

THE NEW CARDIOPROTECTIVE DIABETES DRUGS

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DISCLOSURE

No conflict of interest

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WHAT WE'RE COVERING TODAY

- Cardioprotective?
- Basic metabolism and diabetes
- Incretin system
- GLP1 /GIP Drugs

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WHAT WE'RE COVERING TODAY

- Basic kidney function
- SGLT2i
- When to use these drugs
- What's next?

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CARDIOPROTECTIVE?



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CARDIOPROTECTIVE?

The **NEW ENGLAND
JOURNAL of MEDICINE**

Effect of Rosiglitazone on the Risk of Myocardial Infarction
and Death from Cardiovascular Causes

Steven E. Nissen, M.D., and Kathy Wolzki, M.P.H.

Published on-line May 21, 2007

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FDA 2008 RECOMMENDATION

"To establish the safety of a new antidiabetic therapy to treat type 2 diabetes, sponsors should demonstrate that the therapy will not result in an unacceptable increase in cardiovascular risk."

7

HOW TO PROVE A DRUG DOES NOT INCREASE RISK?

Cardio-Vascular Outcome Trial

CVOT

8

WHAT DO CVOTS LOOK FOR?

MACE

Major Adverse Cardiac Events

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MACE INCLUDE...

Non-fatal stroke
Non-fatal MI
CV Death

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BASIC METABOLISM AND DIABETES

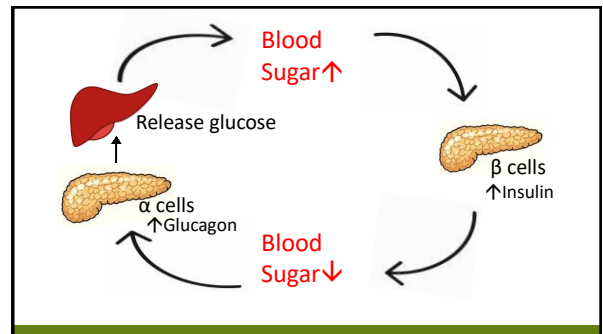
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Insulin
Glucagon

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THREE MAJOR DEFECTS IN TYPE 2 DIABETES

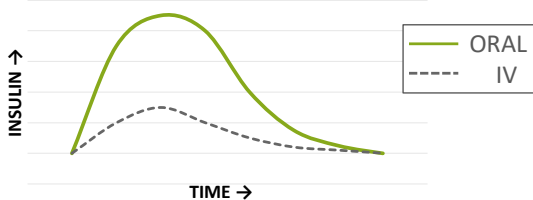
- Pancreas makes too little insulin
- Insulin doesn't work well - "insulin resistant"
- Pancreas makes too much glucagon

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THE INCRETIN SYSTEM AND GLP1 / GIP-RA DRUGS

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NORMAL



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THESE HORMONES WERE NAMED...

Incretins

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Incretins

Gut hormones that increase insulin production by a glucose-dependent mechanism

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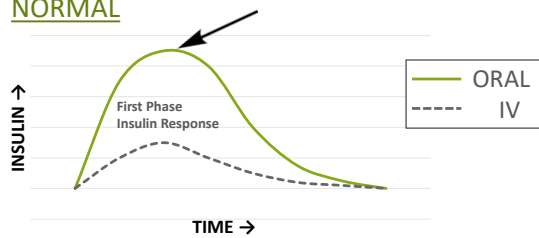
Glucose-dependent

AKA...

Almost no risk of hypoglycemia.

