A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.
# TABLE OF CONTENTS

1. **INTRODUCTION** ......................................................................................... 2  
2. **GLYCAEMIC TARGETS IN TYPE 1 AND TYPE 2 DIABETES**.................... 3  
3. **INITIATING INSULIN THERAPY IN PRIMARY CARE IN TYPE 2 DIABETES** ............................................................................................................. 3  
4. **INSULIN TREATMENT OPTIONS FOR CONVERSION FROM DIET AND ORAL HYPOGLYCAEMIC AGENTS TO INSULIN** ........................................... 4  
5. **INITIATING INSULIN REGIMENS** ............................................................... 5  
6. **INSULIN DOSE ADJUSTMENT** ................................................................. 7  
   6.1. **ONCE DAILY – BASAL REGIMES** ...................................................... 7  
   6.2. **SWITCHING TO ANALOGUE BASAL INSULIN FOR PEOPLE SUFFERING RECURRENT EPISODES OF HYPOGLYCAEMIA** .............................................. 7  
   6.3. **TWICE DAILY BASAL REGIMEN – NPH OR DETEMIR** .................... 7  
   6.4. **PRE-MIXED INSULIN** .......................................................................... 8  
   6.5. **BASAL BOLUS REGIMEN** ................................................................. 9  
   6.6. **GENERAL ADVICE ON INSULIN DOSE ADJUSTMENT** .................. 9  
   6.7. **COMMONLY USED INSULIN PREPARATIONS** .................................... 10  
7. **AVAILABLE INSULIN** .................................................................................. 11-12  
8. **CARE PRE AND POST INITIATION OF INSULIN THERAPY** ................. 13  
   8.1. **EDUCATION PRIOR TO COMMENCING INSULIN** ............................... 13  
   8.2. **EDUCATION ON INITIATING THERAPY** ........................................ 13  
   8.3. **CONTINUING EDUCATION** ............................................................ 14  
   8.4. **BLOOD GLUCOSE MONITORING** .................................................... 15  
9. **HYPOGLYCAEMIA** .................................................................................... 16  
   9.1. **RECOGNISING HYPOGLYCAEMIA** .................................................. 16  
   9.2. **SYMPTOMS** .................................................................................... 16  
   9.3. **PREVENTION OF HYPOGLYCAEMIA** ........................................... 16  
   9.4. **IDENTIFYING THE CAUSE OF HYPOGLYCAEMIA** ....................... 17  
   9.5. **REDUCTION IN AWARENESS OF HYPOGLYCAEMIA** ..................... 18  
   9.6. **HYPOGLYCAEMIA UNAWARENESS AND DRIVING** ..................... 18  
   9.7. **HYPOGLYCAEMIA AND DRIVING** ............................................... 18  
   9.8. **HYPOGLYCAEMIA AND ALCOHOL** .............................................. 19  
   9.9. **NOCTURNAL HYPOGLYCAEMIA** .................................................... 19  
   9.10. **HYPOGLYCAEMIA AND EXERCISE** ............................................ 19  
10. **SICK DAY RULES** ................................................................................. 20  
11. **MISSED INJECTIONS** ............................................................................ 21  
12. **USEFUL CONTACTS** ............................................................................ 22  
REFERENCES .............................................................................................. 23  

APPENDIX 1: **INSULIN INITIATION CHECKLIST** .............................................  
APPENDIX 2: **RECOMMENDATIONS FOR GLUCAGON ADMINISTRATION (ADULTS)**
1. INTRODUCTION

These guidelines were first produced in 2003 by a group of community diabetes specialist nurses to support insulin initiation in primary care.

This latest revision was carried out by community diabetes specialist nurses working on behalf of the Type 2 Subgroup of the Diabetes Managed Clinical Network for NHS Greater Glasgow and Clyde.

Peer review and ratification takes place every 2 years or sooner as new evidence becomes available.

- These guidelines are intended for use in primary care, however they have been written in consultation with local multidisciplinary colleagues from both Primary and Secondary Care.
- These guidelines are not meant to be exhaustive, but are meant to be practical and an easy to use guide for the initiation and adjustment of insulin therapy in Type 2 diabetes.
- This can be read as a stand-alone guideline. However additional guidelines that may be developed in the future will dovetail with this document.
- These guidelines are designed to assist staff in meeting CSBS Standards for Diabetes.¹
2. GLYCAEMIC TARGETS IN TYPE 1 AND TYPE 2 DIABETES

Target HbA1c for intensive insulin therapy derived from the UKPDS and DCCT study is 53 mmol/mol or below in Type 1 and Type 2 patients. In elderly people with diabetes symptom control and freedom from hypoglycaemia are priorities. It is unclear if the HbA1c data from the UKPDS study can be transferred to the elderly.\(^3\) &\(^4\)

SIGN 154 states an HbA1c target of 53mmol/mol for people living with type 2 diabetes is reasonable to reduce the risk of microvascular disease and macrovascular disease. A target of 48mmol/mol may be appropriate at diagnosis. Targets should be individualised in order to balance benefits with harms, in particular hypoglycaemia and weight gain.\(^2\)

The aim of drug and insulin therapy is to achieve the best possible glycaemic control without frequent or severe hypoglycaemia or hyperglycaemia.

<table>
<thead>
<tr>
<th>Elderly patients should avoid hypoglycaemia and symptomatic hyperglycaemia and should aim for an HbA1c of 65-75 mmol/mol(^6) bearing in mind co-morbidities, life expectancy and biological age.</th>
</tr>
</thead>
<tbody>
<tr>
<td>The incidence of hypoglycaemia and/or hyperglycaemia should be monitored and documented, and the results discussed with the patient.</td>
</tr>
</tbody>
</table>

3. INITIATING INSULIN THERAPY IN PRIMARY CARE IN TYPE 2DIABETES

UKPDS \(^4\) demonstrated that

- Beta cell function declines with time
- Good glycaemic control reduces the complications of diabetes
- Optimum glycaemic control becomes more difficult with time and at least 1 in every 25 patients per year need to be transferred to insulin to achieve this

The decision to start people with Type 2 diabetes on insulin is usually due to

- Worsening symptoms of hyperglycaemia
- A persistently elevated HbA1c level despite maximal or near maximal doses of oral glucose lowering agents and / or GLP-1 receptor agonist
- Intercurrent illness or patient commenced on steroid therapy

It is essential to review the patient’s diet and concordance with medication prior to making the decision to commence insulin (CSBS Standard 2, 3, 4 & 8).\(^1\)

It is best practice that a registered dietician should undertake the dietary review.
Step 1
- Discuss with the GP or a consultant diabetologist and agree on the appropriate glycaemic target and insulin for the individual patient.
- Clarify continuing use or discontinuation of oral glucose lowering agents.
- Involve the person starting on insulin in the choice of how often he/she will administer insulin (CSBS Standard 2).

