UKMi North West

# NICE Bites

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## A summary of prescribing recommendations from NICE guidance

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# Type 2 diabetes

## NICE NG28; 2015

This guideline discusses the management of type 2 diabetes in adults.

**Definition of terms**

| | |
|---|---|
| Hb | haemoglobin |
| HbA1c | glycated haemoglobin (A1c) |
| eGFR | estimated glomerular filtration rate |
| CV | cardiovascular |
| BP | blood pressure |
| CI | contraindicated |
| CSII | continuous subcutaneous insulin infusion |
| IV | intravenous |
| ACEi | angiotensin converting enzyme inhibitor |
| PDE-5i | phosphodiesterase-5 inhibitor |
| NPH | neutral protamine Hagedorn |
| mr | modified release |
| U | unlicensed |

### Individualised care – see NICE pathway

### Education and dietary advice – see NICE pathway

- Offer structured education to adults with type 2 diabetes and/or their family members/carers (as appropriate) at diagnosis, with annual reinforcement and review. Explain that structured education is an integral part of diabetes care.
- Provide individualised and ongoing nutritional advice from a healthcare professional with specific expertise and competencies in nutrition.
- Integrate dietary advice with a personalised diabetes management plan, including other aspects of lifestyle modification, such as increasing physical activity and losing weight.

### Monitoring

#### HbA1c measurement

- Measure HbA1c levels every:
  - 3 to 6 months until HbA1c is stable on unchanging therapy,
  - 6 months once HbA1c level and blood glucose lowering therapy are stable.
- Use methods calibrated according to International Federation of Clinical Chemistry standardisation.
- If HbA1c monitoring is invalid because of disturbed erythrocyte turnover or abnormal Hb type, estimate trends in blood glucose control using one of the following:
  - fructosamine estimation,
  - quality-controlled plasma glucose profiles,
  - total glycated Hb estimation (if abnormal haemoglobins).
- Investigate unexplained discrepancies between HbA1c and other glucose measurements. Seek advice from a team with specialist expertise in diabetes or clinical biochemistry.

### Targets

- Involve adults with type 2 diabetes in decisions about their individual HbA1c target. Encourage them to achieve and maintain their target unless any resulting adverse effects or their efforts to achieve their target impair their quality of life.
- Offer lifestyle advice and drug treatment to support adults with type 2 diabetes to aim for a target HbA1c level of:
  - 48mmol/mol (6.5%) if diabetes is managed by lifestyle and diet **OR** lifestyle and diet combined with a single drug not associated with hypoglycaemia,
  - 53mmol/mol (7.0%) if on a drug associated with hypoglycaemia.
- If HbA1c levels are not adequately controlled by a single drug and rise to ≥58mmol/mol (7.5%):
  - reinforce dietary and lifestyle advice and adherence to drug treatment,
  - support the person to aim for a HbA1c level of 53mmol/mol (7.0%), **AND**
  - intensify drug treatment. See **Box 1**
- Consider relaxing target HbA1c level on a case-by-case basis, with particular consideration for people who are older or frail, for adults:
  - who are unlikely to achieve longer-term risk-reduction benefits e.g. people with a reduced life expectancy,
  - for whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, e.g. people at risk of falling, people who have impaired awareness of hypoglycaemia, and people who drive or operate machinery as part of their job,
  - for whom intensive management would not be appropriate, e.g. people with significant comorbidities.
- If adults achieve an HbA1c level below target and are not experiencing hypoglycaemia, encourage them to maintain it. Be aware of other possible reasons for a low HbA1c level, e.g. deteriorating renal function or sudden weight loss.
- For guidance on HbA1c targets for women with type 2 diabetes who are pregnant or planning to become pregnant, see NICE pathway; Diabetes in pregnancy.

### Self-monitoring of blood glucose

- Take into account the DVLA 'At a glance guide to the current medical standards of fitness to drive' when offering self-monitoring of blood glucose levels.

