Lancashire & South Cumbria Medicines Management Group

NHS

Guideline for antihyperglycaemic therapy in adults with type 2 diabetes

Version Control

Version Number	Date	Amendments made
1	January 2018	
1.1 , 1.2 and 1.3	2018 Amendments	Amended to reflect updated SPC advice and the use of combined insulin/GLP-1 agonists
1.4 and 1.5	2019 Amendments	Updated SPC advice and addition of cardiovascular patient factor section
1.6 and 1.7	2021 Amendments	Updated SPC Information, insulin guidance simplified, clarifications
1.8 and 1.9	2023/24 Amendments	Amended to reflect updated NICE guidance (Quality Standard, CKD and tirzepatide) and SPC changes
1.10 and 1.11	2025	Removal of discontinued products. Alogliptin removed as first line. Appendix B updated.

Care after diagnosis and education

- An individualised approach to diabetes care should be adopted taking into account patient factors including frailty, susceptibility to hypoglycaemia, weight, cardiovascular risk and renal function.
- Upon diagnosis **ALL** patients should be offered structured education (DESMOND, X-PERT or locally approved courses) within 6-12 months of diagnosis.
- For those patients who are unable or unwilling to attend such courses further education should be offered including signposting to diabetes.org.uk and/or local interventions such as nutrition and dietetic services, local fitness classes/regimes, mental health services and Local Specialist Obesity Services (for patients with a BMI > 35 kg/m^2).
- In order to achieve the best possible care competent patients should be encouraged to take responsibility for the management of their diabetes and receive comprehensive counselling prior to the initiation of any new medicine. A self management contract (see appendix B) may facilitate patients and prescribers to agree care goals and encourage patients to strive for the best possible outcomes from their treatments.

Initiating and optimising treatments

This guideline does not include all antihyperglycaemic medicines for the management of type 2 diabetes. Where appropriate prescribers may prescribe medicines not considered in this guideline. Medicine preferences stated in the guideline are intended to guide prescribers initiating new treatments. Patients should be able to continue their existing treatments until they and their clinician consider it appropriate to stop.

1. When HbA1c rises above the patients agreed target, **lifestyle advice should be reinforced prior to initiating each new treatment**. (If a patient is symptomatically hyperglycaemic, clinicians should consider insulin or sulfonylurea rescue therapy and review treatment once blood glucose control is achieved).
2. Before adding/switching treatments, prescribers must be satisfied that:
    - the dose of current treatment has been suitably optimised **and**
    - the patient is using existing treatment regularly and correctly.
3. Prescribers should ensure that patients are **reviewed preferably within 3 months** of initiating a new treatment (or no later than 6 months after initiation.
4. In accordance with NICE quality standard 5, adults with type 2 diabetes should be offered an SGLT2 inhibitor if they would benefit because of co-existing chronic heart failure, cardiovascular disease or chronic kidney disease (CKD)
5. Where tolerated and not contraindicated, **metformin should be offered throughout the treatment pathway** (including following insulin initiation).
6. The benefits/risks of other blood glucose lowering therapies should be reviewed at least 6 monthly.

Cost effective prescribing

- Where more than one treatment is suitable based on patient factors, prescribers should prescribe the treatment with the lowest acquisition cost.
- Review patients on modified release preparations of metformin and gliclazide to ascertain whether they could be managed on immediate release preparations.
- Despite the lower acquisition cost of sulfonylureas, the actual cost of treating patients with sulfonylureas will be higher due to the need for blood glucose monitoring. Review patients taking glibenclamide and tolbutamide to establish whether patients could be switched to gliclazide/glimepiride.
- Only consider GLP-1 mimetics/ Tirzepatide if dual therapy has failed to control HbA1c and only continue if HbA1c reduction of ≥ 1% (11mmol/mol) and weight loss of ≥3% at 6 months.
- Patients may be switched to an alternative drug in the same class on the grounds of efficacy and tolerability if the prescriber feels this is appropriate, however drugs of the same class should not be combined (e.g. 2 gliflozins or 2 gliptins).
- Clinicians should:
    - not use combinations of gliptins and GLP-1 mimetics (increased risk of pancreatic cancer for small benefit in treatment)
    - consider titrating the dose of sulfonylureas down and discontinuing in patients who have started bolus insulin therapy or if hypoglycaemia occurs on basal insulin regimens.