Step 2
- Ensure the person starting on insulin understands the broad principle of insulin treatment and is proficient at blood glucose monitoring (CSBS Standard 3 & 4).
- Identify people starting on insulin who may be unable to blood monitor or self-administer insulin and involve District Nurses to initially supervise practical skills or continue to visit long term.

Step 3
- Ideally instruct the person starting on insulin on the use of an insulin delivery device about a week prior to commencing insulin. It is important that they overcome their fears at an early stage as this may hamper further education (CSBS Standard 3 & 4).

Step 4
- Choose the appropriate regimen and calculate a 'safe' dose of insulin using the following tables A - C, for guidance. Ensure a relevant prescription is available (CSBS Standard 2).

Step 5
- If oral glucose lowering agents are to be discontinued instruct patients to take final dose the evening before starting insulin.

Step 6
- Commence Insulin Management Plan/Patient Specific Directive (IMP/PSD) if patient is community nurse dependant, once they are established on their insulin regimen.

4. INSULIN TREATMENT OPTIONS FOR CONVERSION FROM DIET AND ORAL HYPOGLYCAEMIC AGENTS TO INSULIN

For detailed guidance on the insulin treatment options for conversion from diet and oral hypoglycaemic agents to insulin, please refer to the NHS GGC Guidelines for the Management of Diabetes Mellitus 2019.

This is available on StaffNet
5. INITIATING INSULIN REGIMENS

Table A

5.1. Once Daily – Basal Regimen

A basal regimen involves the use of a Neutral Protamine Hagendorn (NPH) or analogue insulin. Choose an intermediate acting insulin, which provides a low background level of insulin. This may be used to supplement the daytime oral glucose lowering agents.

Human Isophane is the background insulin of choice. There is no evidence for improved diabetes control with analogue basal insulin in people living with type 2 diabetes. Analogue basal insulin should only be considered in people living with type 2 diabetes who have recurrent hypoglycaemia or where they require assistance with their insulin injections.

Daily insulin requirements = 0.5 units / kg body weight approximately
e.g. 0.5 x 72kg = 36 units

Of which 50% will be basal requirement
36 x 50% = 18 units

Take 60% of this daily dose for ‘safety’
18 x 60% = 11 units
Rounded up to 12 units for ease of administration.

A safe starting dose would be e.g. 12 units of intermediate acting insulin, usually given at bedtime.

If a District Nurse is administering the insulin it is usually more convenient to give it in the morning.

For titration of insulin dose refer to Table 1.

Table B

5.2. Twice Daily Regimen

For twice daily regimen the most frequently used option is a pre-mixed fixed combination of short and intermediate acting insulin or a rapid acting insulin lispro or aspart mix.8

Insulin is administered as two injections before meals, usually breakfast and evening meal. This is most commonly given as a fixed combination biphasic human isophane insulin e.g. Humulin M3/Insuman Comb 25. Pre-mixed formulations of rapid acting and intermediate acting insulin analogues are also available (e.g. Humalog Mix 25/Novomix 30) which are also suitable for twice daily administration.

Twice-daily basal insulin is an alternative choice and may be appropriate in the elderly where there is a concern regarding the risk of hypoglycaemia.

Daily insulin requirements = 0.5 units / kg body weight approximately
e.g. 0.5 x 72kg = 36 units
Take e.g. 60% ‘for safety’ 36 units x 60% = 22 units

Split the dose 50% : 50% before breakfast and evening meal. i.e. 11 units twice daily.
Rounded up to 12 units for ease of administration.

Generally the final insulin dose required will be nearer to 60%:40% divide but this would become apparent when titrating insulin against Table 2 & 3.

Table C

5.3. Basal Bolus Regimen

This is the most intensive regimen with three pre-prandial doses of short/rapid acting insulin and a bedtime dose of intermediate or long acting insulin. While this regimen offers no improvement in metabolic control compared to any other insulin regimen, this may be the most suitable regimen for people who do not have a stable daily routine as the time and dose of insulin can be varied according to when the meal is taken and its carbohydrate content.

Generally 30 - 50% of the total daily insulin requirements should be given as intermediate or long acting insulin at bedtime with the remaining insulin being given as short / rapid acting before breakfast, lunch and evening meal depending on the needs of the individual.

Daily Insulin requirements = 0.5 units / kg body weight approximately.

e.g. 0.5 x 72kg = 36 units
Take e.g. 60% ‘for safety’ 36 units x 60% = 22 units

When commencing a basal bolus regimen where three pre-prandial doses of short/rapid acting insulin are to be taken prior to breakfast, lunch and evening meal and intermediate acting/long acting analogue insulin at bedtime the total daily dose may be calculated as follows:

22 units as above. 50% of the total daily dose is basal = 11 units e.g. ‘rounding down’ for ease of administration = 10 units

Daily bolus insulin dose therefore is 22 -10 (basal dose) = 12 units of short acting insulin.
This is divided into 3 for pre breakfast, lunch and evening meal = 4 units each meal.
10 units of intermediate/long acting analogue are given prior to bed.

The insulin can then be increased to the requirement of the individual using Table 6.
It is generally beneficial to commence the individual with Type 2 diabetes on a twice-daily insulin regimen initially until they feel comfortable with injections.

For titration of insulin dose refer to Table 4.
6. INSULIN DOSE ADJUSTMENT

6.1. Once Daily – Basal Regimes

Table 1

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Breakfast</td>
<td>Reduce insulin by 4 units</td>
<td>Optimal</td>
<td>Increase insulin by 2 units</td>
<td>Increase insulin by 4 units</td>
</tr>
</tbody>
</table>

These target ranges need to be individualised. It may be for example that the “optimal” glucose range is 7-10mmol/L in certain people. Blood glucose monitoring should be carried out in accordance with GGC Blood Glucose Monitoring Guidelines recommended once daily if not experiencing hypoglycaemia.5

Refer to General Advice on Insulin Dose Adjustment, Section 6.6.