# Type 2 diabetes …….continued

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## Self-monitoring of blood glucose

- **Do NOT** routinely offer self-monitoring of blood glucose levels for adults with type 2 diabetes unless:
  - the person is on insulin, **OR**
  - there is evidence of hypoglycaemic episodes, **OR**
  - the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery, **OR**
  - the person is pregnant, or planning to become pregnant. See NICE pathway; Diabetes in pregnancy.
- Consider short-term self-monitoring of blood glucose levels (and review treatment as necessary):
  - when starting treatment with oral or IV corticosteroids, **OR**
  - to confirm suspected hypoglycaemia.
- Be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia. Review treatment as necessary.
- Carry out a structured assessment at least annually of the:
  - person's self-monitoring skills,
  - quality and frequency of testing,
  - person's knowledge of how to interpret the blood glucose results and what action to take,
  - impact on the person's quality of life,
  - continued benefit to the person,
  - equipment used.

## Treatment and management

## Pharmacological treatment

- Discuss the benefits and risks of drug treatment, and options available. Base choice of drug treatment(s) on:
  - effectiveness in terms of metabolic response,
  - safety (see Medicines and Healthcare products Regulatory Agency guidance) and tolerability,
  - the person's individual clinical circumstances, e.g. comorbidities, risks from polypharmacy, individual preferences and needs,
  - licensed indications,
  - cost (if 2 drugs in the same class are appropriate, choose the option with the lowest acquisition cost).

**Drug classification**

| | |
|---|---|
| CCB | calcium channel blocker (e.g.amlodipine) |
| DPP-4i | dipeptidyl peptidase-4 inhibitor (e.g. sitagliptin) |
| SU | sulfonylurea (e.g. gliclazide) |
| SGLT-2i | sodium-glucose cotransporter 2 inhibitor (e.g. canagliflozin) |
| GLP-1 | glucagon-like peptide-1 mimetic (e.g. exenatide) |

**Initial drug treatment**
Treatment with a single non-insulin blood glucose lowering therapy i.e. **monotherapy.**

**First intensification of drug treatment**
Treatment with two non-insulin blood glucose lowering therapies in combination ie.**dual therapy**.

**Second intensification of drug treatment**
Treatment with either three non-insulin blood glucose lowering therapies in combination ie.**triple therapy,** or any treatment combination containing insulin.

**Rescue therapy at any stage of treatment**
If an adult with type 2 diabetes is symptomatically hyperglycaemic, consider insulin or a SU.
Review treatment when blood glucose control has been achieved

## Initial drug treatment

- Offer standard-release metformin. Gradually increase the dose over several weeks to minimise the risk of gastrointestinal (GI) side effects.
- If standard-release metformin is not tolerated due to GI side effects consider a trial of mr metformin.
- Review dose of metformin if eGFR is <45ml/minute/1.73m$^2$.
- Stop metformin if eGFR is <30ml/minute/1.73m$^2$.
- Prescribe metformin with caution for those at risk of a sudden deterioration in kidney function and those at risk of eGFR falling below 45ml/minute/1.73m$^2$.
- If metformin is CI/not tolerated, consider initial drug treatment* with:
  - a DPP-4i **or** pioglitazone** **or** SU.

**Box 1** Treatment algorithm

**Rescue therapy:** if symptomatically hyperglycaemic consider insulin or a SU. Review treatment when blood glucose control has been achieved.

**If HbA1c rises to 48mmol/mol (6.5%) on lifestyle interventions**

**Offer**: standard release metformin**, or** if not tolerated
**Consider:** trial of metformin mr
Target HbA1c: 48mmol/mol (6.5%)

**Metformin CI /not tolerated***
**Consider** : DPP-4i **or** pioglitazone**
Target HbA1c: 48mmol/mol (6.5%)
**or** SU
Target HbA1c: 53mmol/mol (7.0%)

**First Intensification: if HbA1c ≥58mmol/mol (7.5%)**

**Consider:** dual therapy with, metformin + DPP-4i, or metformin + pioglitazone**, or metformin + SU, or metformin + SGLT-2i***
Target HbA1c: 53mmol/mol (7.0%)

