professionals involved in the management of people with diabetes in hospital. Since the introduction of the original guideline in 2010, use of 50% intravenous (IV) glucose for the treatment of hypoglycaemia has reduced substantially. Case reports have reported extravasation injuries with the use of hyperosmolar solutions such as 50% glucose (4,5). Furthermore using 10% glucose appears to reduce the incidence of post-treatment hyperglycaemia, even when the amount of carbohydrate administered is the same (6). For these reasons 10% or 20% glucose solutions are preferred. The authors recommend the IV glucose preparation chosen is prescribed on an 'as required' (PRN) basis for all people with diabetes in hospital (PWDiH).

If agreed locally, IM glucagon (and/or IV glucose) may be given without prescription in an emergency for the purpose of saving a life or via a Patient Group Directive (7). While intramuscular (IM) glucagon is only licensed for the treatment of hypoglycaemia in people treated with insulin therapy; it is acknowledged that it is often used to treat hypoglycaemia in people taking other medications, principally sulfonylureas.

Healthcare professionals using this guideline must work within their professional codes of conduct and within their own competencies.

This guideline is designed to enable adaptation to suit local practice where required.

Hypoglycaemia in adults with diabetes

Hypoglycaemia results from an imbalance between glucose supply, glucose utilisation and current insulin levels. Hypoglycaemia is the commonest side-effect of insulin or sulfonylurea therapy used to treat diabetes. Because of their modes of action (i.e. they prevent glucose from rising rather than lowering glucose concentrations); metformin, pioglitazone, DPP-4 inhibitors, acarbose, SLGT-2 inhibitors and GLP-1 analogues prescribed without insulin or an insulin secretagogue (sulfonylurea and repaglinide) are unlikely to result in hypoglycaemia. Hypoglycaemia presents a major barrier to satisfactory long-term glycaemic control and remains a feared complication of diabetes treatment. Hypoglycaemia must be excluded in any person with diabetes who is acutely unwell, drowsy, unconscious, unable to co-operate, presenting with aggressive behaviour or a seizure. For this reason, a capillary blood glucose measurement forms part of the systematic "ABCDE" initial approach to the management of the acutely ill adult (8).

Definition

Hypoglycaemia is a level of blood glucose below normal. Normal blood glucose levels in a person without diabetes are 3.5-7.0mmol/L. To avoid potential hypoglycaemia, Diabetes UK recommends a practical policy of "make four the floor", i.e. 4.0mmol/L is the lowest acceptable blood glucose level in people with diabetes. In clinical practice, it can be defined as "non-severe" if the episode is self-treated and "severe" if unable to self-treat and assistance by a third party is required (9). For the purposes of PWDiH, any blood glucose less than 4.0mmol/L should be treated. Blood glucose levels between 4.0-6.0mmol/L may indicate looming hypoglycaemia and require special consideration in PWDiH; see section on glycaemic targets for PWDiH for further details.

Frequency

People with type 1 diabetes mellitus (T1DM) experience around two episodes of mild hypoglycaemia per week. In unselected populations, the annual prevalence of severe hypoglycaemia has been reported consistently to be 30-40% in several large studies (10).

While severe hypoglycaemia is less common in people with insulin-treated type 2 diabetes mellitus (T2DM), people with insulin-treated T2DM are more likely to require hospital admission as part of their treatment than those with T1DM (11,12). Over one third of 2000 ambulance call outs for severe hypoglycaemia represented repeat call outs, suggesting a significant minority are having recurrent problems (13).

The risk of hypoglycaemia with sulfonylurea therapy is often underestimated and due to the duration of action of these tablets, is frequently prolonged. Older people or those with renal impairment are at particular risk. The UK Hypoglycaemia Group Study showed equivalent levels of severe hypoglycaemia in people with T2DM treated with sulfonylurea therapy compared with insulin therapy of less than two years duration (14).

Hypoglycaemia frequency during hospital admissions

Most hypoglycaemia occurs in people admitted to hospital for another reason, it is much less common for it to be the primary cause of admission. Capillary blood glucose testing on admission demonstrated hypoglycaemia in 9.5% of PWDiH although only a minority of these had hypoglycaemia mentioned in the discharge summary or given as the principal cause of admission (15). Hypoglycaemia was given as the cause of admission for 5% of admissions for people with T1DM and 1.5% of admissions for people with T2DM (16).

Eighteen percent of all hospital inpatients in England and Wales have known diabetes compared to a background population prevalence of around 6%; only 8% of these peoples' admissions were directly attributed to their diabetes (17). NaDIA (National Diabetes Inpatient Audit 2019) data shows a year on year reduction in the frequency of hypoglycaemic episodes experienced over the 7 days prior to the day of audit. However, 18.4% of PWDiH still reported one or more hypoglycaemic episodes (blood glucose <4.0mmol/L) with 7.0% reporting one or more hypoglycaemic episodes <3.0mmol/L. There has been no significant reduction in episodes of hypoglycaemia (<3.0mmol/L) in

people with T1DM (28.0% in 2010 versus 27.0% in 2019). Injectable treatment (i.e. intravenous glucose or intramuscular glucagon) was required to treat hypoglycaemia in 1.4% of PWDiH. Figure 1 shows the skewed distribution of hypoglycaemic episodes (<3.0mmol/L) experienced by PWDiH arranged by diabetes type and treatment breakdown; people receiving insulin therapy were much more likely to experience hypoglycaemia (17). Studies from other countries have reported similar figures, with 12-18% of PWDiH (type 1 or type 2) experiencing hypoglycaemia (18).

Hypoglycaemia with a glucose <3.0mmol/L recurred in in 39% and 45% of people with T2DM and T1DM respectively, in a study of over 17,000 PWDiH (19). The high risk of recurrence offers an opportunity for intervention in people experiencing hypoglycaemia while in hospital.