6.2. Switching to analogue basal insulin for people suffering recurrent episodes of hypoglycaemia

The GGC Formulary (http://www.ggcprescribing.org.uk/formulary/endocrine-system/drugs-used-diabetes/) advises that analogue basal insulin is not for routine use in people living with type 2 diabetes unless they suffer recurrent episodes of hypoglycaemia. These insulins should only be initiated following discussion with a Consultant Diabetologist or GP. People with type 2 diabetes experiencing more than one episode of severe hypoglycaemia (i.e. requiring third party assistance) require specialist secondary care input.

Although current evidence suggests no dose change is required when converting from a once daily Neutral Protamine Hagedorn (NPH) regime, common custom and practice would be to reduce the analogue insulin dose by 20%. This is to ensure patient safety and maintain patient confidence in the new regime/therapy. Thereafter titrate the dose, if required, at no sooner than 3 day intervals to assess the impact on blood glucose as per Table 1.

6.3. Twice Daily Basal Regimen – NPH or Detemir

Patients who do not achieve an agreed HbA1c target may be considered for an additional injection (morning & evening).5

Adjust as per Table 2.
### Table 2

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Bed and / or Before Breakfast</td>
<td>Reduce evening meal insulin by 4 units</td>
<td>Optimal</td>
<td>Increase evening meal insulin by 2 units</td>
<td>Increase evening meal insulin by 4 units</td>
</tr>
<tr>
<td>Before Lunch and / or Before Evening Meal</td>
<td>Reduce morning insulin by 4 units</td>
<td>Optimal</td>
<td>Increase morning insulin by 2 units</td>
<td>Increase morning insulin by 4 units</td>
</tr>
</tbody>
</table>

These target ranges need to be individualised. It may be for example that the “optimal” glucose range is 7-10 mmol/L in certain people.

Refer to General Advice on Insulin Dose Adjustment, Section 6.6.

### 6.4. Pre-Mixed Insulin

### Table 3

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Bed and / or Before Breakfast</td>
<td>Reduce evening meal insulin by 4 units</td>
<td>Optimal</td>
<td>Increase evening meal insulin by 2 units</td>
<td>Increase evening meal insulin by 4 units</td>
</tr>
<tr>
<td>Before Lunch and / or Before Evening Meal</td>
<td>Reduce morning insulin by 4 units</td>
<td>Optimal</td>
<td>Increase morning insulin by 2 units</td>
<td>Increase morning insulin by 4 units</td>
</tr>
</tbody>
</table>

These target ranges need to be individualised. It may be for example that the “optimal” glucose range is 7-10 mmol/L in certain people.

Refer to General Advice on Insulin Dose Adjustment, Section 6.6.
6.5. Basal Bolus Regimen

Table 4 (example of 4 injections daily adjustments)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Breakfast</td>
<td>Reduce bedtime intermediate insulin by 4 units</td>
<td>OPTIMAL</td>
<td>Increase bedtime intermediate insulin by 2 units</td>
<td>Increase bedtime intermediate insulin by 4 units</td>
</tr>
<tr>
<td>Before Lunch</td>
<td>Reduce morning short acting insulin by 2-4 units</td>
<td>OPTIMAL</td>
<td>Increase morning short acting insulin by 2 units</td>
<td>Increase morning short acting insulin by 4 units</td>
</tr>
<tr>
<td>Before Evening Meal</td>
<td>Reduce lunchtime short acting insulin by 2-4 units</td>
<td>OPTIMAL</td>
<td>Increase lunchtime short acting insulin by 2 units</td>
<td>Increase lunchtime short acting insulin by 4 units</td>
</tr>
<tr>
<td>Before Supper/ Bedtime</td>
<td>Reduce evening meal short acting insulin by 2-4 units</td>
<td>OPTIMAL</td>
<td>Increase evening meal short acting insulin by 2 units</td>
<td>Increase Evening meal short acting insulin by 4 units</td>
</tr>
</tbody>
</table>

These target ranges need to be individualised. It may be for example that the “optimal” glucose range is 7-10mmol/L in certain people.

6.6. General Advice on Insulin Dose Adjustment

- Insulin dose may need adjusting for exercise, meal composition, patterns in blood sugar levels, during illness and weight loss or gain episodes.
- **Do NOT adjust dose on a SINGLE raised blood glucose.**
- Adjust according to the chart above and monitor for at least 72 hours to judge the effect before further adjustment
- In the event of hypoglycaemia review the insulin adjustment after 48 hours.
- Blood glucose target range should be individualised for each patient.
- Dose adjustment is individual and needs to be monitored closely.
- People living with diabetes should be educated to adjust their own insulin.
- Document all changes of insulin dose in nursing notes.
- If problems persist in controlling the blood glucose level seek advice from the General Practitioner or link Diabetologist.
### 6.7. Commonly Used Insulin Preparations

<table>
<thead>
<tr>
<th>TYPE</th>
<th>NAME</th>
<th>SOURCE</th>
<th>ONSET</th>
<th>DURATION OF ACTION</th>
<th>GGC FORMULARY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short Acting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short Acting Analogue Insulin</td>
<td>Insulin lispro (Humalog®)</td>
<td>A</td>
<td>0-5 min</td>
<td>3 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin aspart (NovoRapid®)</td>
<td>A</td>
<td>10-20 min</td>
<td>3-5 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin glulisine (Apidra®)</td>
<td>A</td>
<td>12-30 mins</td>
<td>3-4 hours</td>
<td>Yes</td>
</tr>
<tr>
<td>Soluble Insulin (Short Acting)</td>
<td>Actrapid®</td>
<td>H</td>
<td>30 mins</td>
<td>7-8 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Humulin-S®</td>
<td>H</td>
<td></td>
<td>6-8 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Hypurin Neutral</td>
<td>B,P</td>
<td>30-60 min</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insuman Rapid®</td>
<td>H</td>
<td>30 mins</td>
<td>7-9 hours</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Intermediate or Long Acting</strong></td>
<td>Insulatard®</td>
<td>H</td>
<td>90 mins</td>
<td>24 hours</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Humulin-I®</td>
<td>H</td>
<td>1-2 hrs</td>
<td>Intermediate</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Hypurin Isophane</td>
<td>B,P</td>
<td>8-12 hrs or longer</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Insuman Basal</td>
<td>H</td>
<td>1 hour</td>
<td>11– 20 hours</td>
<td>No</td>
</tr>
<tr>
<td>Long Acting Analogue Insulin</td>
<td>Insulin Detemir (Levemir®)</td>
<td>A</td>
<td></td>
<td>20-24 hrs</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin Glargine (Lantus®)</td>
<td>A</td>
<td></td>
<td>24 hrs</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Insulin Degludec (Tresiba®)</td>
<td>A</td>
<td></td>
<td>Up to 42 hrs</td>
<td>Yes</td>
</tr>
<tr>
<td>Protamine Zinc Insulin</td>
<td>Hypurin PZI</td>
<td>B</td>
<td></td>
<td>24 hrs</td>
<td>No</td>
</tr>
<tr>
<td>Insulin Zinc Susp</td>
<td>Hypurin Lente</td>
<td>B</td>
<td></td>
<td>24 hrs +</td>
<td>No</td>
</tr>
</tbody>
</table>