**Metformin CI/not tolerated***
**Consider:** dual therapy with: DPP-4i + pioglitazone**, or DPP-4i + SU, or Pioglitazone** + SU
Target HbA1c: 53mmol/mol (7.0%)

**Second intensification: if HbA1c ≥58mmol/mol (7.5%)**

**Consider:** triple therapy with, metformin + DPP-4i + SU, or metformin + pioglitazone** + SU, or metformin + pioglitazone** or SU, + SGLT-2i, or
insulin-based treatment[a]
Target HbA1c: 53mmol/mol (7.0%)

**Metformin CI/ not tolerated**
**Consider**: insulin-based treatment[a]
Target HbA1c: 53mmol/mol (7.0%)

Triple therapy not effective/not tolerated/CI.
**Consider:** metformin + SU + GLP-1 mimetic**** if:
**BMI ≥35kg/m$^2$**[b] **AND** specific psychological or other medical problems associated with obesity **OR,**
**BMI <35kg/m$^2$ AND** insulin therapy would have significant occupational implications **OR** weight loss would benefit other significant obesity-related comorbidities

a when starting insulin continue to offer metformin (unless CI/not tolerated). Review continued need for other blood glucose lowering therapies

b adjust accordingly for people from black/Asian/other minority ethnic groups

*
**
***
**** See **Prescribing** box

# Type 2 diabetes …….continued

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### First intensification of drug treatment

- If initial drug treatment with metformin has not continued to control HbA1c to below the person's individually agreed target consider **dual therapy** with **metformin AND**:
  - DPP-4i **or** pioglitazone** **or** SU **or** SGLT-2i***
- If metformin is CI/not tolerated, consider **dual therapy*** with:
  - a DPP-4i + pioglitazone**, **or**
  - a DPP-4i + SU, **or**
  - pioglitazone** + SU.
- Introduce drugs in a stepwise manner, checking for tolerability and effectiveness of each drug.

### Second intensification of drug treatment

- If dual therapy with metformin and another oral drug has not continued to control HbA1c to below the person's individually agreed threshold for intensification, consider either:
  - **triple therapy** with **metformin AND**:
    DPP-4i + SU, **or**
    pioglitazone** + SU, **or**
    pioglitazone** or SU, +SGLT-2i***, **or**
  - start insulin-based treatment.
- If metformin is CI/not tolerated, consider insulin-based treatment.
- If triple therapy is not effective/not tolerated/CI consider combination therapy with; metformin, + SU + GLP-1 mimetic**** for adults who have a:
  - BMI ≥35kg/m$^2$ (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity,**OR**
  - BMI <35kg/m$^2$ **AND** insulin therapy would have significant occupational implications, **OR** weight loss would benefit other significant obesity-related comorbidities.

### Insulins

- When starting insulin therapy, use a structured programme employing active insulin dose titration that encompasses:
  - injection technique, including rotating injection sites and avoiding repeated injections at same point within sites,
  - continuing telephone support,
  - self-monitoring,
  - dose titration to target levels,
  - dietary understanding,
  - DVLA guidance (At a glance guide to the current medical standards of fitness to drive),
  - management of hypoglycaemia,
  - management of acute changes in plasma glucose control,
  - support from an appropriately trained and experienced healthcare professional.
- Continue to offer metformin for people without CIs or intolerance. Review continued need for other blood glucose lowering therapies.
- If insulin is used in combination with pioglitazone observe person for signs and symptoms of heart failure, weight gain and oedema. Discontinue pioglitazone if any deterioration in cardiac status occurs. See MHRA guidance
- Start insulin therapy from a choice of insulin types and regimens:
  - offer intermediate acting (NPH) insulin injected once or twice daily according to need,
  - consider starting both intermediate acting (NPH) and short-acting insulin (particularly if HbA1c is ≥75mmol/mol [9.0%]), administered either separately or as a pre-mixed (biphasic) human insulin preparation.