In the hospital setting, studies conducted in both the United States and the UK show that significant hypoglycaemia (glucose <2.9mmol/L) is most likely to occur overnight and first thing in the morning. Nocturnal hypoglycaemia (blood glucose <3.9mmol/L) was more common in PWDiH treated with sulfonylurea therapy than insulin therapy (75.3% versus 59.3% respectively). The long gap between the evening meal and breakfast has been suggested as a potential contributing factor; access to bedtime snacks could help address this problem (17,19,20).

Although intravenous (IV) insulin is often used by medical teams to manage perceived problematic glycaemic control; it does itself substantially increase the risk of inpatient hypoglycaemia of <3.0mmol/L compared with all other medication groups. For example, in PWDiH with type 2 diabetes, the usage of an IV insulin infusion for those normally on basal bolus insulin regimens increases the likelihood of inpatient hypoglycaemia from under 20% to over 30% (19). Clearly there is likely to be some confounding as people receiving IV insulin are often more unwell, but it should not be considered a "safe" option particularly when it comes to inpatient hypoglycaemia. The use of intravenous insulin infusions is discussed in other JBDS guidance (21).

Temporary substitution of insulin therapy for oral agents (particularly using DPP-IV inhibitors) in the inpatient setting has been shown to reduce rates of hypoglycaemia while maintaining glycaemic control. However, introducing new treatment options may confuse the PWDiH and may not be practical for many of the common agents such as metformin (GI side effects, caution with renal impairment and slower onset of action), SGLT-2 inhibitors (risk of euglycaemic DKA) and GLP-1 agonists (GI side effects) (22).

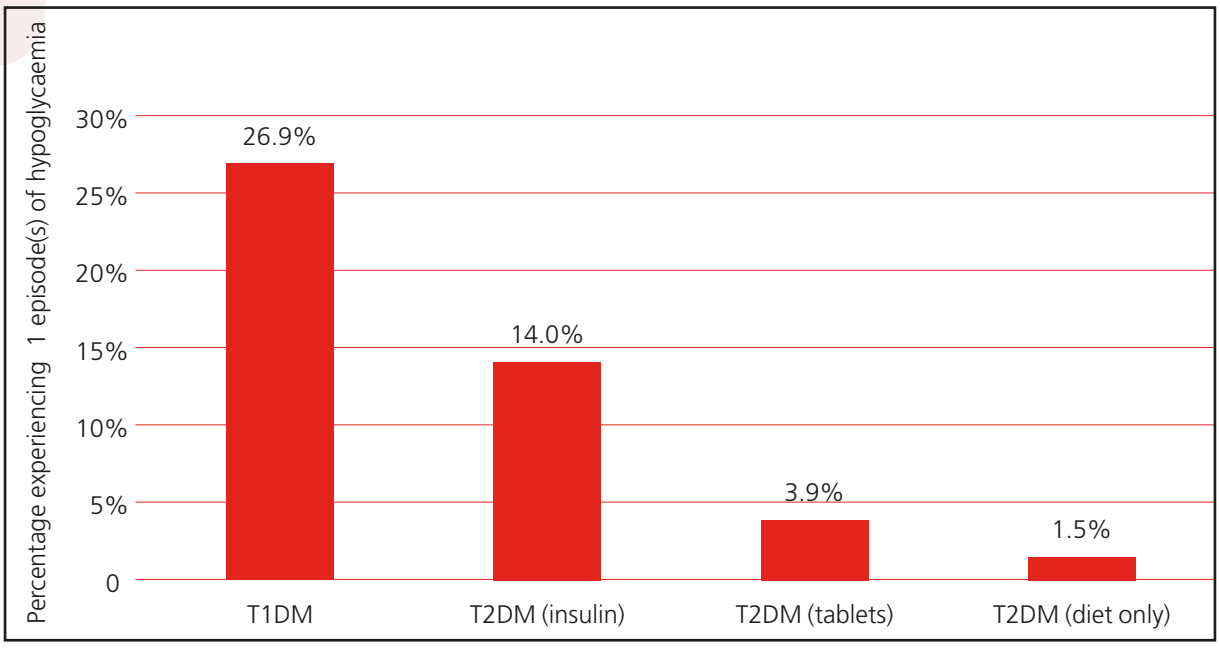


Figure 1: Percentage of PWDiH experiencing ≥1 episode(s) of hypoglycaemia (<3.0mmol/L) (17).

Glycaemic targets for people with diabetes in hospital (PWDiH)

Clearly, the glycaemic target chosen for PWDiH will impact the frequency of hypoglycaemia. There may be occasions where more relaxed glycaemic control is appropriate with target blood glucose levels increased to a higher range (23). For PWDiH the Joint British Diabetes Societies (JBDS) for Inpatient care suggest a target blood glucose of 6.0-10.0mmol/L (24). The American Diabetes Association suggest less stringent target blood glucose levels of 7.8-10.0mmol/L for PWDiH on insulin therapy (25). It is important to emphasise the glycaemic target should be adjusted according to the individual circumstances of the PWDiH; a frail, elderly person with multiple comorbidities may benefit from less stringent glycaemic control.

"Looming" hypoglycaemia

Concern over the risk of hypoglycaemia and potentially increased mortality has been highlighted by studies examining intensive glucose control for people being treated in a critical care environment. The NICE-SUGAR study of over 6000 people treated in intensive care reported an increased incidence of hypoglycaemia and 90-day mortality in people randomised to intensive glucose control (target glucose 4.5-6.0mmol/L) (26). This has led to many critical care societies and guidelines to relax the targets for glycaemic control (21).

