Switching gliclazide modified release to gliclazide and metformin modified release to metformin

This bulletin focuses on gliclazide modified release and provides the rationale for new patients to be commenced on gliclazide standard release and for current patients to be considered for a switch to either metformin or gliclazide (or both depending on where the patient is on the treatment pathway). It also reviews the use of metformin modified release and offers advice on switching appropriate patients to standard release metformin. Although metformin modified release was not originally on the DROP-List, it has been incorporated into this bulletin due to the similarities in the audit and review processes as part of the review on all oral hypoglycaemic and antidiabetic drugs.

Information on the adverse effects of gliclazide modified release, metformin modified release and options for dose conversion in support of the switch and potential switch savings are provided. Further bulletins, including the DROP-List, are available on the PrescQIPP website, available at [www.prescqipp.info](http://www.prescqipp.info).

**Background**

Gliclazide modified release features as number 10 in the PrescQIPP DROP-List.¹ In the NHS Midlands and East, £1.5 million was spent on gliclazide modified release over the course of a year, (March 2012 - February 2013) and accounts for 13% of all gliclazide prescribing costs across the NHS Midlands and East. In addition, £8.9 million was spent on all metformin modified release products which accounts for 22% of all metformin spend.²

In this bulletin we provide the rationale for a switch from gliclazide modified release to gliclazide standard release (hereafter referred to as gliclazide) and metformin modified release to metformin standard release (hereafter referred to as metformin). As with all switches, individual patient circumstances need to be borne in mind, however, with tight switching criteria, assistance from practice nurses, support from your local CCG prescribing teams and the experiences of CCGs/GPs that have already undertaken this work, it is hoped that GPs will participate in realising the cost savings in appropriate patients.

**Recommendations**

- Review prescribing of gliclazide modified release and metformin modified release for patients with type 2 diabetes.
- All new patients requiring metformin or a sulfonylurea should be prescribed metformin or gliclazide standard release products.
- All patients, currently prescribed gliclazide modified release or metformin modified release to be reviewed for suitability of a switch to formulations.
- Monitor blood glucose levels before switching and carefully after switching to avoid hypoglycaemia.
- 30mg gliclazide modified release is therapeutically equivalent to 80mg gliclazide. When switching to treatment with gliclazide 80mg tablets, a starting dose of 80mg/day, followed by a stepwise increase in dose, depending on the metabolic response is advised, this applies to higher doses as well to avoid hypoglycaemia.
Ensure that prescribing of metformin modified release and gliclazide modified release is in line with current guidance. Commence new patients requiring gliclazide onto gliclazide. Review all patients on gliclazide modified release for suitability for switching to gliclazide. As with all switches, these should be tailored to the individual patient and regular blood monitoring to ensure that the therapeutic effect required is achieved.

Rationale for switching gliclazide modified release to gliclazide

The National Collaboration Centre for Chronic Conditions (2008)\textsuperscript{3,5} also compared gliclazide modified release with gliclazide in people with Type 2 diabetes who had been on diet control or on treatment with oral hypoglycaemic agents and found that:

- Both versions were associated with significant reductions in HbA1c (non-significant difference between the two groups).
- No clinically significant changes were seen in terms of lipid profile (non-significant difference between the two groups).
- Hypoglycaemic events were only reported by patients receiving gliclazide modified release (9%) (non-significant difference was reported between the two groups).

Gliclazide modified release 30mg is approximately therapeutically equivalent to gliclazide 80mg. Gliclazide can be taken once daily as a single dose up to 160mg, higher doses should be divided.\textsuperscript{4}

Rationale for switching metformin modified release to metformin

The National Collaboration Centre for Chronic Conditions (2008)\textsuperscript{3,5} also compared metformin modified release with metformin in people with Type 2 diabetes. This comparison was based on one study, which found patients achieved comparable glycaemic control if switched from metformin to metformin modified release. There were no statistically significant differences in the treatment outcomes.

NICE guidance\textsuperscript{6} suggests that metformin modified release may be of benefit for patients unable to tolerate metformin after appropriate titration but who would benefit from being on metformin.

Costs

Table 1 below illustrates the cost differences between the standard release and modified release formulations of metformin and gliclazide.

Table 1: Metformin and gliclazide standard release and modified release price comparison\textsuperscript{7}

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost per 28 tablets</th>
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<tbody>
<tr>
<td>Metformin 500mg tablets</td>
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<td>Metformin 850mg tablets</td>
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<td>Metformin 750mg modified release</td>
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<td>Metformin 1g modified release</td>
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<td>Gliclazide 40mg (only for dose titration)</td>
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<tr>
<td>Gliclazide 80mg</td>
<td>£1.08</td>
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<tr>
<td>Gliclazide modified release 30mg</td>
<td>£2.04</td>
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Switching options

- Switching metformin modified release to metformin.
- Switch gliclazide modified release 30mg to gliclazide 80mg depending on dose, bearing in mind that 30mg gliclazide modified release is therapeutically equivalent to gliclazide 80mg.\textsuperscript{8}
Switch savings

There is a significant difference in cost between modified release and standard formulations. In NHS Midlands and East, around £1.5 million is spent on gliclazide modified release per year. Switching from gliclazide modified release to gliclazide could release savings of up to £800,000 across the NHS Midlands and East.