Note: This list is not exhaustive. Please check current Formulary Status.
7. AVAILABLE INSULIN

Please refer to the most recent BNF for an up to date list of preparations. NHS GGC Formulary status can be checked online at www.ggcprescribing.org.uk

When prescribing insulin it is important to always prescribe by the brand name to ensure the correct preparation is dispensed &administered

### Human and Analogue Insulin Preparation

<table>
<thead>
<tr>
<th>Long-acting insulin analogues</th>
<th>Pack of</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin detemir (Levemir®) (Novo Nordisk)</td>
<td>3 ml cartridge (for NovoPen® 4 or NovoPen Echo® devices)</td>
<td>£42.00</td>
</tr>
<tr>
<td>Insulin detemir 100units/ml (Levemir Flexpen)</td>
<td>3ml Flexpen pre-filled pen</td>
<td>£42.00</td>
</tr>
<tr>
<td>Insulin detemir 100units/ml (Levemir Innolet)</td>
<td>3ml pre-filled pen</td>
<td>£44.85</td>
</tr>
<tr>
<td>Insulin glargine 100 units /ml (Lantus®) (Sanofi-Aventis)</td>
<td>3 ml cartridge (for ClikSTAR® and Autopen 24®)</td>
<td>£37.77</td>
</tr>
<tr>
<td>Insulin glargine 100units/ml (Lantus Solostar)</td>
<td>3ml pre-filled pen</td>
<td>£37.77</td>
</tr>
<tr>
<td>Insulin glargine 100units/ml (Lantus)</td>
<td>10ml vials</td>
<td>£27.92</td>
</tr>
<tr>
<td>Insulin glargine 100 units /ml (biosimilar) (Abasaglar®) (Lilly)</td>
<td>3ml</td>
<td>£35.28</td>
</tr>
<tr>
<td>Insulin glargine 100units/ml (Abasaglar Kwikpen)</td>
<td>3ml Kwikpen pre-filled pen</td>
<td>£35.28</td>
</tr>
<tr>
<td>Insulin glargine 300 units /ml(Toujeo®) (Sanofi)</td>
<td>1.5ml</td>
<td>£33.13 (pack of 3)</td>
</tr>
<tr>
<td>Insulin glargine 100units/ml (Semglee)</td>
<td>3ml pre-filled pen</td>
<td>£29.99</td>
</tr>
<tr>
<td>Insulin degludec (Tresiba®) (NovoNordisk) 100units/ml</td>
<td>3 ml cartridge (Penfill®, for NovoPen® 4 or NovoPen Echo® devices)</td>
<td>£46.60 (pack =3)</td>
</tr>
<tr>
<td>Insulin degludec (Tresiba®) (NovoNordisk) 200units/ml</td>
<td>3ml cartridges (FlexTouch® Pen)</td>
<td>£55.92 (pack =3)</td>
</tr>
<tr>
<td>Insulin degludec (Tresiba® FlexTouch) (NovoNordisk)</td>
<td>3ml pre-filled pen</td>
<td>£46.60</td>
</tr>
<tr>
<td>Insulin degludec and Liraglutide (Xultophy) 100units/ml/3.6mg/ml</td>
<td>3ml pre-filled pen</td>
<td>£95.53 (pack of 3)</td>
</tr>
</tbody>
</table>

### Isophane insulins (intermediate-acting insulins)

<table>
<thead>
<tr>
<th>Isophane insulins</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insuman Basal® (Sanofi)</td>
<td>3 ml cartridge (for Autopen 24® and ClikSTAR®)</td>
</tr>
<tr>
<td>Insuman Basal® (Sanofi)</td>
<td>5ml vial</td>
</tr>
<tr>
<td>Insuman Basal® (Sanofi) Solostar</td>
<td>3ml pre-filled pen</td>
</tr>
<tr>
<td>Humulin I® (Lilly)</td>
<td>3 ml cartridge (for Autopen Classic® and HumaPen®)</td>
</tr>
<tr>
<td>Humulin I® (Lilly) Kwikpen</td>
<td>3ml pre-filled pen</td>
</tr>
<tr>
<td>Humulin I® (Lilly)</td>
<td>10ml vial</td>
</tr>
<tr>
<td>Insulatard® (Novo Nordisk)</td>
<td>3 ml cartridge (Penfill®, for NovoPen® 4 or NovoPen Echo® devices)</td>
</tr>
<tr>
<td>Insulatard® (Novo Nordisk) Innolet</td>
<td>3ml pre-filled pen</td>
</tr>
<tr>
<td>Insulatard® (Novo Nordisk)</td>
<td>10ml vial</td>
</tr>
</tbody>
</table>

### Soluble insulin (short-acting insulin)

<table>
<thead>
<tr>
<th>Soluble insulin (short-acting insulin)</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actrapid® (Novo Nordisk)</td>
<td>10ml vial</td>
</tr>
<tr>
<td>Humulin S® (Lilly)</td>
<td>3ml cartridge (for Autopen Classic® and HumaPen®)</td>
</tr>
<tr>
<td>Humulin S®</td>
<td>10ml vial</td>
</tr>
<tr>
<td>Insuman Rapid® (Sanofi-Aventis)</td>
<td>3ml cartridge</td>
</tr>
</tbody>
</table>