While the treatment threshold for hypoglycaemia remains at less than 4.0mmol/L, for PWDiH, it may be appropriate to act proactively to prevent hypoglycaemia at higher blood glucose levels. This would be especially relevant for those on glucose lowering medications such as insulin secretagogues (e.g. sulfonylureas) or insulin therapy. A blood glucose value between 4.0 to 6.0mmol/L could indicate looming hypoglycaemia; particularly if repeated episodes showed a particular pattern of glucose measurements below 6.0mmol/L were occurring. This may require oral or intravenous carbohydrate depending on the clinical situation; if the PWDiH is fasting for a procedure or operation

then intravenous glucose would be preferred to reduce the risk of their procedure or operation being postponed. This should also trigger a review of diabetes treatment to see if any adjustment is necessary. Other interventions could include carbohydrate containing snacks, adding glucose to an intravenous infusion or simply rechecking blood glucose levels sooner than planned (27). An individualised approach is often helpful and advice should be sought from the inpatient diabetes team if unsure.

As with glycaemic targets, the concept of looming hypoglycaemia is a contentious one and should be personalised to suit the circumstances of the PWDiH and their individual risk of hypoglycaemia. Case examples might include:

- A middle-aged man with T2DM on metformin with an HbA1c usually around 48mmol/L would not be expected to be at high risk of hypoglycaemia and so may not need any action following blood glucose readings in the range of 4.0-6.0mmol/L.

- An 84-year-old woman with T2DM on high dose sulfonylurea therapy admitted with a urinary tract infection and acute kidney injury would be at substantially higher risk of hypoglycaemia. Dose adjustment may well then be appropriate, possibly proactively but certainly if readings in the range of 4.0-6.0mmol/L were being recorded.

- Similarly, a man with T1DM on a basal bolus insulin regimen who normally self- manages his diabetes with a usual HbA1c around 53mmol/L. He has been admitted with delirium secondary to a chest infection. His temporary cognitive impairment is likely to make self-management more difficult. He might need to relax his glycaemic control. Blood glucose levels in the range of 4.0-6.0mmol/L might trigger a reduction of insulin doses.

The learning point of these fictitious yet familiar case examples is that a "one size fits all" approach is unlikely to work and highlights the need for early involvement of the inpatient diabetes team. For some PWDiH, especially those using insulin pumps and/or wearable glucose sensors, a range of 4.0-6.0mmol/L may be within their normal glycaemic range when they are not eating. For these PWDiH it is important to have a discussion with them about the need to avoid severe hypoglycaemia, they may need to aim for higher levels than they are used to. The decision as to whether to intervene at a blood glucose of <6.0 or <5.0mmol/L should ideally be a joint decision between the PWDiH and inpatient diabetes team.

Clinical Features

The symptoms of hypoglycaemia warn an individual of its onset and vary considerably between individuals. Particular care must be taken with older PWDiH (particularly those who are frail with cognitive impairment) as the clinical features may be subtle and mistaken for other problems. Autonomic symptoms are generated by the activation of the sympatho-adrenal system and neuroglycopenic symptoms are the result of cerebral glucose deprivation. The brain is dependent on a continuous supply of circulating glucose as the substrate to fuel cerebral metabolism and to support cognitive performance. If blood glucose levels fall sufficiently, cognitive dysfunction is inevitable (28). The 11 most

Table 1: Edinburgh Hypoglycaemia Scale		
Autonomic	**Neuroglycopenic**	**General malaise**
• Sweating	• Confusion	• Headache
• Palpitations	• Drowsiness	• Nausea
• Shaking	• Odd behaviour	
• Hunger	• Speech difficulty	
	• Incoordination	

commonly reported symptoms were used to form the Edinburgh Hypoglycaemia Scale and are reproduced in the table above (29).

Impaired awareness of hypoglycaemia

Impaired awareness of hypoglycaemia (IAH) is an acquired syndrome associated with insulin treatment. IAH results in the warning symptoms of hypoglycaemia becoming diminished in intensity, altered in nature or lost altogether. This increases the vulnerability of affected individuals of progression to severe hypoglycaemia. The prevalence of IAH increases with duration of diabetes and is more common in type 1 than in type 2 diabetes (30).

Table 2: Risk Factors for Hypoglycaemia	
Medical issues	**Lifestyle issues**
• Strict glycaemic control	• Increased exercise (relative to usual)
• Previous history of severe hypoglycaemia	• Increasing age
• Long duration of type 1 diabetes	• Alcohol
• Duration of insulin therapy in type 2 diabetes	• Early pregnancy
• Lipohypertrophy at injection sites	• Breast feeding
• Impaired awareness of hypoglycaemia	• No or inadequate blood glucose monitoring
• Severe hepatic dysfunction	**Reduced Carbohydrate intake/absorption**
• Impaired renal function (including those people requiring renal replacement therapy)	• Food malabsorption e.g. gastroenteritis, coeliac disease, gastroparesis
• Sepsis	• Bariatric surgery involving bowel resection
• Inadequate treatment of previous hypoglycaemia	**Endocrine disorders**
• Terminal illness	• Addison's disease
• Cognitive dysfunction/dementia	• growth hormone deficiency
• C-peptide negativity	• hypothyroidism
	• hypopituitarism

A review article has examined the risk factors and causes of hypoglycaemia occurring in PWDiH (19). Multivariable logistic regression analysis showed that age >70 years, cognitive dysfunction and nephropathy were independently associated with hypoglycaemia for PWDiH with T2DM (34). A British study used a similar technique to show that age >75 years, insulin & sulfonylurea therapy, black and Asian ethnicity, emergency (rather than elective) admission, lower eGFR, raised inflammatory markers, hyponatraemia (<125mmol/L) and low albumin were the strongest predictors of hypoglycaemia in people with diabetes admitted to medical or surgical wards (not intensive therapy units) (35).

