

APPENDICES

APPENDIX A: Protocol for re-introduction of blood glucose lowering medications

Blood glucose levels were monitored by participants and reviewed at each trial contact. Insulin and oral hypoglycaemic agents were adjusted as outlined below. This protocol is based on guidance published by Baldry et al in 2020 (28).

Oral hypoglycaemic agents

- At the commencement of dulaglutide, sulphonylurea dose was reduced by 50% if HbA_{1c} < 75mmol/mol
- At the commencement of dulaglutide, DPP-IV inhibitors were ceased
- All oral hypoglycaemic agents were ceased at the commencement of LED
- If BSL >7mmol/L for 7 consecutive days or >10mmol/L for 3 consecutive days, agents were reintroduced in the following order:
 1. Metformin
 2. SGLT2 inhibitor
 3. Sulphonylurea, pioglitazone or basal insulin

Insulin

- At time of initiating dulaglutide, the insulin total daily dose was reduced by 20%
- At the initiation of LED, insulin was ceased
- If insulin reintroduction was required, dosing decisions were made at the discretion of the responsible investigator

References

28. Baldry EL, Davies MJ, Khunti K, et al. Pragmatic management of low-energy diets in people with type 2 diabetes in primary care: a decision aid for clinicians. *Diabet Med*. 2020;37(5):747–51.

APPENDIX B: Protocol for re-introduction of blood pressure lowering medications

Antihypertensives were stopped at the initiation of the low energy diet except if prescribed for another indication. The blood pressure (BP) was measured at each face-to-face study visit. For ease, only the systolic BP was considered when making decisions regarding medication reintroduction. If the systolic BP was >165mmHg in the first two weeks of the LED or >140mmHg thereafter, antihypertensives were reintroduced according to the order of reintroduction below. Doses were increased to achieve target BP before another agent was added.

Order of reintroduction of previously used drugs

1. Angiotensin converting enzyme inhibitor
2. Angiotensin receptor blocker
3. Thiazide type
4. Spironolactone
5. Calcium channel blocker
6. Beta blocker
7. Alpha blocker
8. All other

APPENDIX C: Overview of Study Visit Protocol

Week 0	Week 2	Week 2.5	Week 3	Week 4	Week 6	Week 8	Week 10	Week 11	Week 14
In-person	In-person	In-person	In-person	By phone	In-person	By phone	In-person	By phone	In-person
Group or individual information session.	Completion of dulaglutide run-in	Measure weight, BP, and BSL	Measure weight, BP, and BSL	Adverse event screen (pre-determined and/or other)	Measure weight, BP, and BSL	Adverse event screen (pre-determined and/or other)	Measure weight, BP, and BSL	Adverse event screen (pre-determined and/or other)	Trial completion
Enrolment and consent	Commence LED	Adverse event screen (pre-determined and/or other)	Adverse event screen (pre-determined and/or other)		Adverse event screen (pre-determined and/or other)		Adverse event screen (pre-determined and/or other)		Adverse event screen (pre-determined and/or other)
Baseline QoL, anthropometric and laboratory measures	Cease remaining diabetes medications								Final QoL, anthropometric, and laboratory measures
Education and commence dulaglutide	Measure weight, BP, and BSL								Discuss ongoing diabetes medication plan
Titration of diabetes medications	Adverse event screen (pre-determined and/or other)								(Dietitian follow-up after trial completion)
Cease BP medications									
General feedback collected, respond to arising concerns, reviewing diet adherence									
Diabetes and blood pressure medication review and/or re-introduction and/or titration									

APPENDIX D: Events of special interest, medical events and hospitalisation

At each visit, adverse events were systematically screened for using the below form. All adverse events were graded 0-3 in severity.

Grading System
0 = Not present
1 = Mild (no real interference with daily activities)
2 = Moderate (occasional/minor interference with daily activities)
3 = Severe (frequent/constant/marked interference with daily activities)

Appointment	1	2	3	4	5	6	7	8	9	10
Week	0 (Group Visit)	2	2.5	3	4	6	8	10	12	14
Nausea										
Vomiting										
Abdominal pain										
Diarrhoea										
Constipation										
Dizziness										
Heartburn/Indigestion										
Headache										
Mood changes										
Sensitivity to cold										
Hair loss										
Fatigue										