Monotherapy

If confirmed HbA1c ≥ 48mmol/mol (6.5%) following lifestyle interventions.

If the patient is symptomatically hyperglycaemic, consider insulin or a sulfonylurea first line

Metformin

HYPOGLYCAEMIA RISK	Low
WEIGHT	Neutral/loss
ANNUAL COST	Standard release < £50, Modified release < £200
CARDIOVASCULAR EFFECTS	Associated cardiovascular benefit
USE IN CKD STAGES 3-5 (GFR < 60 ML/MIN)	**Stages 4-5** avoid, **stage 3** dose reduction may be considered
USE IN FRAIL/ELDERLY PATIENTS	Suitable, care in patients with dehydration at risk of age-related anorexia

Reinforce advice on lifestyle and adherence to drug treatment whenever a new treatment is initiated. Aim to review treatment and HbA1c preferably after 3 months (max 6 months)

First intensification

Metformin +

The ordering of agents in the table does not represent prescribing preference

If HbA1c rises to 58 mmol/mol (7.5%) despite optimisation of metformin treatment

*Sulfonylurea	1st Line	Gliclazide
	2nd Line	Glimepiride
*Gliptin	1st Line	Sitagliptin
	2nd Line	Linagliptin (in renal impairment)
*Gliflozin	1st Line	Canagliflozin/ Dapagliflozin /Empagliflozin
	2nd Line	Ertugliflozin

	Sulfonylurea	Pioglitazone	Gliptin	Gliflozin	Insulin (basal)
HYPOGLYCAEMIA RISK	Moderate	Low	Low	Low	High
WEIGHT	Gain	Gain	Neutral	Loss (consider if BMI > 30)	Gain
ANNUAL COST	< £50	< £50	< £400	< £450	£120- £700
CARDIOVASCULAR EFFECTS	Associated with increased risk of cardiovascular events	Can cause fluid retention which may exacerbate or precipitate heart failure	Neutral for overall CV safety measures although slightly increased rates of hospitalisation for heart failure for saxagliptin (cannot be excluded as a class effect)	Associated cardiovascular benefit particularly in patients with established atherosclerotic cardiovascular disease, chronic kidney disease or at risk of heart failure	Associated with increased risk of cardiovascular events
USE IN CKD STAGES 3-5 (GFR < 60 ML/MIN) #	**Stage 5** avoid, **stage 4** use lowest effective dose, **stage 3** no dose adjustment necessary	Suitable for all stages (not licensed in dialysis)	No dose adjustment necessary for linagliptin, dose reductions required for other DDP-4 inhibitors	All agents have demonstrated positive renal outcomes in clinical studies. Dapagliflozin and Empagliflozin have NICE TAs for use in CKD. See Appendix A for further details	Suitable for all stages, blood glucose monitoring should be intensified and dose adjusted on an individual basis
USE IN FRAIL/ELDERLY PATIENTS	Less suitable in frail patients due to increased risk of hypoglycaemia, if used dose should start low and be increased carefully	Avoid in elderly patients likely to have history of fractures, bladder cancer, cardiac failure	Relatively safe. No dose adjustments necessary based on age (unless due to renal function)	Risk of volume depletion and hypotension higher in frail/elderly patients and those taking ACE-inhibitors/ diuretics	Long acting insulin preferred in frail patients where there is a higher risk of hypoglycaemia, or assistance with administration necessary

Use in CKD stages 3-5 section of the table is intended to provide a summary only. For detailed advice please consult appendix A.

Second intensification

Metformin +

If HbA1c rises to 58 mmol/mol (7.5%) despite optimisation of therapy at first intensification

***Preferred drugs included in this guideline are based on cost, safety, inclusion on hospital formularies and current local epact data. Specialists may wish to prescribe alternative agents where they are clinically appropriate**

Sulfonylurea +	Pioglitazone +	Gliptin +	Gliflozin +
Pioglitazone	Sulfonylurea	Sulfonylurea	Sulfonylurea
OR	OR	OR	OR
Gliptin	Gliptin	Pioglitazone	Pioglitazone
OR	OR	OR	OR
Gliflozin	Gliflozin	Gliflozin	Gliptin
		OR	OR
		Insulin (basal)	Insulin (basal)

N.B. The triple therapies to be used at second intensification are based on the licensed indications contained in the products SPCs and ADA Standards of care. Some recommendations may vary from NG28 (Type 2 diabetes in adults: management). There are variations in the licensing of drugs in each of the DDP-4 inhibitor and SGLT-2 inhibitor classes of medicines. Please consult individual SPCs for licensed combinations.

