

**Rescue therapy: Insulin** or **SU** Rescue based therapy if symptomatic or high HbA<sub>1c</sub> Review once symptoms resolved +/- target HbA<sub>1c</sub> achieved

Drug	<b>CKD stage 1</b> eGFR >90 mL/min	CKD stage 2 eGFR 60-90 mL/min	<b>CKD stage 3a</b> eGFR 45-59 mL/min	<b>CKD stage 3b</b> eGFR 30-44 mL/min	CKD stage 4 eGFR 15-29 mL/min	<b>CKD stage 5</b> eGFR <15 mL/min	Mild to moderate hepatic impairment	Severe hepatic impairment
Metformin	$\checkmark$	$\checkmark$	$\checkmark$	✓ Max 500mg BD	×	×	Specialist initiation only	×
Gliclazide	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	Use lowest effective dose	×	$\checkmark$	×
Linagliptin	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$
Sitagliptin	100 mg	100 mg	100mg	50mg	25mg	25mg	$\checkmark$	×
Alogliptin	25mg	25mg	25mg	12.5mg	6.25mg	6.25mg	$\checkmark$	×
Pioglitazone (TZD)	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	×	×
Dapagliflozin	✓ 10mg	✓ 10mg	✓ Continue 10mg	×	×	×	$\checkmark$	✓ 5mg
Canagliflozin	✓ 100-300mg	✓ 100-300mg	✓ 100mg	Initiate 100mg, only if uACR >300mg/g	No new initiation; continue 100mg if uACR >300mg/g	No new initiation; continue 100mg if uACR >300mg/g	$\checkmark$	×
Empagliflozin	✓ 10-25mg	<b>√</b> 10-25mg	✓ Continue 10mg	×	×	×	$\checkmark$	×
Ertugliflozin	<b>√</b> 5-15mg	✓ 5-15mg	✓ Continue 5-15mg	×	×	×	$\checkmark$	×
Liraglutide	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	×	$\checkmark$	×
Semaglutide	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	×	$\checkmark$	Caution: limited information
Dulaglutide	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	×	$\checkmark$	$\checkmark$
Insulin	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$	$\checkmark$

Diminished glycaemic effect of SGLT-2i with eGFR < 45 mL/min, however sustained cardio-renal protection

### Sick Day Guidance - to be reiterated to patients at every opportunity



Increase blood glucose monitoring during acute illness and check for ketones. If you are using daily insulin or an SUs, you may need to increase (or decrease) the amount taken to maintain appropriate glucose control. Ensure fluid intake to minimise dehydration.

Adapted from Imperial College Healthcare NHS Trust Renal Sick Day Rules

Lifestyle Counselling – to be reiterated to patients at every opportunity

<b>Dietary Guidance</b> Seek dietitian input. Individualised approach: low fat diet, low Glycaemic Index diet or Mediterranean diet etc. Alternatives include low calorie total diet replacement programmes (NWL REWIND).	<b>Physical Activity</b> Realistic targets should be set. The benefits of regular exercise should be explained and people should be advised to perform regular aerobic activity. Clinical studies show that walking for 30 minutes every day has cardiovascular benefits.			
Weight Management Weight loss can help the patient	Smoking Cessation & Alcohol consumption			

achieve Type 2 diabetes remission. Realistic initial weight loss target of 5% to 10% of starting weight. Consider drug therapy, e.g SLGT-2i or GLP-1. Consider surgical intervention.

## essation & nsumption

and refer to Smoking Cessation

## **Medication review**

Reassess the person's needs and circumstances at each review (3-6 months) and think about whether to stop any medicines that are not effective. Adjustments for Renal & Hepatic Impairment - see page 2.



# **Diabetes Remission Programme**



Diabetes remission is a practical target for primary care<sup>2</sup>. Consider enrolment into NWL REWIND Programme for either low calorie total diet replacement or low carb pathway<sup>3</sup>. For more details, click here For full pathways, click here

Given the recent wealth of publications regarding cardiovascular & renal outcome trials in type 2 diabetes, this Type 2 Diabetes Management Algorithm is meant as a quick reference guide as we move away from glucose-centric prescribing, based on current evidence as of August 2020. For more in-depth guidance please refer to full <u>North</u> <u>West London Diabetes Guidelines</u>, the <u>EASD-ADA Consensus Document</u>, or other [inter]national guidelines. <u>Also see CaReMe multi-association position statement</u>.