Be aware the following can also precipitate hypoglycaemia:

- Concurrent use of medicines with hypoglycaemic agents e.g. warfarin, quinine, salicylates, fibrates, sulphonamides (including cotrimoxazole), linezolid, monoamine oxidase inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), probenecid, somatostatin analogues, selective serotonin reuptake inhibitors. Do not stop or withhold medication, discuss with the medical team or pharmacist
- Endocrine disorders associated with diminished counterregulatory responses (e.g. Addison's disease, growth hormone deficiency, hypothyroidism, hypopituitarism)

Table 3: Potential causes of inpatient hypoglycaemia

Insulin Prescription Errors

- Inappropriate use of 'stat' or 'PRN' rapid/ short-acting insulin (i.e. repeated doses of rapid- acting insulin without leaving sufficient time between to allow for onset of action and duration of effect)
- Confusing the insulin name with the dose (e.g. Humalog Mix25 becoming Humalog 25 units) and insulins with similar sounding names (e.g. Novorapid & Novomix 30)
- Confusing the concentration with the dose (be very careful if dose is written as 100units, it could be the insulin concentration instead which is usually 100units per ml
- Only insulin syringes should be used to withdraw insulin from a vial, syringes used for intravenous administration should never be used for insulin.
- Inappropriately withdrawing insulin using a standard insulin syringe (100units/ml) from prefilled insulin pens containing higher insulin concentrations (e.g. 200units/ml or 300 units/ml)
- Misreading poorly written prescriptions – when 'U' is used for units (i.e. 4U becoming 40 units); always write "UNITS" in full
- Confusion regarding the indications for prescription of glucose and insulin infusion to control blood glucose and a glucose and insulin infusion for hyperkalaemia treatment (i.e. 50units in 50ml sodium chloride 0.9% instead of 10units of insulin with 25g glucose)
- Incorrect drug history and failure to correctly reconcile on admission

Medical issues

- Acute discontinuation of long-term corticosteroid therapy
- Recovery from acute illness/stress
- Mobilisation after illness
- Major amputation of a limb
- Incorrect type of insulin or oral hypoglycaemia therapy prescribed and administered
- Inappropriately timed insulin or oral hypoglycaemia therapy in relation to meal or enteral feed
- Change of insulin injection site
- IV insulin infusion with or without glucose infusion
- Inadequate mixing of intermediate-acting or mixed insulins
- Regular insulin doses or oral hypoglycaemia therapy being given in hospital when these are not routinely being taken at home
- Failure to monitor blood glucose adequately whilst on IV insulin infusion

Carbohydrate intake issues

- Missed or delayed meals
- Less carbohydrate than normal
- Change of the timing of the biggest meal of the day (i.e. main meal at midday rather than evening)
- Lack of access to usual between meal or before bed snacks
- Prolonged starvation time e.g. 'Nil by Mouth'
- Vomiting
- Reduced appetite
- Reduced carbohydrate intake
- Omitting glucose while on IV insulin infusion

Morbidity and mortality of hypoglycaemia affecting PWDiH

Hypoglycaemia can cause coma, hemiparesis and seizures. If the hypoglycaemia is prolonged the neurological deficits may become permanent. Acute hypoglycaemia impairs many aspects of cognitive function, particularly those involving planning and multitasking (28). The long-term effect of repeated exposure to severe hypoglycaemia on cognitive function is being investigated. A meta-analysis including 15 studies showed PWDiH remain in hospital for 4.1 days longer if they experience hypoglycaemia with almost double the risk of in-hospital mortality (36). Clearly hypoglycaemia may be associated with an increased risk of mortality rather than a causative factor.

Management of hypoglycaemia

Introduction

People experiencing hypoglycaemia require a rapid-acting carbohydrate to restore euglycaemia (usually 4.0-7.0mmol/L). The rapid-acting carbohydrate should be followed up by giving long-acting carbohydrate either as a snack or as part of a planned meal. All PWDiH experiencing hypoglycaemia should be treated without delay. Where it is safe to do so, a blood glucose measurement should be taken to confirm hypoglycaemia (especially if there is any suspicion the person may also be under the influence of alcohol). If measurement is difficult (e.g. in a PWDiH having a seizure) then treatment should not be delayed.

After acute treatment, consideration should be given to whether the hypoglycaemia is likely to be prolonged, i.e. as a result of long-acting insulin or sulfonylurea therapy; these PWDiH may require a continuous infusion of glucose to maintain blood glucose levels. Regular blood glucose monitoring enables detection of asymptomatic biochemical hypoglycaemia. For the majority of people with diabetes in hospital, a blood glucose between 4.0-6.0mmol/L should act as an alert value, especially if a repeated finding.

Preventing hypoglycaemia in people with diabetes in hospital (PWDiH)

Most PWDiH are not looked after by diabetes specialists. Various studies have shown knowledge by non-specialist healthcare professionals is suboptimal (37). While in hospital, more than half of people with diabetes reported not feeling in control of their diabetes with less trust in the diabetes knowledge of healthcare professionals who were caring for them (38). A recent review article divides the approaches to reduction in hypoglycaemia affecting PWDiH into human approaches, computerised approach and a medical device approach (33).

Human approaches to reducing hypoglycaemia in PWDiH

Allowing PWDiH to easily identify the amount of carbohydrate consumed (by providing easily identified 10g "bricks" of carbohydrate) can allow PWDiH to carbohydrate count. The amount of carbohydrate consumed was often less than predicted, delaying their meal time insulin injection until after their meal reduced hypoglycaemia in the hospital setting (39). Using a variety of measures including proactive identification of admissions involving people with diabetes, online referral system, use of web-linked glucose meters, an enhanced diabetes team and diabetes training for non-specialist medical staff, a hospital in England was able to demonstrate a reduced length of stay over and above improvements seen across all hospital patients (40). Similar multi-faceted approaches have been adopted by many diabetes teams across the UK.