Insulin/GLP-1 mimetic therapy

If treatment optimisation and still above target HbA1c. Continue to offer metformin and review other blood glucose lowering therapies

Insulin based therapy

See insulin algorithm (page 7)

Additional annual cost for bolus insulin £200-400

OR

GLP-1 mimetic and Tirzepatide

See guidance on page 6

Annual cost GLP-1 mimetics - £700-1400, Tirzpatide £1200 -£1600

Low risk of hypo, reduce weight, avoid GLP-1 mimetics in **CKD stage 5** (limited experience with tirzepatide in stage 5), associated cardiovascular benefit for liraglutide/semaglutide/dulaglutide

For patients in whom metformin is contraindicated or not tolerated

Monotherapy

The ordering of agents in the table does not represent prescribing preference

If confirmed HbA1c ≥ 48mmol/mol (6.5%) following lifestyle interventions.

If the patient is symptomatically hyperglycaemic, consider insulin or a sulfonylurea first line

	Sulfonylurea	Pioglitazone	Gliptin	Gliflozin	Insulin (basal)
HYPOGLYCAEMIA RISK	Moderate	Low	Low	Low	High
WEIGHT	Gain	Gain	Neutral	Loss (consider if BMI > 30)	Gain
ANNUAL COST	< £50	< £50	< £400	< £450	£120- £700
CARDIOVASCULAR EFFECTS	Associated with increased risk of cardiovascular events	Can cause fluid retention which may exacerbate or precipitate heart failure	Neutral for overall CV safety measures although slightly increased rates of hospitalisation for heart failure for saxagliptin (cannot be excluded as a class effect)	Associated cardiovascular benefit particularly in patients with established atherosclerotic cardiovascular disease, chronic kidney disease or at risk of heart failure	Associated with increased risk of cardiovascular events
USE IN CKD STAGES 3-5 (GFR < 60 ML/MIN) #	**Stage 5** avoid, **stage 4** use lowest effective dose, **stage 3** no dose adjustment necessary	Suitable for all stages (not licensed in dialysis)	No dose adjustment necessary for linagliptin, dose reductions required for other DDP-4 inhibitors	All agents have demonstrated positive renal outcomes in clinical studies. Dapagliflozin and Empagliflozin have NICE TAs for use in CKD. See Appendix A for further details	Suitable for all stages, blood glucose monitoring should be intensified and dose adjusted on an individual basis
USE IN FRAIL/ELDERLY PATIENTS	Less suitable in frail patients due to increased risk of hypoglycaemia, if used dose should start low and be increased carefully	Avoid in elderly patients likely to have history of fractures, bladder cancer, cardiac failure	Relatively safe. No dose adjustments necessary based on age (unless due to renal function)	Risk of volume depletion and hypotension higher in frail/elderly patients and those taking ACE-inhibitors/ diuretics	Long acting insulin preferred in frail patients where there is a higher risk of hypoglycaemia, or assistance with administration necessary

Use in CKD stages 3-5 section of the table is intended to provide a summary only. For detailed advice please consult appendix A.

Reinforce advice on lifestyle and adherence to drug treatment whenever a new treatment is initiated. Aim to review treatment and HbA1c preferably after 3 months (max 6 months)

First intensification

If HbA1c rises to 58 mmol/mol (7.5%) despite optimisation of monotherapy

***Preferred drugs included in this guideline are based on cost, safety, inclusion on hospital formularies and current local epact data. Specialists may wish to prescribe alternative agents where they are clinically appropriate**

*Sulfonylurea	1st Line	Gliclazide
	2nd Line	Glimepiride
*Gliptin	1st Line	Sitagliptin
	2nd Line	Linagliptin (in renal impairment)
*Gliflozin	1st Line	Canagliflozin/ Dapagliflozin /Empagliflozin
	2nd Line	Ertugliflozin

Sulfonylurea +	Pioglitazone +	Gliptin +	Gliflozin +
Pioglitazone	Sulfonylurea	Sulfonylurea	Sulfonylurea
OR	OR	OR	OR
Gliptin	Gliptin	Pioglitazone	Pioglitazone
OR	OR	OR	OR
Gliflozin	Gliflozin	Gliflozin	Gliptin
		OR	OR
		Insulin (basal)	Insulin (basal)

N.B. The dual therapy options at first intensification are based on the licensed indications contained in the products SPCs. Some recommendations may vary from NG28 (Type 2 diabetes in adults: management). There are variations in the licensing of some drugs. Please consult individual SPCs for licensed combinations.