Lifestyle management should be part of the ongoing discussion with individuals with T2DM at each visit. Increasing physical activity and reducing body weight improves glycaemic control and should be encouraged in all people with T2DM<sup>1</sup>. Glycaemic treatment targets should be individualised based on patient preferences and patient characteristics, including frailty and comorbid conditions<sup>1</sup>. All drugs can cause side effects, consult BNF or summary of product characteristics for full side effect profile of individual drugs. Always offer advice on sick day guidance for patients on Metformin and/or SGLT-2i<sup>1</sup>. Stop SGLT-2is peri-operatively or if restricted food intake or dehydration<sup>1</sup>. Patients on insulin treatment should always be advised never to stop or significantly reduce their insulin as part of the sick day response<sup>1</sup>. SU & TZD both have low acquisition cost, this should be taken into consideration alongside increased risk of weight gain and hypoglycaemia risk (SU).

#### Abbreviations:

T2DM; type 2 diabetes mellitus; NWL REWIND; North West London Reducing Weight with Intensive Dietary support, eGFR, estimated glomerular filtration rate; SGLT-2i, sodium-glucose cotransporter-2 inhibitor; DPP-4i, dipeptidyl peptidase 4 inhibitor (gliptin); SU, sulfonylurea; TZD, thiazolidinedione; BMI, body mass index; GLP-1, glucagon-like peptide-1 receptor agonist; +ive, positive; CVD, cardiovascular disease; eCVD, established cardiovascular disease; MI, myocardial infarction; Cana, canagliflozin; Dapa, dapagliflozin; Empa, empagliflozin; HF, heart failure; CKD, chronic kidney disease; HbA<sub>1c</sub>, hemoglobin A1C; BD, twice daily; ACEi, Angiotensin-converting enzyme inhibitors; ARB, Angiotensin II receptor blocker; NSAID, Non-steroidal anti-inflammatory drug; DKA, diabetic ketoacidosis.

#### References:

- 1. For further guidance please refer to full North West London Diabetes Guidelines http://tiny.cc/p4egfz
- 2. DiRECT; Lancet 2018; 391: 541–51 https://doi.org/10.1016/S0140-6736(17)33102-1
- 3. NWL REWIND Programme (Reducing Weight with Intensive Dietary support) For more details, click here For full pathways, click here.
- 4. When prescribing an SGLT-2i, consider risk of volume depletion, euglycemia DKA in insulin deficient cohorts and lower limb amputation (class warning, but only observed in Cana and Eurtu). Caution in frail patients and always follow sick day rules. For more information, refer to full North West London Diabetes Guidelines
- 5. DECLARE TIMI 58; N Engl J Med 2019; 380:347-357; DOI: https://doi.org/10.1056/NEJMoa1812389
- 6. Saxagliptin to be avoided in patients with heart failure. SAVOR; N Engl J Med. 2013 Oct 3;369(14):1317-26. doi: https://doi.org/10.1056/NEJMoa1307684
- 7. TZD (Pioglitazone) to be avoided in patients with heart failure. PROactive; Lancet. 2005 Oct 8;366(9493):1279-89 https://doi.org/10.1016/S0140-6736(05)67528-9
- 8. REWIND (Dulaglutide CVOT); Lancet 2019; 394: 121–30; DOI: <u>https://doi.org/10.1016/S0140-6736(19)31149-3</u>
- 9. Patients with established atherosclerotic cardiovascular disease having had an ischemic event (e.g myocardial infarction or stroke)
- 10. Consider initiating Met + SGLT-2i rather than stepwise. This is in line with Position Statement by Primary Care Diabetes Europe; S. Seidu, et al., A disease state approach to the pharmacological management of Type 2 diabetes in primary care: A position statement by Primary Care Diabetes Europe, Prim. Care Diab. (2020), https://doi.org/10.1016/j.pcd.2020.05.004. Alternatively, the European Society of Cardiology (ESC) diabetes guideline states that SGLT-2i could be considered as first line ahead of metformin in patients with eCVD, HF or CKD - European Heart Journal (2019) 00, 169; doi: <a href="https://doi.org/10.1093/eurhearti/ehz486">https://doi.org/10.1093/eurhearti/ehz486</a>
- 11. EMPA-REG; N Engl J Med 2015; 373:2117-2128; DOI: https://doi.org/10.1056/NEJMoa1504720
- 12. CANVAS; N Engl J Med 2017; 377:644-657; DOI: https://doi.org/10.1056/NEJMoa1611925
- 13. Dapa has shown MACE benefit in a post MI analysis; DECLARE prior MI; Circulation. 2019 May 28;139(22):2516-2527; DOI: https://doi.org/10.1161/CIRCULATIONAHA.119.039996
- 14. SUSTAIN 6; N Engl J Med. 2016 Nov 10;375(19):1834-1844 DOI: https://doi.org/10.1056/NEJMoa1607141
- 15. LEADER; N Engl J Med 2016; 375:311-322; DOI: https://doi.org/10.1056/NEJMoa1603827
- 16. DAPA HF; September 19, 2019; DOI: https://doi.org/10.1056/NEJMoa1911303
- 17. CREDENCE; N Engl J Med 2019; 380:2295-2306; DOI: https://doi.org/10.1056/NEJMoa1811744