### Prescribing

***Repaglinide**

- If metformin is CI/not tolerated, repaglinide is both clinically and cost effective. However, if considering this treatment discuss that there is no licensed non-metformin-based combination containing repaglinide that can be offered at first intensification

****Pioglitazone**

- When prescribing pioglitazone exercise particular caution if the person is at high risk of adverse effects of this drug (heart failure, bladder cancer, bone fracture). Known risk factors for these conditions including increased age should be carefully evaluated before treatment. MHRA advise that prescribers should review treatment after 3 to 6 months and only continue if patient is deriving benefit.
- **Do NOT** offer or continue pioglitazone if any of the following are present:
  - current or history of heart failure,
  - hepatic impairment,
  - diabetic ketoacidosis,
  - current, or history of, bladder cancer,
  - uninvestigated macroscopic haematuria.

*****SGLT-2i**

- Treatment with combinations of medicines including SGLT-2i may be appropriate for some people with type 2 diabetes.See NICE TA288 Dapagliflozin, TA315 Canagliflozin, TA336 Empagliflozin in combination therapy for treating type 2 diabetes.

******GLP-1 mimetic**

- Only offer a GLP-1 mimetic in combination with insulin with specialist advice and ongoing support from a consultant-led multidisciplinary team.
- Only continue GLP-1 mimetic therapy if the person has had a beneficial metabolic response (a reduction of at least 11mmol/mol [1%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months.

- Consider pre-mixed (biphasic) preparations that include short-acting insulin **analogues**, rather than short-acting **human** insulin preparations, if:
  - a person prefers injecting insulin immediately before a meal**, OR**
  - hypoglycaemia is a problem, **OR**
  - blood glucose levels rise markedly after meals.
- Consider switching to long-acting insulin detemir or insulin glargine° from intermediate-acting (NPH) insulin in adults with type 2 diabetes who:
  - do not reach their target HbA1c because of significant hypoglycaemia, **OR**
  - experience significant hypoglycaemia on intermediate-acting (NPH) insulin irrespective of the level of HbA1c reached, **OR**
  - cannot use the device needed to inject intermediate-acting (NPH) insulin but who could administer their own insulin safely and accurately if a switch was made, **OR**
  - need help from a carer or healthcare professional to administer insulin injections and for whom switching would reduce the number of daily injections, **OR**
  - if the person would otherwise need twice-daily intermediate-acting (NPH) insulin injections in combination with oral glucose-lowering drugs.

° This recommendation also applies to any current or future biosimilar product(s) with a marketing authorisation for use in the same indication.

# Type 2 diabetes …….continued

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- Monitor adults with type 2 diabetes:
  - who are on a basal insulin regimen (intermediate-acting NPH insulin/insulin detemir/insulin glargine°) for the need for short-acting insulin before meals (or a pre-mixed [biphasic] insulin preparation),
  - who are on pre-mixed (biphasic) insulin for the need for a further injection of short-acting insulin before meals or for a change to a basal bolus regimen with intermediate-acting (NPH) insulin or insulin detemir or insulin glargine° if blood glucose control remains inadequate.

## Insulin delivery – see NICE pathway:Type 1 diabetes

## CSII or 'insulin pump'

- CSII therapy is **NOT** recommended for treatment of people with type 2 diabetes.

## CVS risk prevention

- **Do NOT** offer antiplatelet therapy (aspirin or clopidogrel) for adults with type 2 diabetes without CV disease.
- For guidance on primary and secondary prevention of CV disease in adults with type 2 diabetes, see NICE pathway: cardiovascular disease prevention and myocardial infarction: secondary prevention.