Second intensification

If HbA1c rises to 58 mmol/mol (7.5%) despite optimisation of therapy at first intensification

Insulin based therapy

See insulin algorithm (page 7)

Additional annual cost for bolus insulin £200-400

OR

GLP-1 mimetic and Tirzepatide

See guidance on page 6

Annual cost GLP-1 mimetics - £700-1400, Tirzpatide £1200 -£1600

Low risk of hypo, reduce weight, avoid GLP-1 mimetics in **CKD stage 5** (limited experience with tirzepatide in stage 5), associated cardiovascular benefit for liraglutide/semaglutide/dulaglutide.

Guidance for use of GLP-1 mimetics and Tirzepatide

NICE Criteria for GLP-1 mimetics and Tirzepatide

BMI > 35kg/m^2 and specific psychological or medical problems associated with obesity
OR BMI < 35kg/m^2 and insulin would have significant occupational implications
OR weight loss would benefit other obesity-related comorbidities.
Oral GLP-1 mimetic is recommended for patients who are unable to use subcutaneous formulations or patients who prefer oral administration.
GLP-1 mimetic in combination with insulin only on advice of specialist with ongoing support from a consultant-led multidisciplinary team

Local Criteria for the use of GLP-1 mimetics and Tirzepatide

Preference of agent should be decided based on the clinician's judgement about patient characteristics. **Local specialists have suggested the following**:

1. Semaglutide (or other available GLP-1 RAs) may be preferred in patients with lower BMIs e.g. < BMI 35 kg/m^2 or patients who have established CVD or are at high risk of CV events and require an agent with proven CV benefit.
2. Tirzepatide may be preferred in patients with higher BMIs e.g. > BMI 40 kg/m^2 or who despite optimisation of all other therapies still require further glycaemic control.

Please note: Rybelsus® (semaglutide) tablets are now available in sufficient quantities to support initiation of GLP1 RA treatment in people with type 2 diabetes (T2DM) in whom new initiation of GLP-1 RA therapy would be clinically appropriate.

Review and stopping treatment

- Careful consideration **MUST** be given to stopping GLP-1 mimetics and tirzepatide if ineffective or not tolerated (evidence of poor tolerance as dose escalates). GLP-1 mimetics and tirzepatide should be reviewed after 6 months, and the deprescribing of other agents, e.g. sulfonylureas and gliptins, should be considered where possible.
- As a minimum expectation, it is recommended that GLP-1 mimetics and tirzepatide are only continued if the adult with type 2 diabetes has had a beneficial metabolic response **(a reduction of at least 11 mmol/mol [1.0%] in HbA1c and weight loss of at least 3% of initial body weight in 6 months).**

Insulin-based treatment in type 2 diabetes

Insulin therapy should be commenced by a healthcare professional who is appropriately trained and experienced in the initiation of insulin.

GLP-1 mimetic in combination with insulin only on advice of specialist with ongoing support from a consultant-led multidisciplinary team

When starting insulin, use a structured programme and continue metformin for people without contraindications or intolerance. Review the continued need for other blood glucose lowering therapies. Prescribers should consider selection of cost-effective insulins (biosimilars) and reusable cartridge pens (penfills) as a sustainable alternative to disposable pens

Preferred basal treatment

Offer NPH (isophane) insulin once or twice daily – Humulin I KwikPen

Monitor patients who are on a basal insulin (and pre-mixed insulin) for the need for short-acting insulin before meals

Alternative basal treatments

Consider insulin glargine (1st line – Abasaglar KwikPen)/detemir (2nd line – Levemir FlexPen) if:

- Patient needs assistance to inject insulin **or**
- lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes **or**
- Patient would otherwise need twice-daily NPH insulin + oral antihyperglycaemic agents

Specialists may exceptionally consider initiating insulin degludec if:

- Patient is experiencing poor glycaemic control or recurrent hypoglycaemic episodes with their existing long-acting insulin analogue **or**
- Patient is unable to take basal insulin at the same time each day

Specialists may consider high strength formulations (Toujeo or Tresiba 200) if:

Patient experiencing symptomatic nocturnal hypoglycaemia whilst being treated with a first line long-acting insulin analogue

Preferred biphasic treatment

Offer pre-mixed (biphasic) human insulin if HbA1c > 75mmol/mol (9.0%)*
1st line – Humulin M3 KwikPen

* If preferred patients may be started on separate NPH and short acting insulin

Alternative biphasic treatment

Consider pre-mixed preparations that include short-acting analogues (rather than short acting human insulin) if:

- Patient prefers injecting before a meal **or**
- Blood glucose levels rise markedly after meals **or**
- Hypoglycaemia is a problem

1st line – NovoMix 30 FlexPen
2nd line – Humalog Mix KwikPen

Preferred insulins included in this guideline are based on cost, safety, inclusion on hospital formularies and local epact data. Specialists may wish to prescribe alternative agents where they are clinically appropriate

Preferred bolus insulin treatment

Offer a choice of rapid-acting insulin analogues
1st line – Apidra SoloStar
2nd line – Humalog KwikPen
3rd line – Trurapi SoloStar

Alternative bolus insulin treatment

Consider Fiasp (insulin aspart) or Lyumjev (insulin lispro) exceptionally if patient not managed on existing bolus insulin and:

- The prescriber believes a faster onset of action would be beneficial to the patient **or**
- A patient requires "tight" control of blood glucose levels **or**
- A patient has rapid post meal increases in blood glucose levels

Patients currently receiving insulin products other than those recommended in this guideline should still continue their treatment unless their clinician considers it appropriate to stop.

Appendix A

Impact of renal function on antihyperglycaemic treatment

	CKD stage 1 and 2 GFR ≥ 60 mL/min	CKD stage 3a GFR 45- 59 mL/min	CKD stage 3b GFR 30- 44 mL/min	CKD stage 4 GFR 15-29 mL/min	CKD stage 5 GFR < 15 mL/min or dialysis
Metformin	< 89 mL/min - dose reduction may be considered	Consider risk factors for lactic acidosis before initiation. Reduce dose (starting dose ≤ 1/2 maximum dose)		Not recommended at GFR < 30mL/min	
Glimepiride					Change over to insulin is indicated
Gliclazide				Change over to insulin is indicated	
Sitagliptin			Reduce dose to **50mg** if GFR < 45 mL/min	Reduce dose to **25mg** if GFR < 30mL/min	
Alogliptin		Reduce dose to **12.5mg** if GFR < 50 mL/min		Reduce dose to **6.25mg** if GFR < 30mL/min	
Linagliptin					
Saxagliptin			Reduce dose to **2.5mg** for moderate to severe renal impairment		Not recommended in end-stage renal disease requiring haemodialysis
Vildagliptin		Reduce dose to **50mg** once daily if GFR < 50 mL/min			
Pioglitazone					Not licensed for dialysis patients
Empagliflozin (Type 2 diabetes only)		Initiate/maintain on 10mg if GFR < 60 mL/min, if GFR falls below 45 ml/min, additional glucose lowering treatment should be considered		Not recommended if < 20mL/min	
Empagliflozin (Heart failure+/- Type 2 diabetes)	GFR ≥ 20mL/min Recommended daily dose 10 mg			Not recommended if < 20mL/min	
Canagliflozin	Initiate with **100 mg**. In patients tolerating **100 mg** and requiring additional glycaemic control, the dose can be increased to **300 mg**.	Use 100 mg *		Continue **100 mg** for patients already taking canagliflozin Do not initiate. Continue dosing until dialysis or renal transplantation. *	
Dapagliflozin			If GFR falls below 45 mL/min/1.73m2, additional glucose lowering treatment should be considered		Do not initiate if GFR < 15 mL/min
Ertugliflozin		eGFR ≥ 45 to < 60 mL/min initiate at 5 mg and up-titrate to 15 mg as needed for glycaemic control.	Initiation not recommended if GFR < 45 mL/min. Discontinued if GFR persistently less than 30 mL/min.		
Liraglutide					Not recommended for use in end-stage renal disease
Exenatide MR				Not recommended if GFR <30 mL/min	
Dulaglutide					Not recommended for use in end-stage renal disease
Semaglutide					Not recommended for use in end-stage renal disease
Tirzepatide					Caution in end stage renal disease and dialysis
Insulin	Requirements may reduce in renal disease, monitor and adjust dose accordingly				