### Rapid-acting analogues (short-acting insulin)

<table>
<thead>
<tr>
<th>Rapid-acting analogues (short-acting insulin)</th>
<th>Price</th>
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<tbody>
<tr>
<td>Insulin aspart (Novorapid®)</td>
<td>3ml cartridge (Penfill®, for NovoPen® devices)</td>
</tr>
<tr>
<td>Insulin aspart (Novorapid®) PumpCart</td>
<td>1.6ml cartridge</td>
</tr>
<tr>
<td>Insulin aspart (Novorapid®) FlexTouch</td>
<td>3ml pre-filled pen</td>
</tr>
<tr>
<td>Insulin aspart (Novorapid®) Flexpen</td>
<td>3ml pre-filled pen</td>
</tr>
<tr>
<td>Insulin aspart (Novorapid®)</td>
<td>10ml vial</td>
</tr>
</tbody>
</table>
### Insulin aspart (Fiasp) 100units/ml
- 10ml vial: £14.08
- Flextouch: 3ml pre-filled pen: £30.60
- 3ml cartridges: £28.31
- 3ml cartridge (for Autopen 24° and ClikSTAR): £28.30
- 3ml pre-filled pen: £28.30
- 10ml vial: £16.00
- Insulin lispro (Humalog®) (Lilly)
  - 3ml cartridge (for Autopen Classic® or Humapen® ranges): £28.31
  - 3ml pre-filled pen: £29.46
  - Kwikpen/Junior Kwikpen 200UNITS/ML: £58.92
- 10ml vial: £16.61
- Insulin lispro sanofi 100units/ml
  - 10ml vial: £14.12
  - 3ML CARTRIDGES: £24.06
  - 3ml pre-filled pen: £25.04

### Biphasic isophane preparations
- Humulin M3® (Lilly)
  - 3ml cartridge (for Autopen Classic® and Humapen®): £19.08
- Humulin M3® (Lilly) Kwikpen
  - 3ml pre-filled pen: £21.70
- Humulin M3® (Lilly) 10ml vial: £15.68
- Insuman Comb 15e, 25e (Sanofi)
  - 3ml cartridge (for Autopen 24° and ClikSTAR®): £17.50
- Insuman Comb 25 (Sanofi)
  - 5ml vial: £5.61
- Insuman Comb 25 Solostar (Sanofi) 883 3633
  - 3ml pre-filled pen: £19.08

### Biphasic insulin aspart preparations
- Novomix 30e (Novo Nordisk)
  - 3ml cartridge (Penfill® for Novopen® devices): £28.79
- Novomix 30e (Novo Nordisk) Flexpen
  - 3ml pre-filled pen: £29.89

### Biphasic insulin lispro preparations
- Humalog Mix 25e and 50e (Lilly)
  - 3ml cartridge (for Autopen Classic® or Humapen®): £29.46
- Humalog Mix 25e (Lilly)
  - 10ml vial: £16.61
- Humalog Mix 25e and 50e (Lilly) Kwikpen
  - 3ml pre-filled pen: £30.98

### Animal Insulins
Please note: Animal insulin is no longer used to initiate insulin therapy.

### Animal insulin short acting
- Hypurin Bovine Neutral (Wockhardt)
  - 3ml cartridge (for Autopen Classic®): £41.58
- Hypurin Bovine Neutral (Wockhardt) 10ml vial: £27.72 (1 vial)
- Hypurin Porcine Neutral (Wockhardt)
  - 3ml cartridge (for Autopen Classic®): £46.95
- Hypurin Porcine Neutral (Wockhardt) 10ml vial: £31.30 (1 vial)

### Animal insulin intermediate acting
- Hypurin Porcine Isophane (Wockhardt)
  - 3ml cartridge (for Autopen Classic®): £46.95
- Hypurin Porcine Isophane (Wockhardt) 10ml vial: £31.30 (1 vial)

### Animal insulin premixed
- Hypurin Porcine 30/70 Mix (Wockhardt)
  - 3ml cartridge (for Autopen Classic®): £46.95
- Hypurin Porcine 30/70 Mix (Wockhardt) 10ML VIAL: £31.30 (1 VIAL)

### Animal insulin long acting
- Hypurin Bovine Lente (Wockhardt)
  - 1 x 10ml vial: £27.72
- Hypurin Bovine Protamine Zinc Insulin (PZI)
  - 1 x 10ml vial: £27.72

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*All prices from BNF on medicinescomplete.com accessed 08/02/19*
8. CARE PRE AND POST INITIATION OF INSULIN THERAPY

Before insulin conversion, people living with type 2 diabetes should be seen by a registered dietician for dietary education.

They should be given contact numbers and details of the individual nurse initiating therapy, together with back up contact numbers, numbers for out of hours services (i.e. NHS 24) and staff names.

They will be contacted/ reviewed by the nurse initiating therapy, or a colleague, within 72 hours or sooner, of commencing insulin, depending on patient competency.

Generally insulin initiation in people with Type 2 diabetes is a planned procedure, therefore, patients should not be started on insulin on a Friday unless absolutely essential.

Education is a continuing process and should be given as and when necessary.

8.1. Education Prior to Commencing Insulin

Education prior to commencing insulin should include the following and be documented in the patient’s SCI Diabetes record:

- The proposed benefits and aims of treatment, including an individualised definition of good glucose control.
- Ensure proficiency in blood glucose monitoring. This may include the patient, family member or carer or district nurse.
- Pen device choice / suitability.
- Advice on recognition, treatment and causes of hypoglycaemia.
- Dietetic review.
- Implications for employment should be discussed (e.g. taxi drivers, emergency services employees, armed forces personnel, train drivers, airline pilots etc.)
- Provide all people starting insulin with written information on the DVLA guidance for insulin and driving.
- Advise patient they are legally required to inform the Driver and Vehicle Licensing Agency (DVLA) and insurance company. It is their responsibility to do so. Legal implications of not doing so should be emphasised.
- Drivers with a Group 2 entitlement license may continue to hold this as long as qualifying conditions are met. (see DVLA website: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/491028/aagv1.pdf)
- Contact numbers of appropriate healthcare professionals.

8.2. Education on Initiating Therapy

Education on initiating therapy should include the above points plus:
• Injection techniques, rotation of sites to prevent lipohypertrophy, times of insulin administration, storage of insulin, disposal of equipment and items available on prescription. Emphasise the need to invert, rock and roll the vial/pen device for cloudy insulin at least 20 times in order to mix the insulin completely.
• Sick day rules, illness at home and alternative fluid or diet measures. Awareness of the need to ketone test, if appropriate, and action to take if ketonuria/blood ketones present.
• Glucagon administration should be taught to carers/family where appropriate.
• Eating out and appropriate information for adjusting insulin times.
• ID cards.
• Cultural considerations e.g. Ramadan

8.3. Continuing Education

• Self-management of insulin titration
• Refer to secondary care, all women requiring pre-conceptual and pregnancy advice
• Cardiovascular risk education
• Smoking
• Exercise
• Holidays and travel
• Retinopathy screening and eye care
• Information about annual review
• Dental care
• Foot care
8.4. Blood Glucose Monitoring

1. It would be reasonable for people living with type 2 diabetes to carry out blood glucose monitoring for at least 2 – 4 weeks prior to the initiation of insulin therapy.