Computerised approaches to reducing hypoglycaemia in PWDiH

Ruan et al used electronic data capturing the demographics, medications, laboratory results and medical procedures of PWDiH to identify those at highest risk of inpatient hypoglycaemia. One of the strongest predictors of hypoglycaemia affecting PWDiH was previous inpatient hypoglycaemia. The hope is that the best performing algorithm could utilise available data in the electronic patient record to highlight those at risk of hypoglycaemia to the medical team (41).

Continuous subcutaneous insulin infusions (CSII)

CSII or "insulin pumps" administer rapid-acting insulin on a continuous basis via a subcutaneous cannula. CSII is used by some people with type 1 diabetes and some PWDiH are taught that long-acting carbohydrate may not always be required following hypoglycaemia. If PWDiH are to continue using their CSII devices they must be well enough to self-manage their diabetes. If they are not then alternatives such as a variable rate insulin infusion or subcutaneous insulin administration should be considered. If there are concerns then advice from the diabetes inpatient specialist team should be sought (42).

Evidence for oral treatment options

Quantity of rapid-acting carbohydrate

There is limited evidence regarding the quantity of rapid-acting carbohydrate required to successfully treat an episode of hypoglycaemia. The initial quantities chosen were the result of expert consensus subsequently backed up with glucose clamp studies (43,44). Vindedzis et al compared 15g versus 20g and found that 32-63% of episodes resolved after one treatment with 15g carbohydrate compared with 55-89% of episodes with 20g carbohydrate (45). Larsen et al used continuous glucose monitoring (CGM) to monitor 125 adults with T1DM over 6 days; adequate treatment was defined as ingesting 10-20g of quick-acting carbohydrate. Thirty percent of hypoglycaemia episodes were under-treated (i.e. <10g carbohydrate consumed) and 38% were over-treated (i.e. > 20g carbohydrate consumed). Participants who were under-treated had a 57% chance of remaining hypoglycaemic at the repeat test, this compares with 30% for those adequately treated and 26% for those over-treated (46). This reinforces the suggestion that treatment of hypoglycaemia with less than 10g of rapid-acting carbohydrate is likely to be inadequate.

Anecdotally, over-treatment of hypoglycaemic episodes is often seen both in the community and hospital. Seventy-three percent of hypoglycaemic episodes were over-treated (i.e. more than 20g of rapid-acting carbohydrate consumed) in adults with T1DM; the mean amount of carbohydrate used to treat was 32g (47).

In the community, treating hypoglycaemia using a weight-adjusted carbohydrate quantity has been proposed. A small study involving 21 adults with T1DM and insulin pump therapy used 0.3g carbohydrate per kg of body weight (so a 70kg adult would receive 21g of carbohydrate) compared with standard fixed quantities (48). While this approach could be considered for individuals in the community, it would add an additional layer of complexity for PWDiH.

Type of rapid-acting carbohydrate

Chocolate is no longer recommended for the treatment of hypoglycaemia. Chocolate contains rapid-acting carbohydrate and fat; the addition of fat has been shown to slow the absorption of quick-acting carbohydrate (49,50). Orange juice (which contains fructose) remains a popular treatment for hypoglycaemia although caution should be exercised in PWDiH with chronic kidney disease (CKD) stage 4 or CKD stage 5 due to the potassium content. The results of two studies using a modified glucose clamp technique have suggested orange juice may not be the most effective treatment in adults with T1DM (43,44). Brodows et al reported almost double the amount of orange juice was required to produce a similar increment compared with glucose tablets. The total sugar content of any fruit juice varies according to the ripeness of the fruit, the season it is picked and the addition of any sugar when packaged (44). A more recent study showed fructose (in the form of a fruit bar) was less effective than sucrose in successfully treating hypoglycaemia in children with T1DM. The fibre in the bar may have slowed down the absorption of the fructose, reducing its efficacy as a treatment for hypoglycaemia (51). By contrast, a recent "real-world" study of children with type 1 diabetes attending a diabetes camp found orange juice to be as effective as other treatments (52). Pragmatically, orange juice remains a widely used treatment and treatment should not be delayed while looking for alternative options.

Time to resolution and retesting interval

Several studies have examined the time interval between treatment and re-testing to confirm resolution of hypoglycaemia. All are supportive of a minimum interval of at least 10 minutes before re-testing to ensure resolution of hypoglycaemia (52). Slama et al concluded that repeating carbohydrate intake every 5-10 minutes would not allow adequate time for the treatment to take effect thus leading to over-treatment (44). Vindedzis et al reported when hypoglycaemia was treated with 20g of carbohydrate, 55% were adequately treated after a 5 minute wait, compared with 89% after a 10 minute wait (45).

Compliance with optimum re-testing time has been examined in the inpatient setting, only 23% of capillary blood glucose measurements were repeated within 20 minutes of the initial hypoglycaemic value suggesting a delayed confirmation of recovery (53). A Scottish study examined the gap between recognition of hypoglycaemia (by capillary blood glucose monitoring) and repeat blood glucose monitoring (as a surrogate for successful and timely treatment of hypoglycaemia). The gap was largest in those with T2DM taking sulfonylurea therapy and smallest in those with T1DM; especially when the initial glucose was between 3.0-3.9 mmol/L (54). This suggests a difference in perceived importance in treatment response according to treatment and diabetes type.

Hypoglycaemia requiring third party assistance and driving

Further clarification is awaited from the DVLA as to whether episodes of hypoglycaemia requiring third party assistance occurring while in hospital have any implications for PWDiH who hold a current driving licence.