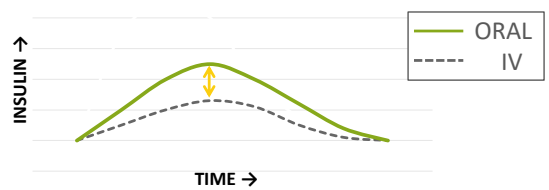
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NORMAL



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INCRETIN EFFECT BLUNTED WITH TYPE 2 DIABETES

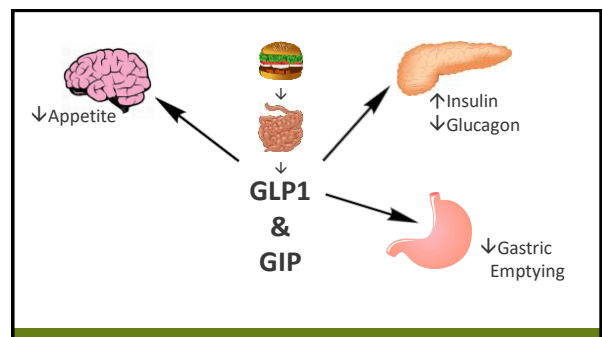


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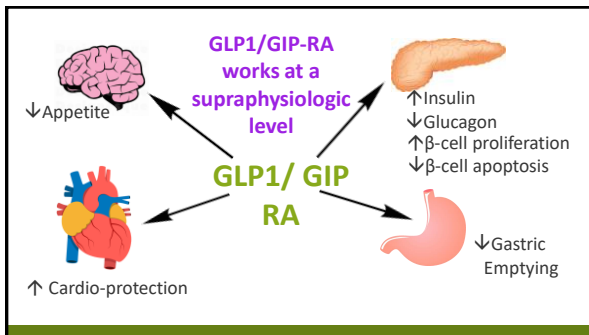
THE INCRETINS!

- **GLP1**
(glucagon-like peptide 1)
- **GIP**
(glucose-dependent insulinotropic polypeptide)

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LET'S MEET THE INCRETIN DRUGS!

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GLP1 / GIP RA Drugs		
exenatide	Bydureon BCise	1 x week injection
dulaglutide	Trulicity	1 x week injection
liraglutide	Victoza	1 x day injection
	Saxenda (Wt)	1 x day injection
semaglutide	Ozempic	1 x week injection
	Rybelsus	1 x day pill
	Wegovy (Wt)	1 x week injection
tirzepatide	Moujaro	1 x week injection
	Zepbound (Wt)	1 x week injection

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Once-weekly 
BYDUREON® BCise™
 exenatide extended-release
 injectable suspension 2 mg



28


trulicity™
 dulaglutide once-weekly injection



29

VICTOZA®
 liraglutide injection 1.2 mg/1.8 mg



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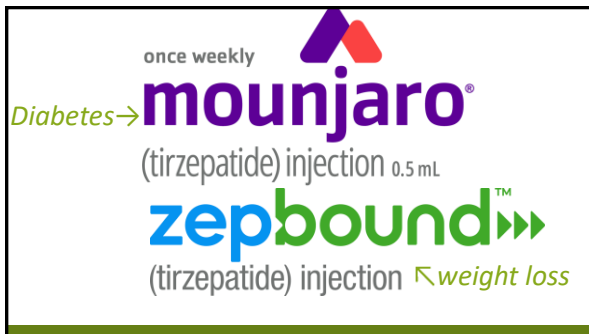
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A1C	A1C%
	9
	8.5
	8
	7.5
	7
	6.5
	6

41

A1C to Estimated Average Glucose (eAG)	A1C%	eAG
	9	212
	8.5	197
	8	183
	7.5	169
	7	154
	6.5	140
	6	126

From the American Diabetes Association https://professional.diabetes.org/diapro/glucose_calc

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Diabetes A1C goals (general)

ADA – Less than 7% →

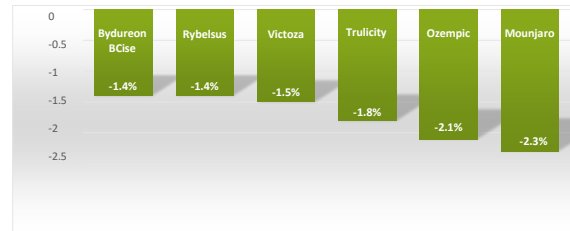
AACE – 6.5% or less →

A1C%	eAG
9	212
8.5	197
8	183
7.5	169
7	154
6.5	140
6	126

ADA – American Diabetes Association AACE – American Association of Clinical Endocrinologists