In addition £8.9 million is spent on metformin modified release each year. Switching from metformin modified release to metformin could release further savings of £2.8 million across the NHS Midlands and East.

Summary

There is an opportunity to potentially save £3.6 million across the NHS Midlands and East by switching gliclazide modified release to gliclazide and metformin modified release to metformin.

A 100% switch would not be achievable particularly for the modified release metformin which may have a place in therapy for certain patients, however there may be some inappropriate prescribing of metformin modified release which is worth reviewing as even a 50% switch would release significant savings.

There is no robust evidence to support the use of gliclazide modified release over gliclazide.

The National Collaboration Centre for Chronic Conditions (2008) found no significant difference between gliclazide modified release and gliclazide in the effects on HbA1C, lipid profile and incidence of hypoglycaemic effects.

Appendix 1 provides an audit tool to identify potential patients who may be switched from gliclazide modified release to gliclazide. It also looks at the potential for switching metformin modified release to metformin.

References

4. BNF 65, March 2013
Appendix 1

Modified release anti-diabetic agent audit

The National Institute for Health and Care Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN) suggest that the use of metformin and gliclazide are used as first line options and that the modified release preparation of metformin should be reserved for those patients who are intolerant to the preparations but would benefit from a dose of metformin. Gliclazide modified release has no benefits over gliclazide and is therefore is not recommended for use. Around £3.6 million could be saved if metformin and/or gliclazide were used instead of the less favourable modified release preparations based on March 2012-February 2013 figures for the NHS Midlands and East.

Reviewing patients on oral metformin and/or gliclazide provides a vehicle for assessing practice against the recommendations set out in the PrescQIPP Bulletin on newer oral hypoglycaemics in type 2 diabetes. This audit is suitable for being carried out in GP practices by GPs or a nurse or in conjunction with a secondary care diabetes consultant or diabetes specialist nurse.

Aim

This audit aims to identify whether new patients with type 2 diabetes requiring drug treatment as well as lifestyle modification are prescribed metformin or gliclazide compared to modified release preparations and whether there is a need to amend prescribing practice.

Objectives

This audit can be modified according to local objectives. The main objectives of this audit are to:

- Identify patients currently taking metformin modified release and/or gliclazide modified release that may be suitable for metformin and/or gliclazide and have not previously taken metformin and/or gliclazide.
- Identify patients with type 2 diabetes currently taking metformin modified release and/or gliclazide modified release and would not be suitable for a switch to metformin and/or gliclazide.

Step 1: If required obtain consent to proceed with oral hypoglycaemic audit

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Step 2: Patient identification and data collection

Undertake a computer search to identify adult patients (over 18 years) with type 2 diabetes receiving repeat prescriptions for the following drugs within the past 12 months:

- Metformin modified release (including Glucophage SR®)
- Gliclazide modified release (including Diamicron MR®, Dicardis MR® Vitile XL®)
Data collection
Record on the data collection form (Appendix 2), the following information for each patient identified by the search:

- Patient ID
- Patient date of birth/age
- Diagnosis of Type 2 diabetes recorded? (Yes or No)
- Record any lifestyle measures or risk factors
- Oral antidiabetic prescribed: metformin modified release, gliclazide modified release
- Has the patient previously been prescribed metformin? (Yes or No)
- Has the patient previously been prescribed gliclazide (Yes or No)
- Reason for use of modified release formulation
  » Consider switch back to metformin or gliclazide
- Record the most recent HbA1c
- Is the HbA1C within target for this patient? (Yes or No)
- Record your action plan for a switch from metformin modified release to metformin and/or gliclazide modified release to gliclazide
- If required, the GP should initial under GP approved the suggested action plan which have been proposed
- Once action plans are completed, record date of completion

Step 3: Patient exclusions
This list is not exhaustive and other local exclusions may be added. The following patients should be excluded from the audit:

- Patients who are not able to use insulin as third line therapy.
- Patients who cannot tolerate metformin or gliclazide standard release formulations after appropriate dose titration.
- Any other exclusions agreed by the GP practice.

Step 4: Switch reviewed patients
- Patients identified in the audit as potentially suitable for a switch to metformin and/or gliclazide from modified release preparations should be called in for a diabetes review to assess their suitability for a switch by the GP or NMP.
- Patients suitable for a switch include those who have not tried metformin and/or gliclazide standard release formulations.
- Review and switch all appropriate patients on modified release preparations to metformin and/or gliclazide, adjusting dose as per the SPC if metformin or gliclazide are not tolerated.
- Ensure that the switch is explained to the patient and accurately recorded in the patient’s notes/GP system.
- Destroy any additional patient confidential/identifiable data generated during the switch process e.g. patient log sheets etc.
- Inform the local community pharmacists that switches have taken place with an indication of the number of patients involved.

Step 5: Follow up
- All patients switched to metformin and/or gliclazide should be followed up at an agreed interval e.g. one month and two months post switching to assess their HbA1C, number of hypoglycaemic episodes and any adverse effects/tolerability issues.
- Re-check prescribing patterns in 6 months’ time to ensure intervention has continued to be successful.