"Sugar tax"

The Soft Drinks Industry Levy (SDIL) came into effect in the U.K. from April 2018. Many soft drinks companies changed the formulation of their products to reduce sugar content. Lucozade® was commonly used to treat hypoglycaemia but is no longer recommended due to the quantities required to deliver 15-20g carbohydrate and variation in carbohydrate content between different types of Lucozade®. Fruit juices and products specifically designed for the treatment of hypoglycaemia only, will be exempt from this sugar tax and are therefore recommended in this guideline.

Evidence for parenteral treatment options

Glucagon

Intramuscular glucagon and intravenous glucose in varying concentrations are the main treatment options. A randomised trial of people attending the Emergency Department with hypoglycaemia found glucagon almost as effective as intravenous glucose with no difference in adverse events (e.g. vomiting) although recovery of blood glucose levels was slower with glucagon (55,56). Faster recovery of blood glucose levels using intravenous glucose compared with intramuscular glucagon was shown in two subsequent studies into the pre-hospital treatment of hypoglycaemia (57,58).

More recently nasal glucagon has been suggested as an alternative with ease and success of administration reported as significantly better; particularly among lay caregivers. Efficacy in terms of resolution of hypoglycaemia was comparable with IM glucagon. Nasal irritation and headaches were the most common side effects (59). At the time of writing, nasal glucagon is not yet available in the UK.

Repeated administration of glucagon is not advised (and unlicensed), only 1% of people responded to a second injection of glucagon who had not responded to the first injection (60). Glucagon will be less effective in those people with depleted glycogen reserves such as those with impaired hepatic function (i.e. people with excessive alcohol consumption or severely malnourished). In summary glucagon is an effective and useful treatment option, especially if intravenous access is not available (e.g. in community or rehabilitation hospitals). However, it can only be used once with the slower recovery and higher treatment failure rate making intravenous glucose the preferred option (59). Caution should also be exercised in PWDiH receiving anticoagulation due to the bleeding risk following an intramuscular injection.

Intravenous glucose

The increment in blood glucose after administration of 50ml of 50% glucose varies widely between individuals with hypoglycaemia. The mean increment in people with diabetes was 9.8mmol/L with a large standard deviation of 4.4mmol/L (61). Further evidence has become available comparing 10% or 20% glucose with 50% glucose. Moore and Wollard administered 5g aliquots of either 10% or 50% glucose at 1-minute intervals to people with hypoglycaemia until recovery of consciousness level had occurred. Participants were selected on the basis of confusion or impaired consciousness level sufficient to make treatment with oral carbohydrate inadvisable. Using 10% glucose resulted in lower post treatment glucose levels (6.2 versus 9.4mmol/L) (62). Ten grams of carbohydrate delivered as 10% glucose in the pre-hospital setting resulted in adequate treatment of hypoglycaemia for most people, only 18% required an additional 100ml of 10% glucose (63). Giving a similar mean dose using 10% glucose (21.6g) or 50% glucose (20.3g) resulted in no difference in the retreatment rates (very low for both groups at 2% or less) but did result in higher blood glucose levels after treatment with 50% glucose compared with 10% glucose

(8.4mmol/L compared with 6.9mmol/L) (6). The lower retreatment rates observed with 20g of 10% glucose compared with smaller amounts forms the basis of recommending 15-20g of glucose is administered intravenously.

Fifty percent glucose solution is a hypertonic solution with the potential to cause significant tissue damage from extravasation and even skin necrosis. Phlebitis increases the risk of extravasation as it causes endothelial damage making the vein more permeable or even leading to rupture (64). The potential risks have led to recommendations that 50% glucose should only be administered through central venous access; clearly this may not be a practical recommendation, particularly in the context of emergency treatment.

The risk of extravasation injury with any hypertonic solution may make 10% glucose safer than 50% glucose (65). Ten percent glucose preparations are considerably less hypertonic than the 50% preparation and therefore less destructive to the venous endothelium (66). Ten percent glucose has an osmolality of 506mOsm/L compared with 2522mOsm/L for 50% glucose (67). Fifty percent glucose also has a pH range of 3.2-6.5. These two factors are thought to increase the risk of phlebitis and therefore extravasation. For these reasons, 10% or 20% glucose solutions are preferred for intravenous administration.

It is important to emphasise that in the emergency situation IV glucose or glucagon can be given without a prescription to treat hypoglycaemia but that your local organisation might not permit this (68).

"Hypo" boxes

These boxes are often in a prominent place e.g. on resuscitation trolleys and are brightly coloured for instant recognition. They contain all the equipment required to treat hypoglycaemia from cartons of fruit juice to IV cannulas (69). Suggested contents of a typical "hypo box" can be found in Appendix 1. Introduction of "Hypo boxes" has been shown to improve the management of hypoglycaemia with an increase from 42% to 82% of episodes being correctly managed following the introduction of hypo boxes (70). There are now commercially available hypo boxes.

Conclusion

Although most people with diabetes are admitted to hospital for reasons not directly related to their diabetes, adequate management of their diabetes while in hospital, including timely recognition, treatment and prevention of hypoglycaemia, will help reduce morbidity and prevent lengthy inpatient stays.

A review of international guidelines on the treatment of hypoglycaemia in adults (including this one) notes the lack of high-quality randomised controlled trial evidence to inform treatment options (12). These guidelines are intended only to guide the assessment and management of PWDiH; each person should be individually assessed and management altered where necessary.

Many episodes of hypoglycaemia are avoidable so every preventable measure should be taken. Many people with diabetes carry their own supplies of oral carbohydrate and should be supported to self-manage when capable and appropriate; this decision should be recorded in their hospital care plan. PWDiH capable of self-care should alert nursing staff an episode of hypoglycaemia has occurred so their management plan can be altered if necessary. You may want to agree local guidance for the self-management of hypoglycaemia in conjunction with certain other medical conditions (e.g. renal impairment, congestive cardiac failure).