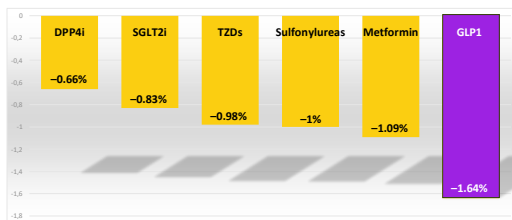
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Average A1C Reduction on Highest Dose of Each Medication



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Average A1C Reduction for Highest Dose in Each Drug Category

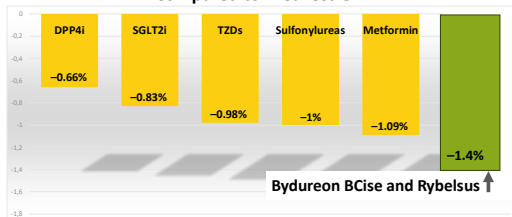


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The weakest GLP1s are stronger than all other diabetes medication categories.

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Average A1C Reduction for Highest Dose in Each Drug Category Compared to Weakest GLP1



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And remember
Incretins are...

glucose-dependent...
aka almost no risk of hypoglycemia

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ASCVD Risk Reduction

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Shown to Be Cardioprotective?

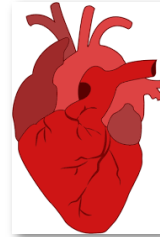
YES

Trulicity

Victoza

Ozempic

Wegovy (wt↓)



NO

Bydureon BCise

Rybelsus

Mounjaro

50

Trulicity

12%

Victoza

13%

Ozempic

26%

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GLP1 / GIP RA Drugs Cheat Sheet

Drug Name	Medical Name	How Taken	↓A1c*	↓Wt*	Cardio-protective?
Saxenda (Wt)	liraglutide	1 x day injection	X	↓6.4%	NO
Wegovy (Wt)	semaglutide	1 x wk injection	X	↓15%	YES
Zepbound (Wt)	tirzepatide	1 x wk injection	X	↓26%	NO
Bydureon BCise	exenatide	1 x wk injection	↓1.4%	X	NO
Trulicity	dulaglutide	1 x wk injection	↓1.8%	X	YES
Victoza	liraglutide	1 x day injection	↓1.5%	X	YES
Ozempic	semaglutide	1 x wk injection	↓2.1%	X	YES
Rybelsus	semaglutide	1 x day pill	↓1.4%	X	NO
Mounjaro	tirzepatide	1 x wk injection	↓2.3%	X	NO

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GLP1 / GIP RA Drug Contraindications

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Contraindications Thyroid

All GLP1 drugs

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Contraindicated If...

A personal or family history of medullary thyroid carcinoma (MTC)

or

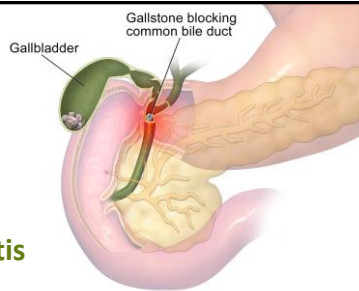
Multiple Endocrine Neoplasia syndrome type 2 (MEN2)

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Warnings and Precautions

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Cholelithiasis And Cholecystitis



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Pancreatitis



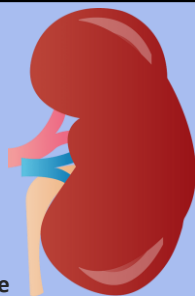
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Retinopathy



CREATED BY VECTORPORTAL.COM

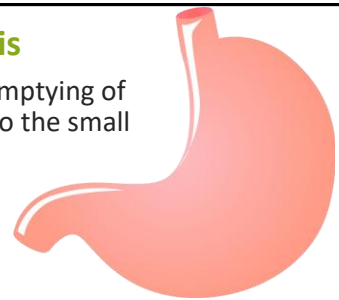
Renal Disease



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Gastroparesis

A delay in the emptying of the stomach into the small intestine.