## Blood pressure management

### Monitoring

- In adults with type 2 diabetes without previously diagnosed hypertension or renal disease measure BP at least annually. Offer and reinforce preventive lifestyle advice.
- For an adult on antihypertensive drug treatment when diabetes is diagnosed, review BP control and medications. Make changes only if there is poor control or current drug treatment is not appropriate because of microvascular complications or metabolic problems.
- Provide lifestyle advice and repeat BP measurements within:
  - 1 month if BP >150/90mmHg
  - 2 months if BP >140/80mmHg
  - 2 months if BP >130/80mmHg and there is kidney, eye or cerebrovascular damage.
- Provide lifestyle advice if BP is confirmed as being consistently >140/80mmHg (>130/80mmHg if there is kidney, eye or cerebrovascular damage).
- Add medications if lifestyle advice does not reduce BP to <140/80mmHg (<130/80mmHg if there is kidney, eye or cerebrovascular damage).
- Monitor BP every 1 to 2 months, and intensify therapy if the person is already on antihypertensive drug treatment, until BP is consistently <140/80mmHg (<130/80mmHg if there is kidney, eye or cerebrovascular damage).
- For someone who has attained and consistently remained at his or her BP target monitor BP every 4 to 6 months. Check for possible adverse effects of antihypertensive drug treatment, including risks from unnecessarily low BP.

### Pharmacological treatment

- ***First-line*** antihypertensive drug treatment should be a once-daily, generic ACEi. Exceptions to this are:
  - people of African or Caribbean origin**β**: use ACEi plus either a diuretic or a generic CCB,
  - women for whom there is a possibility of becoming pregnant: use CCB.
- For a person with continuing intolerance to an ACEi (other than renal deterioration or hyperkalaemia), substitute an angiotensin II-receptor antagonist for the ACEi.
- **Do NOT** combine an ACEi with an angiotensin II-receptor antagonist to treat hypertension.
- If BP is not reduced to the individually agreed target with first-line therapy, add a CCB or a diuretic (usually a thiazide or thiazide-related diuretic). If the target is not reached with dual therapy add the other drug (that is, the CCB or diuretic)
- If BP is not reduced to the individually agreed target with triple therapy, add an alpha-blocker, a beta blocker or a potassium-sparing diuretic (the last with caution if the person is already taking an ACEi or an angiotensin II-receptor antagonist).

## Managing complications

Eye disease, chronic painful diabetic neuropathy, autonomic neuropathy, acute painful neuropathy, diabetic foot problems, psychological problems – see NICE pathway:Type 2 diabetes.

## Gastroparesis

- Think about a diagnosis of gastroparesis in adults with type 2 diabetes with erratic blood glucose control or unexplained gastric bloating or vomiting, taking into account possible alternative diagnoses.
- For people with vomiting explain that: there is no strong evidence that any available antiemetic therapy is effective.
- Some people have had benefit with domperidone∞, erythromycin**U** or metoclopramide∞∞
- The strongest evidence for effectiveness is for domperidone∞, but prescribers must take into account its safety profile, in particular cardiac risk and potential interactions with other medicines.
- For treating vomiting caused by gastroparesis;
  - consider alternating use of erythromycin**U** and metoclopramide∞∞,
  - consider domperidone∞ only in exceptional circumstances and in accordance with MHRA guidance.
- Consider referral to specialist services if:
  - differential diagnosis is unclear, **OR**
  - persistent or severe vomiting occurs.

## Erectile dysfunction

- Offer men with type 2 diabetes the opportunity to discuss erectile dysfunction as part of their regular review.
- Offer a PDE-5i to men with type 2 diabetes with isolated erectile dysfunction unless CI. Choose one with lowest acquisition cost.
- Consider referral to a service offering further assessment and other management options of erectile dysfunction if PDE-5i treatment is unsuccessful or CI.

∞ See MHRA guidance: domperidone prescribing

∞∞ See MHRA guidance: metoclopramide prescribing

**β Editorial note:** this recommendation remains unchanged from the previous guideline (2009) but does not reflect current clinical practice. See NICE pathway: Hypertension

**Recommendations –** wording used such as 'offer' and 'consider' denote the strength of the recommendation.

**Drug recommendations –** the guideline assumes that prescribers will use a drug's Summary of Product Characteristics (SPC) to inform treatment decisions.

° This recommendation also applies to any current or future biosimilar product(s) with a marketing authorisation for use in the same indication.