2. This should take into account age, other illnesses, physical and mental dexterity etc. Although blood glucose monitoring gives a quantitative measurement that bears some relation to HbA1c, there is no evidence that it improves overall blood glucose control. However, many patients welcome the opportunity to know more clearly what their blood glucose control is. Blood glucose monitoring can detect worsening trends in glycaemic control.

3. The pattern of blood glucose monitoring in insulin treated patients depends on the individual and the insulin regimen they are using. The timing of blood glucose measurements depends on the insulin regimen. See NHSGGC Guidelines for The Self Monitoring of Blood Glucose available on Staffnet for suggested times to monitor. Measurements of between 4.0 and 7.0 mmol/l pre-prandially and rarely above 8.5 mmol/l two hours post-prandially are reasonable. Targets need to be individualised, taking into account age, co-morbidities and aims of insulin therapy.

4. People starting insulin should be warned against making insulin adjustments on a daily basis and should be helped to understand that the HbA1c measurement is by far the most useful assessment of their overall glycaemic control.

5. During the initiation of insulin therapy it is necessary for blood glucose measurements to be carried out more frequently to enable the Diabetes Specialist Nurse to suggest the necessary adjustments to insulin doses.

6. It is reasonable to suggest that during periods of illness the person with diabetes should carry out blood glucose monitoring more often.
9. HYPOGLYCAEMIA

9.1. Recognising Hypoglycaemia

Hypoglycaemia is defined as a blood glucose level of less than 4 mmol/l.\(^5\)

Individuals with diabetes may experience hypoglycaemia due to the side effects of treatment with Insulin, or Sulphonylureas or combination thereof.

Severe hypoglycaemia is defined as any episode requiring external assistance for recovery.\(^10\) See Appendix 1 for Recommendations for Glucagon Administration (Adults)

The United Kingdom Prospective Diabetes Study (UKPDS)\(^4\) and the Diabetes Control and Complications Trial (DCCT)\(^3\) have conclusively shown that intensive glucose lowering therapy significantly reduces the risk of diabetes related complications.

However, intensive glucose-lowering therapy can also lead to an increased incidence of hypoglycaemia.

9.2. Symptoms

<table>
<thead>
<tr>
<th>Autonomic</th>
<th>Neuroglycopenic</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activating sympathetic or para-sympathetic nervous system</td>
<td>Caused by glucose deprivation to the brain</td>
<td>Non Specific</td>
</tr>
<tr>
<td>Sweating</td>
<td>Confusion</td>
<td>Weakness</td>
</tr>
<tr>
<td>Tremor/Shaking</td>
<td>Lack of Concentration</td>
<td>Dry Mouth</td>
</tr>
<tr>
<td>Palpitations</td>
<td>Drowsiness</td>
<td>Headaches</td>
</tr>
<tr>
<td>Hunger</td>
<td>Atypical behaviour</td>
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<tr>
<td></td>
<td>Inco-ordination</td>
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<tr>
<td></td>
<td>Speech Difficulty</td>
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<tr>
<td></td>
<td>Diplopia</td>
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</tr>
</tbody>
</table>

Hypoglycaemia unawareness increases with duration of diabetes.\(^5\)

Severe hypoglycaemia may adversely affect quality of life in patients treated with insulin. Improvements in blood glucose control are associated with improvements in quality of life, providing there is no increase in hypoglycaemic symptoms.\(^2\)

9.3. Prevention of Hypoglycaemia

The individual should be informed of the following:

- Blood glucose should be monitored where possible to confirm hypoglycaemia.
- If taking Sulphonylureas, or Insulin, carry some form of fast acting glucose e.g. dextrose tablets, and a diabetes identification card at all times.
- The importance of eating regular meals.
• Observation and rotation of injections sites.
• Appropriate dosage adjustment and administration of insulin.
• Effects of any external temperature changes.
• Hypoglycaemia risk during and after exercising, including sex
• The risks involved if hypoglycaemic while driving or operating machinery.
• The significance of alcohol related hypoglycaemia.

9.4. Identifying the Cause of Hypoglycaemia

Most people with diabetes are understandably more frightened of hypoglycaemia, than mild hyperglycaemia and nothing causes more loss of confidence than a severe hypoglycaemic episode after a doctor or nurse has suggested a change in tablet or insulin regimen.

According to the Clinical Standards Board for Scotland 2001 acute complications of diabetes can cause distress, disability and death. Therefore appropriate initial management of diabetes emergencies including severe hypoglycaemia can improve the outcome of the event (CSBS Standard 3, 4, 8 & 10).¹

If there is an explanation for a severe hypoglycaemic episode(s), or for recurrent near hypoglycaemia then appropriate action can usually be taken. Protecting people from further severe hypoglycaemia takes precedence over achieving “good” glycaemic control in the short term. Patients who have sustained an episode of severe hypoglycaemia have an increased risk of a further episode of severe hypoglycaemia in the future. Patients experiencing more than one episode of severe hypoglycaemia (i.e. requiring third party assistance) should be referred to secondary care.⁵

The following points should be considered:

- Is the injection device working properly?
- Was insulin given at the appropriate time before meals?
- Are insulin dosages being missed and overcompensated for later?
- Is extra insulin being taken to reduce high blood glucose?
- Are tablets being missed and overcompensated for later?
- Are meals being missed?
- Are meals changing in quantity/quality without a planned change in insulin?
- Are hypoglycaemic events occurring at the weekend rather than weekdays?
- Was alcohol responsible?
- Was exercise/increased activity responsible?
- Was the hypoglycaemia related to pre or postmenstrual blood glucose changes?
- Have the injection sites been checked?
- Does the patient rotate injection sites?
- Does the patient have Lipohypertrophy/Lipoatrophy?
- Is the blood glucose monitoring machine working properly?
- Is blood glucose monitoring technique acceptable?
- Does the patient need a dietary review?
- Does hot weather, bath or showers pre injection affect control?
- Is this insulin regime suitable for this patient?
- Is this oral hypoglycaemic agent suitable for this patient?
- Has the patient recently started taking their tablets?
• If oral hypoglycaemic agents still being taken in conjunction with insulin ensure they are being taken at the appropriate time and dose.
• Does the person drive and what does this episode mean for their license?