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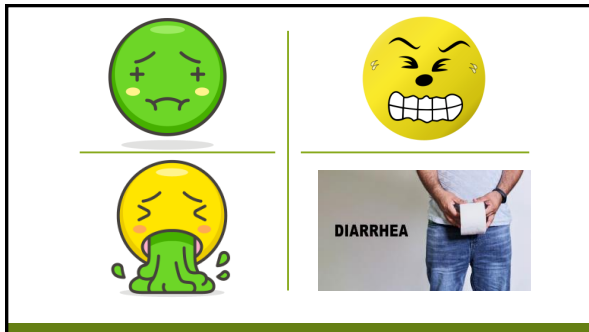


- Hold GLP-1 agonists on the day of the procedure/surgery for patients who take the medication daily.
- Hold GLP-1 agonists a week prior to the procedure/surgery for patients who take the medication weekly.

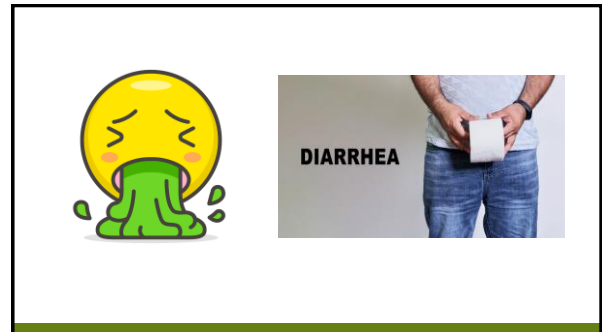
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Side Effects

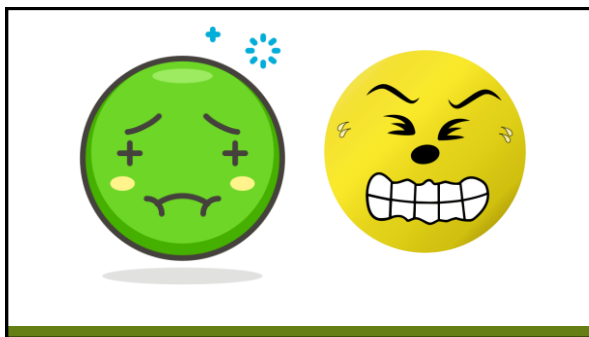
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Titrate to Minimize GI Symptoms

How bad is it?
For all GLP1 drugs except one....

~4-10% discontinued due to GI symptoms

66

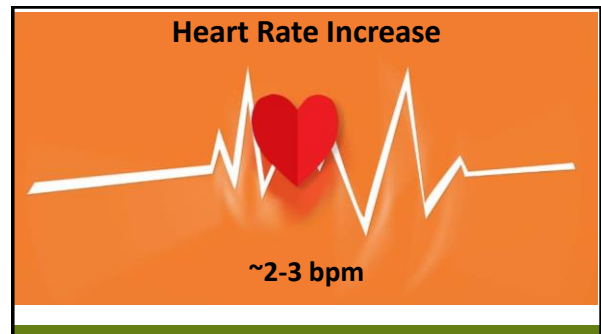
Once-weekly 

BYDUREON® BCise™

- Only 2% D/C due to GI symptoms
- Not as strong for weight loss
- Still 1.4% A1C reduction

 **EASY**
Proven A1C reductions with no titration¹

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**General Guidelines
and
FAQs**

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Can They Be Left Out of The Refrigerator?

Yes! – up to 86°F for at least 2 weeks

Bydureon BCise	28 days
Victoza	30 days
Saxenda	30 days
Trulicity	14 days
Ozempic	56 days
Wegovy	28 days
Mounjaro	21 days
Zepbound	21 days

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What if I missed a dose?

Depends on how many days since this missed dose

If up to this many days since missed dose – take missed dose.
If more take next schedule dose.

Bydureon BCise	4 days
Trulicity	4 days
Ozempic	5 days
Wegovy	5 days
Mounjaro	4 days
Zepbound	5 days

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Missed a DAILY dose?

Victoza		Skip and take next daily dose.
Saxenda		
Rybelsus		

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Can I Switch the Day I Take it?

Yes – as long as the time between doses is at least....

