

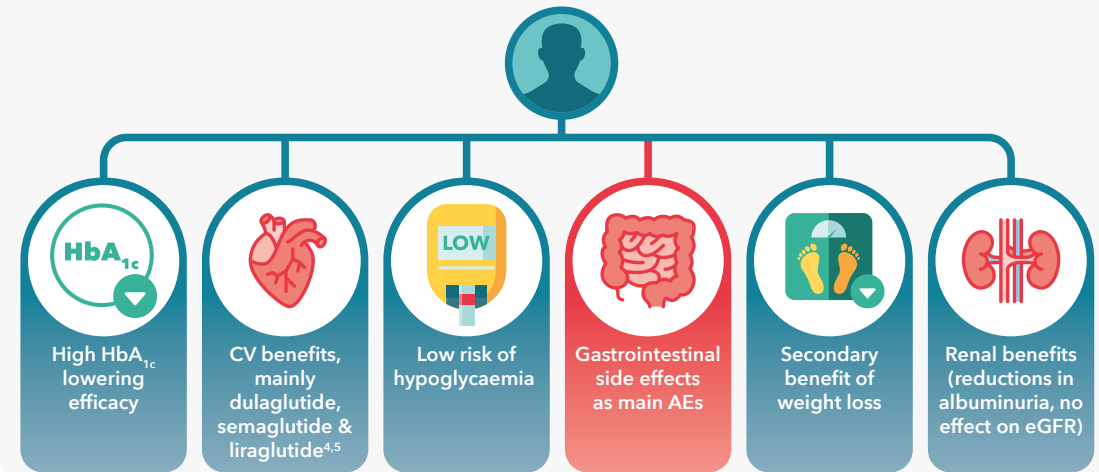
When should GLP-1 RAs be used?

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Early intensive therapies with incretin-based drugs, **DPP-4is** and **GLP-1 RAs** has been adopted by many guidelines, but the recommendations on the use of these agents vary across major guidelines

Guideline	2019: ADA/EASD ¹	2019: ESC/EASD ²	2015: NICE ³
Incretin-based therapies	DPP-4is	2 nd line if no ASCVD/CKD but minimised hypoglycaemia required	2 nd /3 rd line as combination depending on existing therapy and CV risk
	GLP-1 RAs	2 nd line if with ASCVD or at high ASCVD risk 2 nd line if minimised hypoglycaemia or weight loss required	1 st line if with ASCVD or at (very) high CV risk - To reduce CV events use liraglutide, semaglutide, dulaglutide - To reduce mortality risk use liraglutide
			2 nd or 3 rd line combination therapy 4 th line if weight loss required

GLP-1RA impact on patient outcomes



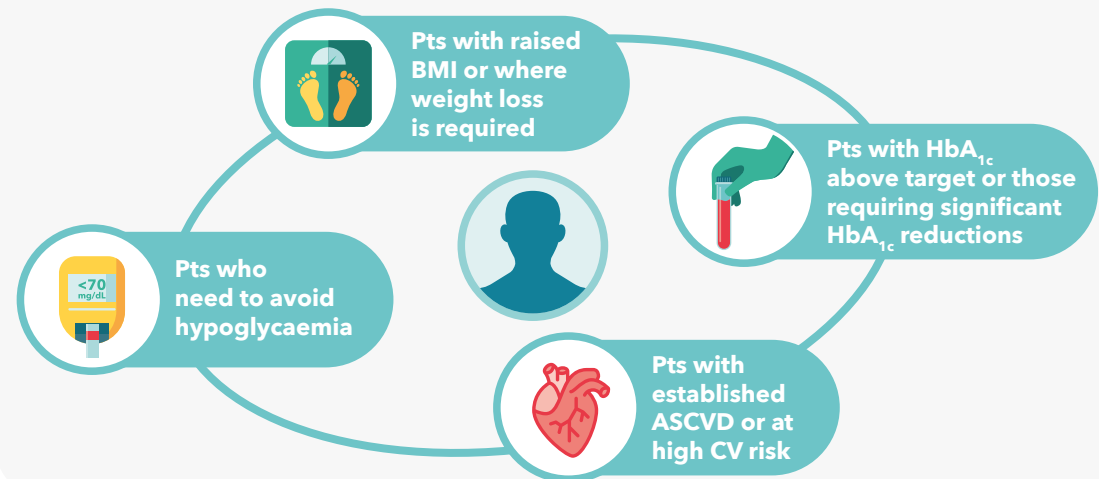
Main differences in guidelines for use of GLP-1 RAs

- Both ADA/EASD (2019)¹, and ESC/EASD (2019)² guidelines recommend the use of **GLP-1 RAs** in patients with established ASCVD or at (very) high CV risk
 - ADA/EASD as an add-on therapy to metformin
 - ESC/EASD as **first-line therapy in treatment-naïve patients**
- NICE³ guideline recommendations were last updated 2015 hence do not reflect the latest evidence indicating CV protection, so recommends **GLP-1RAs** only as 4th line therapy and only if weight loss is required

What about other therapies?

- In patients with no risk or established ASCVD or CKD, **DPP-4is** are recommended as 2nd or 3rd line combination therapy, particularly when hypoglycaemia should be minimised^{1,3}
- Where HF or CKD predominates, **SGLT-2is** are preferred¹
 - If **SGLT-2is** are not tolerated, **GLP-1RAs** are recommended
 - GLP-1RAs** can be used in CKD stage 3 (down to low eGFR) with no requirements for dose reduction

Which patients are suitable for treatment with GLP-1RAs?



Abbreviations: ADA, American Diabetes Association; AE, adverse event; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; DPP-4i, dipeptidyl peptidase-4 inhibitor; eGFR, estimated glomerular filtration rate; EASD, European Association for the Study of Diabetes; GLP-1, glucagon-like peptide-1; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA_{1c}, Hemoglobin A_{1c}; HF, heart failure; NICE, National Institute for Health & Care Excellence; Pts, patients; SGLT2i, sodium-glucose cotransporter-2 inhibitor.

References: 1. Buse JB et al. *Diabetes Care*. 2020;43(2):487–493. 2. Cosentino F et al. *Eur Heart J*. 2019;41(2):255–323. 3. National Institute for Health and Care Excellence. 2015. Available at: <https://www.nice.org.uk/guidance/ng28> [Accessed 10th September 2021]. 4. Evans LM et al. *Endocrinol Diab Metab*. 2021;4:e00259. 5. Buse JB et al. *Diabetes Care* 2020; 43(7): 1546-1552.