

Draft SIGN guideline on pharmacological management of glycaemic control in people with type 2 diabetes

Response from the Royal College of Physicians of Edinburgh

3.1 – Evidence for treating to glycaemic targets

There is no mean duration of diabetes for the VADT study – is this consistent?

3.5 - hypoglycaemia

This section only discusses problems with major hypoglycaemia for T2DM - mild / moderate hypoglycaemia also has significant QOL issues for type 2 patients.

4.1.2 – Glycaemic control compared with other glucose-lowering agents

We are not sure why canagliflozin, dulaglutide and DPP-4 i data are included when none of these drugs are being promoted as monotherapy. To be consistent, similar data for insulin, meglitinides and alpha-glucosidase inhibitors should be included.

This is the only mention of meglitinides in the guideline.

4.3 – Cardiovascular morbidity and mortality

There is no discussion about renal dysfunction and what level of eGFR Metformin needs reduced / withdrawn. There is also no mention of starting Metformin at a low dose and increasing slowly - this is important as these guidelines will be read by non-diabetologists.

5. - Sulphonylureas

The American Diabetes Association guidelines mention low durability SUs (see UK Prospective Diabetes Study). There is no mention of this in these guidelines.

There is no mention of renal dysfunction and withdrawing therapy. Clinically we still see patients on SUs at very low eGFRs. GPs tend to follow eGFR guidelines for gliptins and SGLT2i and forget SUs.

6 - Thiazolidinediones

There is no mention of TZD withdrawal with macular oedema.

We are surprised there is no mention of risk of bladder cancer in relation to pioglitazone.

7.1 – Dipeptidyl peptidase-4 inhibitors Glycaemic control

DPP4i are recognized clinically as poor drugs in patients with longer duration of diabetes. As a group they are the least effective anti-diabetic agents.

There is no mention of DPP4i and renal dysfunction with change in dosage.

8.1 Alpha-glucosidase inhibitors - Glycaemic control

The inclusion of Alpha-glucosidase inhibitor inclusion is surprising as there are very few patients on this class of drug because of side-effects.

9. Glucagon like peptide-1 agonists

There is mention of CV protection with SGLT2i but not with GLP analogues. Data is available on this from a number of studies and more are coming out soon. This section therefore needs future proofed. For example, LEADER demonstrated a superior 13% cardiovascular risk reduction compared

to standard treatment of care. There is also no mention that LEADER also showed a 22% reduction in nephropathy - one of the most common complications in T2D.

9.3 Cardiovascular morbidity and mortality

This states that in LEADER - ‘a limitation was significantly greater use of insulin and sulphonylureas and a consequent higher rate of hypoglycaemia in the placebo group which may have influenced event rates’.

However; it is relevant to mention that in the EMPA-REG nearly double the number of patients in the placebo vs the empagliflozin arm received the addition of insulin (11.5% vs 5.8%) or a sulphonylurea (7% vs 3.8%) with 1.5% of patients in the placebo arm vs 1.3% in the empagliflozin arm experiencing a severe hypoglycaemic event. Therefore the statement referring to the limitation of the LEADER trial could be removed.

Two large international guideline bodies (American Diabetes Association Standards of Medical Care in Diabetes 2017 and Canadian Diabetes Association Clinical Practice Guidelines) have both endorsed liraglutide and empagliflozin in the use with T2D adults with established CVD.

GLP1 analogue should be considered as an add-on therapy to metformin in patients with type 2 diabetes when hypoglycaemia is a concern or weight loss is considered to be potentially beneficial. In individuals with type 2 diabetes and established cardiovascular disease, GLP1 RA with proven cardiovascular benefit (currently only liraglutide) in diabetes.

SWITCH data now included in the smpc for degludec yet there is no mention of this.

10. Sodium Glucose Co-Transporter 2 inhibitors

We are unsure why there is so much on SGLT2i as monotherapy as the Scottish Medicines Consortium (SMC) has not approved any SGLT2i for monotherapy.

Tables presented are as monotherapy and could direct people to an area that SIGN is not recommending usage. Text appears to present NICE meta-analysis. The evidence review group within NICE were clear that there were uncertainties with the analysis and it should be treated with caution.

Monotherapy not recommended by SMC or within SIGN – more emphasis should be placed in reviewing data from SMC approvals for the Add onto Met SIGN recommendation. It would be better to use Detailed Advice Document from SMC (as below).

	Baseline	24/26week
Dapa 10	7.92%	0.84
CannaSU 100	7-7.9%	0.82
CannaSU 300		0.93%
Canna D 100	7-10%	0.79%
Canna D 300		0.94%

With SGL2i there is no comment on fractures/amputations.

General comments

- There is no data on or mention of fixed dose combinations, which have the potential benefits to patients and may improve adherence as well as saving money.
- Language does future proof parts of the guideline but it should be generalised further as the guideline could be out of date very quickly.
- We look forward to seeing the algorithm that was not included in this draft.