9.5. Reduction in Awareness of Hypoglycaemia

Some people, especially with diabetes of long duration, may lose the early warning signs of falling blood glucose and thus be at greater risk of more severe hypoglycaemia. On average patients with reduced hypoglycaemia awareness are six times more likely to experience severe hypoglycaemia.

9.6. Hypoglycaemia Unawareness and Driving

If a patient has reduced warning symptoms of hypoglycaemia, they are a risk to themselves and other road users. In accordance with current driving regulations, patients experiencing hypoglycaemia unawareness should notify the DVLA. Group 2 drivers must have full awareness of hypoglycaemia.

9.7. Hypoglycaemia and Driving

For full information refer to DVLA website. 

Advise patients to avoid low blood glucose while driving by:

• Checking blood sugar levels less than 2 hours before driving and every 2 hours after driving has started.
• Using a blood glucose meter with memory for holders of Group 2 license.
• If blood glucose less than 4.0mmol/l or they feel hypoglycaemic they should not drive and treat the hypoglycaemic episode.
• If blood glucose 5.0 mmol/l or less, take a snack
• Not driving for more than 2 hours without checking blood glucose and eating a snack if necessary.
• Not missing, or delaying, a meal or snack. Always carrying some form of fast and long acting carbohydrate food, within reach, in the car.

If hypoglycaemia occurs while driving advise the person they should:

• Stop driving as soon as it is safe to do so
• Remove the car key from the ignition and move into the passenger seat if safe to do so. This is not advisable if motorway driving
• Treat hypo with fast acting carbohydrate
• Check blood glucose if possible
• Follow that up with a long acting carbohydrate
• Check blood glucose every 15 minutes
• Wait at least 45 minutes after blood glucose returns to normal (at least 5 mmol/l), before driving again. It takes 45 minutes for the brain to fully recover.
Severe Hypoglycaemia means the assistance of another person is required. By law a Group 2 license holder must stop driving Group 2 vehicles and tell DVLA if: they have a single episode of hypoglycaemia requiring the assistance of another person, even if this happened during sleep or one episode of severe hypoglycaemia while driving. All Group 1 license holders must inform the DVLA if they experience more than one episode of severe hypoglycaemia in the last 12 months.7

9.8. Hypoglycaemia and Alcohol

Individuals with diabetes should be made aware of the hypoglycaemia risk following significant ingestion of alcohol. Alcohol inhibits the process of gluconeogenesis and blood glucose levels may fall dangerously low. Alcohol can impair hypoglycaemia awareness.

To reduce the risk of hypoglycaemia, give the following advice:

- Do not drink more than 2 units of alcohol (men) per day
- Do not drink more than 2 units of alcohol (women) per day
- Ensure some form of long acting carbohydrate is taken along with alcohol
- Have a long acting carbohydrate snack before bed

9.9. Nocturnal Hypoglycaemia

Hypoglycaemia can happen during the night, while sleeping, just as it can during the day. How someone reacts to hypoglycaemia during sleep can vary from person to person. It may

- wake them from sleep
- cause vivid dreams
- cause sweating and confusion

Treat it as you would advise for any hypoglycaemic episode.

Others may sleep right through hypoglycaemia, waking in the morning with

- a headache
- a hangover sensation
- a high blood glucose

This is a result of the body releasing stores of glucose as a response to hypoglycaemia. Family members may recognise symptoms, if person becomes restless, noisy or non-responsive. In these cases it is best to wake the person and get them to treat the hypoglycaemia.

9.10. Hypoglycaemia and Exercise

The acute effects of exercise on blood glucose are variable, with some people experiencing a rise in blood glucose (perhaps mediated by catecholamine excretion) while others note a fall in blood glucose, presumably due to increased utilisation of glucose as a metabolic fuel. Most people taking insulin therapy are aware of the effects of their own usual exercise pattern and can take steps to avoid hypoglycaemia,
either by increasing food ingestion before or during exercise, or reducing insulin doses prior to exercise.

Relevance of using appropriate injection sites prior to exercise should be discussed with the individual patient.

Significant exercise (sustained and/or vigorous) has an effect on the sensitivity of target tissues to the action of insulin, producing increased insulin sensitivity, which lasts for several hours after the exercise and may need to alter food ingestion or insulin dose post exercise as well as pre-exercise. As exercise is often taken during the early evening there is the possibility of significant post-exercise hypoglycaemia occurring while in bed, a time when many subjects are at risk of severe hypoglycaemia.

See Appendix 1 for Recommendations for Glucagon Administration (Adults).

10. SICK DAY RULES

People with diabetes do not get any more illnesses than other people, but if they get ill their glycaemic control may become erratic. This includes common illnesses such as flu, sore throats or stomach trouble. Blood glucose levels will return to normal once the patient has recovered.

What Should the Patient Do if They Are Ill?

Blood glucose levels may rise even if the patient is unable to eat and drink normally. It is therefore important that they are advised to never stop taking their insulin. Continuing use of all oral medication should be discussed with their GP or Consultant Diabetologist. People taking insulin for their diabetes should be further advised to:-

- Test their blood glucose levels every 2-4 hours and act on the result as discussed with their diabetes nurse or doctor
- Try to drink 3 litres (4-6 pints) of sugar free liquid throughout the day
- If they don’t feel like eating, they should replace their meals with carbohydrate containing drinks such as soup, milk or fruit juice with sugar free drinks in between
- If they are being sick and cannot keep anything down, they should take regular sips of sugary drinks such as lemonade
- Consult their diabetes nurse or doctor if
  - they have ketones in their urine or blood
  - they are vomiting and unable to keep their tablets down
  - their blood glucose levels remain high or low
  - they don’t improve quickly or are worried

Ketones

If the patient’s blood glucose is more than 17 mmol/l or if they are vomiting, they should test their urine or blood for ketones if they are able (if instructed to do so by the DSN).

Ketones are acid substances produced when the body is short of insulin. Shortage of insulin means the body cannot get sugar into the cells and starts to burn fat stores to
provide energy. This can lead to ketoacidosis which is dangerous if not treated quickly. If the person has ketones they should contact their diabetes nurse or doctor.

Can They Adjust Their Insulin?

If they are on insulin and have discussed this with their diabetes nurse or doctor, they should follow their guidelines.

If they are not sure, they should contact their diabetes nurse or doctor.