Easily accessible quick- and long-acting carbohydrate must be available in your clinical area (ideally located in a hypo box) and all staff should be aware of its location.

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Appendix 1

Example contents of a hypo box

- Copy of hypoglycaemia algorithm (laminated and attached to inside of lid)
- 2x 200ml carton of pure fruit juice
- 2x packets of dextrose tablets
- 1x mini pack of biscuits (source of long-acting carbohydrate)
- 3 x tubes (1 box) 40% glucose gel
- 20% dextrose IV solution (100ml vial) with infusion set
- 1x green cannula 18G
- 1x grey cannula 16G
- 1x 10ml sterile syringe
- 3 x 10ml sodium chloride 0.9% ampoules for flush
- 1x green sterile needle 21G
- Chlorhexidine spray/alcohol wipes
- 1x IV dressing (cannula cover)
- 10% dextrose for IV infusion (500ml bag) with infusion set
- Audit form
- Instructions on where to send audit form and replenish supplies
- 1x Glucagon pack – to be kept in the nearest drug fridge or labelled with reduced expiry date of 18 months if stored at room temperature

"Hypo box" contents should be checked on a daily basis to ensure it is complete and in date. It is the responsibility of the member of staff who uses any contents to replenish them after use.

Chosen preparation of IV glucose should also be included or kept nearby with appropriate giving set.

Appropriate portable sharps disposal equipment should also be kept nearby.

A hard plastic hypo box can be cleaned with a damp cloth or clinell wipe, and should be cleaned in accordance with your Trust's equipment cleaning procedures.

Appendix 2

Audit standards

	Processes
Protocol	Availability of diabetes management guidelines based on national examples of good practice including management of patients who are nil-by-mouth or enterally fed
Implementation	Availability of hospital-wide pathway agreed with diabetes speciality team Defined rolling education programme for ward staff and regular audit of key components including staff knowledge of correct treatment targets, blood glucose meter calibration, and quality assurance Percentage of wards with "hypo boxes" (or equivalent) Percentage of people with diabetes able to access treatments to manage their own hypos
Specialist review	People with diabetes who are admitted to hospital with hypoglycaemia are reviewed by a specialist diabetes physician or nurse prior to discharge
	Outcome measures
Incidence	Benchmark incidence of severe hypoglycaemia against equivalent national and regional data for admissions using widely available local and national datasets
Income	Percentage of hospital discharges delayed by in-patient hypoglycaemia episode
Identification and prevention	Cause of hypoglycaemia identified and recorded Percentage of appropriate insulin/ anti-hyperglycaemia medication dose adjustment regarding prevention of hypoglycaemia (snap shot audit of different areas of Trust on monthly basis)
Resolution	Time to recovery

With thanks to Dr Rifat Malik for producing these audit standards

Appendix 3

Hypoglycaemia Audit Form

To be completed by a Healthcare Professional after each hypoglycaemic episode

Patient Details/Sticker:

Hosp No: _____ DoB:

Surname: _____

Forename(s): _____

Male ☐ Female ☐ NHS No _____

Healthcare Professional Details:

Name: _____

Grade/Band: _____

Ward: _____

Consultant: _____

Date of Event: ____ / ____ / ____

Time of Event: ____ : ____ **hrs** (24 hr clock)

Hypoglycaemic episode type please insert letter from key below: ☐

Key:

A. Patient was conscious, orientated and able to swallow
B. Patient was conscious but confused, disorientated, aggressive or had an unsteady gait but was able to swallow
C. Patient was unconscious and/or having seizures and/or was very aggressive
D. Patient was conscious, orientated but 'Nil by Mouth'
E. Patient requiring enteral feeding

	Treatment administered	
Blood Glucose (BG) at time of event:		
BG – 10-15 minutes after treatment:		
BG – 10-15 minutes after further Treatment (if required):		

Was Hypoglycaemia Treatment Guideline followed? Yes ☐ **No*** ☐ (Please tick appropriate box)

***If No, please give details:**

Hypoglycaemia Audit Form (Cont'd)

Did the patient self-manage? **Yes** ☐ **No*** ☐ (Please tick appropriate box)

Patient recovered? **Yes** ☐ **No*** ☐ (Please tick appropriate box)

***If No, please give details:**

What steps were taken to identify the reason for the hypoglycaemia?
Please give details:

What steps were taken to prevent a recurrence?
Please give details:

Please comment on the ease and effectiveness of the Hypoglycaemia Guideline and make any suggestions on how it could be improved.

Thank you

Please return completed form to the Diabetes Inpatient Team

Appendix 4

Example of a Hypoglycaemic Episode Label

Hypoglycaemic Episode

Based on the original from Harrogate and District NHS Foundation Trust'

Ward: _____

Consultant: _____

Completed by: _____

Name: _____

Sign: _____

Date: ____ / ____ / ____

Affix Patient Label

Hypoglycaemic episode code (from key below):

Key:

A. Patient was conscious, orietated and able to swallow
B. Patient was conscious but confused, disorientated, aggressive and had an unsteady gait but was able to swallow
C. Patient was unconscious and/or having seizures and/or was very aggressive
D. Patient was conscious, orientated, but 'Nil by Mouth'
E. Patients requiring enteral feeding

	Blood Glucose (BG)(mmol/L)	Treatment Administered (see options inside hypo kit)
Starting BG Time:____:____ (24hr clock)		
BG after 10/15 mins Time:____:____		
Further BG after further 10/15 mins (if required) Time:____:____		

PLEASE STICK IN MEDICAL NOTES AFTER HYPOGLYCAEMIC EPISODE HAS BEEN TREATED.