Bydureon BCise	3 days
Trulicity	3 days
Ozempic	3 days
Wegovy	2 days
Mounjaro	3 days
Zepbound	3 days

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Supply Issues

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Trying To Get Rx Filled

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Trying To Get Rx Filled

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I couldn't get it
for a month, do
I restart on my
regular dose?

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I can't get it at
my pharmacy,
can I get it
compounded?

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Compounded “semaglutide” may be semaglutide sodium or semaglutide acetate.

These forms have not been shown to be safe or effective.

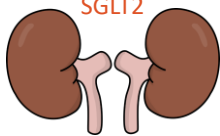
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The Kidneys And SGLT2i

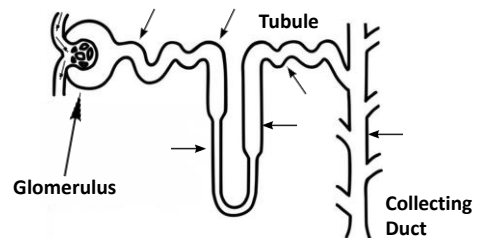
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SGLT2
Sodium Glucose Linked Transporter 2
Inhibitors

SGLT2i
SGLT2

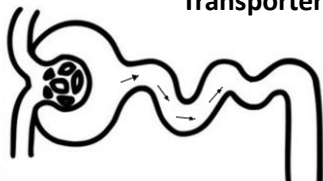


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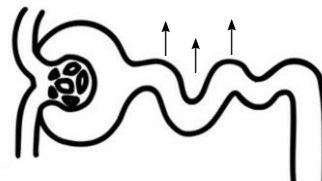
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Sodium Glucose Linked
Transporter 2 (SGLT2)



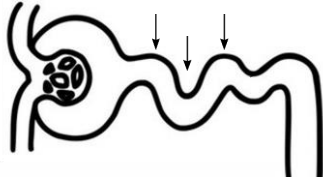
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Sodium Glucose Linked Transporter 2 (SGLT2)
...transports glucose + sodium OUT



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SGL2 Inhibitors



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THE RESULT?

- ↓ blood sugar with very low risk of hypoglycemia
- Pulls out water
 - ↓ blood pressure (a little)
 - Possible dehydration
 - Possible weight loss

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LET'S MEET THE SGLT2i DRUGS!

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SGLT2i Drugs

canagliflozin	Invokana
dapagliflozin	Farxiga
empagliflozin	Jardiance
ertugliflozin	Steglatro
bexagliflozin	Brenzavvy

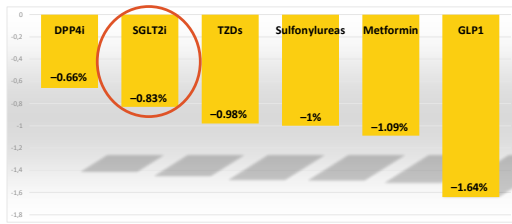
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THE 3 BIG PLAYERS



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A1c Reduction

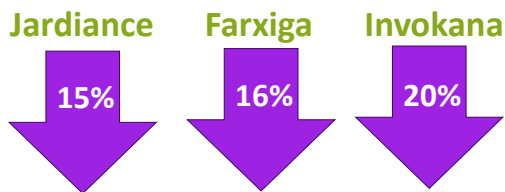


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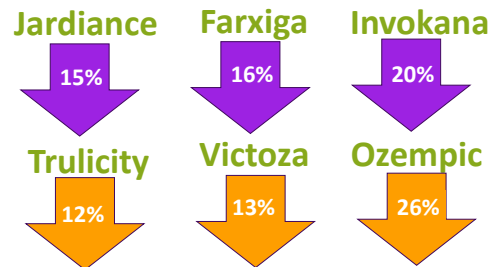
ALL 3 REDUCE MACE