No dose adjustment	
Dose adjustment necessary	
Not recommended	

* In patients with urinary albumin /creatinine ration > 300 mg/g

Appendix B –

GLP-1 patient plan(word version of this document available at https://www.lancashireandsouthcumbriaformulary.nhs.uk/chaptersSubDetails.asp?FormularySectionID=6&SubSectionRef=06&SubSectionID=A100&FC=1)

Patient agreement form – GLP-1 agonists for Type 2 diabetes

At your appointment today we have agreed to start treatment with one of the following medicines to help manage your type 2 diabetes:

- Liraglutide
- Dulaglutide (Trulicity)
- Semaglutide (Ozempic)
- Tirzepatide (Mounjaro)

These medicines all work in a very similar way and are sometimes known as GLP-1 agonists. Further information on how to use the device and any side-effects you should be aware of is included in the patient information provided with your medicine supply.

Although these medicines are given as an injection, they work in a different way to insulin. However, they should help reduce your blood glucose levels and may also help you lose weight, especially if you follow a healthy diet and take regular exercise.

Please ask your diabetes nurse if you would like further information on the use of these medicines to treat type 2 diabetes or help and support with losing weight.

These injections do not work for everyone and if left unchecked may not be the best use of NHS resources. We therefore need to regularly monitor whether they are being effective.

In order to do this, we follow the guidance from the National Institute for Health and Care Excellence (NICE). This states that treatment with these medicines should only be continued after 6 months ***if a patient sees a reduction in their HbA1c (measurement of long-term blood sugar control) of 11mmol/mol (in the old number system that is about 1% HbA1c) and a reduction in their weight of 3% or more***.

If the GLP-1 agonist injection we have agreed to start today does not provide these beneficial outcomes after 6 months, **we will need to consider alternative options to manage your condition and stop the GLP1 agonist injection**.

If treatment is continued after 6 months, we will continue to monitor your HbA1c and weight on a regular basis. If the beneficial effects are not maintained, then again, we will need to consider alternative options to manage your condition and then stop the GLP 1 agonist injection.

PATIENT AGREEMENT:

The information overleaf has been explained to me and I understand that treatment with GLP1 agonist will be stopped and alternative options considered if the beneficial effects on my weight and HbA1c are not achieved after 6 months or continued long-term.

	Today	6 month's target
Weight (3% loss needed by 6 months)		
HbA1c (11mmol/mol (1%) reduction needed by 6 months)		
eGFR (To check your kidney function)		To be measured in 6 months

Patient Name: _____ Patient Signature: _____

Clinician Name: _____ Clinician Signature: _____

Date: Date of 6-month review:

If you have any questions or problems with your treatment, please contact:

Name:

Contact number:

Please give a copy to the patient and keep a copy in the patient's record.

If treatment is started by hospital clinicians, please also send a copy to the patient's GP

References

1. National Institute for Health and Care Excellence (2015) Type 2 diabetes in adults: management NICE guideline (NG28)
2. National Institute for Health and Care Excellence (2015) Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes NICE guideline (NG5)
3. American Diabetes Association (2017) Standards of Medical Care in Diabetes-2017, Diabetes Care, vol 40, supplement 1.
4. Sinclair A et al. European Diabetes Working Party for Older People 2011 Clinical Guidelines for Type 2 Diabetes Mellitus. Diabetes and Metabolism, vol. 37, S27-S38, 2011.
5. Mallery LH et al. Evidence-informed Guidelines for Treating Frail Older Adults with Type 2 Diabetes: From the Diabetes Care Program of Nova Scotia (DCPNS) and the Palliative and Therapeutic Harmonization (PATH) Program. Journal for Post-Acute and Long-Term Care Medicine(JAMDA), vol. 14, issue 11, 801-808, 2013.
6. Abbatecola AM et al. Frailty and Safety The Example of Diabetes. Drug Safety, vol. 35, supplement 1, 63-71, 2012.
7. Ashley C and Currie A. The Renal Drug Handbook Third edition, 2009.
8. Scottish Intercollegiate Guidelines Network (2017) Pharmacological management of glycaemic control in people with type 2 diabetes (SIGN 154).
9. Davies MJ et al. Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia vol. 61, issue 12, 2461-2498, 2018.

The Summary of Product Characteristics for all medicines included in the guideline have been consulted when including product specific information.