CONSIDER REFERRAL TO DISN (DIABETES INPATIENT SPECIALIST NURSE) X5345 / BLEEP 5345 FOR:

REPEATED EPISODES; HYPO - RELATED ADMISSIONS; SEVERE HYPO; PATIENTS ON ENTERAL FEEDS

Cause of Hypoglycaemic episode	Action taken to prevent recurrence

Hypoglycaemic Episode

Based on the original from Harrogate and District NHS Foundation Trust'

Ward: _____

Consultant: _____

Completed by: _____

Name: _____

Sign: _____

Date: ____ / ____ / ____

Affix Patient Label

Hypoglycaemic episode code (from key below):

Key:

A. Patient was conscious, orietated and able to swallow
B. Patient was conscious but confused, disorientated, aggressive and had an unsteady gait but was able to swallow
C. Patient was unconscious and/or having seizures and/or was very aggressive
D. Patient was conscious, orientated, but 'Nil by Mouth'
E. Patients requiring enteral feeding

	Blood Glucose (BG)(mmol/L)	Treatment Administered (see options inside hypo kit)
Starting BG Time:____:____ (24hr clock)		
BG after 10/15 mins Time:____:____		
Further BG after further 10/15 mins (if required) Time:____:____		

PLEASE STICK IN MEDICAL NOTES AFTER HYPOGLYCAEMIC EPISODE HAS BEEN TREATED.

CONSIDER REFERRAL TO DISN (DIABETES INPATIENT SPECIALIST NURSE) X5345 / BLEEP 5345 FOR:

REPEATED EPISODES; HYPO - RELATED ADMISSIONS; SEVERE HYPO; PATIENTS ON ENTERAL FEEDS

Cause of Hypoglycaemic episode	Action taken to prevent recurrence

With kind permission from Laura Dinning, Harrogate and District NHS Foundation Trust

Appendix 5

Dextrose 10% and 20% infusions

Written by Dr Clare Crowley, Consultant Medicines Safety Pharmacist, Oxford University Hospitals NHS Foundation Trust

Sample injectable monograph
To provide healthcare staff with essential technical information in clinical area at point of use, in accordance with NPSA Patient Safety Alert 20 'Promoting safer use of injectable medicines'.

Indication: Management of adult hypoglycaemia, where dose should be prescribed by volume and concentration to minimise confusion.

Available as: 10% dextrose 250ml, 500ml or 1000ml solution for IV infusion (0.1g/ml)
20% dextrose 100ml solution for IV infusion (0.2g/ml)

Example calculations
Should not be required if prescribed via concentration and volume as advised

Usual adult dose: see guidelines

Administration:
IV injection: Not recommended

IV infusion:

20% dextrose - short term peripheral use via a secure cannula into a large vein is acceptable for the emergency management of hypoglycaemia with close monitoring of the infusion site for thrombophlebitis. Central access is preferred where available and is desirable if 20% infusion has to be continued after the initial dose.

10% dextrose - peripherally via a secure cannula into a large vein or central access (preferred where available). If peripheral infusion continues for more than 24 hours change infusion site to minimise thrombophlebitis. Care should be taken to ensure that the whole infusion is not inadvertently administered.

IM injection: Contraindicated

Subcutaneous injection: Contraindicated

Preparation and final concentration
Ready to use infusion. If only part of the infusion is needed discard any unused portion.

Rate of administration
Give 100ml of 20% dextrose* (or 200ml 10% dextrose) over 10-15 minutes. For the initial emergency management of hypoglycaemia this may be administered via a giving set alone. In all other situations, an infusion pump is required. With dextrose bags containing a larger volume than that prescribed, care should be taken to avoid inadvertent administration of the whole bag.

** The entire 100ml infusion bottle should be hung to get this dose due to the dead space in the infusion set*

For persistent hypoglycaemia despite appropriate initial treatment, an infusion of 10% dextrose at 100ml/hr may be required.

Flush
Sodium chloride 0.9%, dextrose 5% - flush well to reduce vein irritation
Remove infusion set and discard once hypoglycaemia corrected

Compatible infusions
Not applicable

Storage and handling
Do not use unless solution is clear, without visible particles and container is undamaged. Discard any unused portion. Do not reconnect any partially used bags.
Do not remove the infusion bag from overwrap until ready to use (inner bag maintains the sterility of the product).
High strength solution – packaging looks similar to other infusion fluids take care to confirm correct strength selected.

Cautions and side effects

- Hyperglycaemia, monitor blood glucose
- Avoid extravasation – may cause tissue damage
- Pain, phlebitis and vein irritation may occur during administration as the solution is hypertonic. This is a particular risk if infused too quickly. Monitor the infusion site, if any signs of phlebitis, stop infusion, remove cannula and re-site
- Hypersensitivity/infusion reactions including anaphylactic/anaphylactoid reactions have been reported with glucose infusions, thought to be from corn allergy. Caution in patients with suspected or know allergy to corn or corn products. Stop the infusion immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Treat reaction and seek urgent medical advice regarding hypoglycaemia treatment
- Fluid and electrolyte disturbances including oedema, hypokalaemia and hypomagnesaemia
- Monitor patients with or at risk of fluid overload

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Appendix 6

Membership of JBDS IP Group

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Dr Ahmed Al-Sharefi, South Tyneside and Sunderland NHS Foundation Trust

Dr Parizad Avari, Imperial College Healthcare NHS Trust

Elizabeth Camfield, Guy's and St Thomas' NHS Foundation Trust

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Dr Sue Manley, University Hospitals Birmingham NHS Foundation Trust

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Philip Newland-Jones, University Hospital Southampton NHS Foundation Trust

Dr Dipesh Patel, Royal Free London, NHS Foundation Trust

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