Additional Advice

• Flu & Pneumovac vaccines are recommended for people with diabetes
• Keep basic medicines in the house such as painkillers and cough medicines
• Keep a supply of test strips and sugary drinks at home for emergencies

11. MISSED INJECTIONS

Following a clinical assessment

Actions:
• Check blood glucose
• Check ketones if appropriate

For once daily basal
• If within 6 hours of usual time give normal dose
• If 6-12 hours late give 50% of normal dose
• If > 12 hours late consider omitting dose and monitor blood glucose

For twice daily regimen
• If within 2 hours of usual time, consider reducing dose by approximately 10%
• If 2-4 hours late, consider reducing dose by approximately 25%
• If 4-6 hours late, consider reducing dose by approximately 50%
• If > 6 hours late, omit dose and monitor BG until next injection
• If overslept, follow above advice

For basal bolus regimen
a) Bolus
• If within 30 minutes of food and on a rapid acting insulin, give normal dose
• If between 30 minutes and 2 hours individual patient assessment required
• If more time has elapsed consider taking next short/rapid acting injection early followed by food.

b) Basal
• If within 6 hours of usual time give normal dose.
• If 6-12 hours late give 50% of normal dose.
• If > 12 hours late consider omitting dose and monitor blood glucose.
Reassure patient that they may take a couple of days to regain normal glucose control. Continue monitoring.

12. USEFUL CONTACTS

Full contact details and services including patient support groups, careline counsellor services, information services and booklets, should be given to the patient.

Contact details include:

Diabetes UK Scotland
Venlaw
349 Bath Street
Glasgow
G2 4AA
Telephone: 0141 245 6380      Careline Scotland: 0141 212 8710

Website: www.diabetes.org.uk
Email: scotland@diabetes.org.uk

Out of Hours Contact: NHS 24 - 111

Websites

www.nhsggc.org.uk

www.mydiabetesmyway.scot.nhs.uk

www.dft.gov.uk/dvla

www.runsweet.com (diabetes and sport)

http://www.diabetes.co.uk/travel.html (diabetes and travel)

http://www.medicines.org.uk/emc/ (pharmaceutical companies)
REFERENCES


### INSULIN INITIATION CHECKLIST

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<tr>
<th>DIABETES</th>
<th>Date</th>
<th>Sign</th>
<th>Date</th>
<th>Sign</th>
<th>HYPOGLYCAEMIA</th>
<th>Date</th>
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<td>What is a hypo</td>
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### ILLNESS / SICK DAY RULES

- Oral Agents Continue Y/N

### INJECTIONS/INSULIN

- Test blood sugar x 4 day

### DIABETES

- Demonstration of insulin device
- Insulin dose adjustment

### Injection technique

- Who to contact for advice

### Injection sites

- Never Stop Insulin

### Time of injections

- Alternative Foods

### Safe disposal of needles

- Miscellaneous

### Storage of insulin

- Exercise

### Type & action of insulin

- Missed meals

### Dose adjustment

- Alcohol

### Discuss work pattern

- Inform DVLA / Insurance

### ID cards given

- Travel Advice

### DUK

- Relevant Company Helpline

### Cultural considerations

- Out of hours contact - NHS 24 - 111

### REFER TO GP / PN

### REFER TO DN
APPENDIX 2: RECOMMENDATIONS FOR GLUCAGON ADMINISTRATION (ADULTS)

For use only by registered first level Nurses.

Hypoglycaemia which causes unconsciousness is considered an acute medical emergency and must be dealt with promptly. Glucagon should be available for all Type 1 patients and for those patients who have been identified by their healthcare professional as requiring glucagon.

Glucagon (Glucagen Hypo Kit 1mg) should be kept at home for hypoglycaemic emergencies ideally stored in a fridge. Glucagon 1mg/1ml can be injected either subcutaneously or intramuscularly for acute insulin induced hypoglycaemia. It increases plasma glucose concentration by mobilising glycogen stored in the liver. Can be given only once. Do not use in oral induced hypoglycaemia.

Situations where Glucagon should be administered
When a patient has a blood glucose level recorded at less than 4 mmol/L, AND including one or both of below:

- The person is displaying signs and symptoms of moderate to severe hypoglycaemia e.g. cold, clammy and confused and where encouraging oral intake of fast acting carbohydrate is considered unsafe.
- The person cannot swallow, is uncooperative, unconscious, or is having convulsions.

Contraindications
- Phaeochromocytoma
- Chronic alcohol abuse
- Where the person can safely swallow fast acting carbohydrate (e.g. 4-5 glucotabs, 170ml original lucozade, 100-150ml cola or 1.5-2 tubes of Glucogel) followed by a long acting carbohydrate (e.g. slice of bread, 2 plain biscuits or next meal)
- Oral hypoglycaemic agent-induced hypoglycaemia

Side effects
Nausea, vomiting, diarrhoea, headache and hypokalaemia may occur following administration of Glucagon.

Action to be taken following Glucagon administration
- Glucagon can sometimes cause vomiting. Ensure the person is alert and orientated before sitting them upright.
- Encourage the person to take fast acting carbohydrate. 20gm of carbohydrates should be given (e.g. 4-5 glucotabs, 170ml original lucozade, 100-150ml cola or 1.5-2 tubes of Glucogel). This should be followed up with 40gm long acting carbohydrate (e.g. 2 slices of bread, 4 plain biscuits or next meal) as soon as they are able.
- Check blood glucose levels every 10-15 minutes until person recovered. Record results in nursing notes/diary.
- Capillary blood glucose levels should be monitored regularly over the next 24-48 hours.
• Do not withheld insulin but dose may need to be adjusted. Contact GP or DSN for advice.
• Blood glucose levels are likely to be high following administration of glucagon. Do not give additional correction doses of insulin.
• Identify where possible reasons for ‘hypo’ (e.g. check injection sites, change in insulin regimen, meal patterns, alcohol and general health).
• Severe episodes of hypoglycaemia requiring Glucagon should be reported to GP/DSN for further advice and investigation. 3
• Ensure patient has a repeat prescription for Glucagen Hypo Kit.
• Ensure adequate supplies of food are available.

An ambulance MUST be called for anyone experiencing a severe hypoglycaemic symptoms NOT responding to use of Glucagon within 10-15 minutes. Place the person in the recovery position and check ABC. Makenil by mouth and do not give anything orally

N.B. Glucagon may take up to 15 minutes to work and may be ineffective in patients who are undernourished, have severe liver disease and in repeated hypoglycaemia. In these circumstances, it is imperative that an ambulance is called without delay.

References