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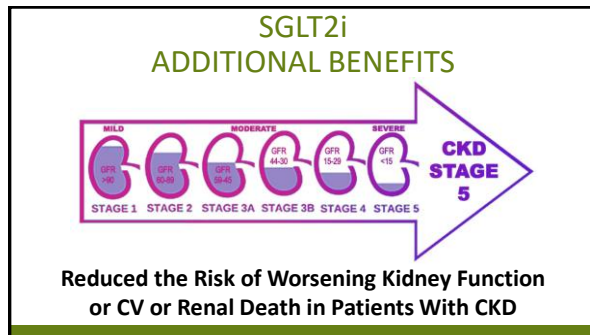
SGLT2i
ADDITIONAL BENEFITS

Reduces CV Death and Hospitalizations
from Heart Failure (HF)

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REDUCES CV DEATH AND HEART
FAILURE HOSPITALIZATIONS

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REDUCES CKD DECLINE

farxiga®
(dapagliflozin) ^{5mg} tablets

Jardiance®
(empagliflozin) tablets
10 mg/25 mg

Approved for CKD with or without type 2 diabetes

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**FOR HEART FAILURE AND
CKD WITHOUT DIABETES**

farxiga®
(dapagliflozin) ^{5mg} tablets

Jardiance®
(empagliflozin) tablets
10 mg/25 mg

FOR DIABETES

Invokana®
(canagliflozin) tablets

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SGLT2i Cheat Sheet					
Drug Name	Medical Name	How Taken	↓A1c*	Indications in addition to Diabetes	Cardio-protective?
Invokana	canagliflozin	1 x day oral	↓1%	None	YES
Farxiga	dapagliflozin	1 x day oral	↓0.7%	CKD HF	YES
Jardiance	empagliflozin	1 x day oral	↓0.8%	CKD HF	YES
Steglatro	ertugliflozin	1 x day oral	↓0.6%	None	NO
Brenzavvy	bexagliflozin	1 x day oral	↓0.56%	None	NO

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**SGLT2i Drug
Contraindications**

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SGLT2i - CONTRAINDICATIONS

Renal Insufficiency

GFR ≥30 – Invokana and Jardiance
GFR ≥45 – Farxiga

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SGLT2i Drug Side Effects

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SGLT2i SIDE EFFECTS

- Glycosuria
- Urinary Tract Infections
- Genital Mycotic Infections (aka Yeast Infections)
- Dehydration

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SGLT2i SIDE EFFECTS

- RARE – Diabetic KetoAcidosis
 - Acute illnesses
 - Surgeries – hold for 3 days prior to surgery
- RARE – Necrotizing fasciitis of the perineum

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Prescribing Recommendations

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Independent of A1C, if...

established or high risk for
ASCVD

...start a GLP1 RA or SGLT2i with proven ASCVD benefit

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Newly Diagnosed?

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Newly Diagnosed?

Independent of A1C, if...

established or high risk for

ASCVD

...start a GLP1 RA or SGLT2i with proven ASCVD benefit

As First Line Therapy

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Recommendations Summary – T2DM with ASCVD or High Risk for ASCVD

GLP1-RA or SGLT2i
with proven benefit

If A1C above
target...
Add metformin

If A1C above target...
If on GLP1-RA add
SGLT2i and vice
versa

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What's Coming!

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Drugs In The Pipeline

<u>Incretin Drugs</u>	<u>Delivery</u>
Cagrisema	Weekly injectable
retatritide	Weekly injectable
orforglipron	Daily pill

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Let's Wrap It Up!

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Incretin Drugs are Game Changers

Unparalleled glycemic benefit

Unparalleled weight loss

Some are cardioprotective

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Incretin Drugs are Game Changers

Make note of contraindications and risks

Most side effects are GI related and do subside over time

If GI side effects are severe or unrelenting, medical intervention is warranted

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SGLT2i Drugs are Game Changers

Not super strong for T2DM

The three major drugs are all cardio-protective

First and only drugs to be approved for HF and CKD with or WITHOUT diabetes

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Diabetes can be difficult, but the newer medications are stronger, safer and come with CVD and other health benefits...

With these new drugs, we can help make it a little easier.

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THANKS FOR JOINING US!

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- <https://www.mounjaro.com/hcg>
- <https://new.novomedlink.com/obesity-treatment/products/saxenda.html>
- <https://www.onglyza-hcg.com/>
- <https://www.ozempicpro.com/>
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