



## Meds for Type 2 – What you need to know

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## Diabetes Meds for Type 2: What You need to Know



1. Describe the main action of the 6 different categories of type 2 diabetes medications.
2. Discuss strategies to determine the right medication for the right patient.
3. List the side effects and clinical considerations of each category of medication.

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## Diabetes Meds for Type 2: What you need to Know



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## ABCs of Diabetes –

- A1c less than 7% (avg 3 month BG)
  - Pre-meal BG 70-130
  - Post meal BG <180
- Blood Pressure < 140/80 (changed in 2013)
- Cholesterol
  - HDL >40
  - LDL <100 (if CHD, <70)
  - Triglyceride < 150
    - [American Diabetes Association Standards of Care](#)

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## Resource Page Underline = Link

- We have added hyperlinks that you can click on for more information.
- So, if you see words underlined click on them to review additional information.
- [Diabetes Medication](#)  
[PocketCards](#)



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## What is Type 2 Diabetes?

- Complex metabolic disorder ....  
(Insulin resistance and deficiency)  
with social, behavioral and environmental risk factors unmasking the effects of genetic susceptibility.



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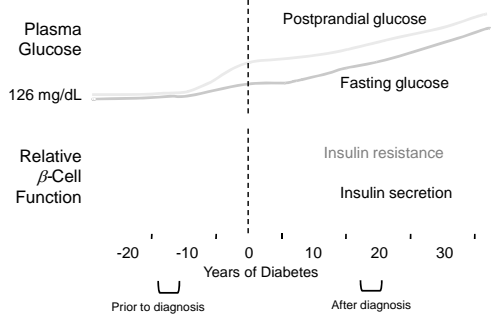
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## Natural Progression of Type 2 Diabetes



Adapted from Bergenstal et al. 2000; International Diabetes Center.  
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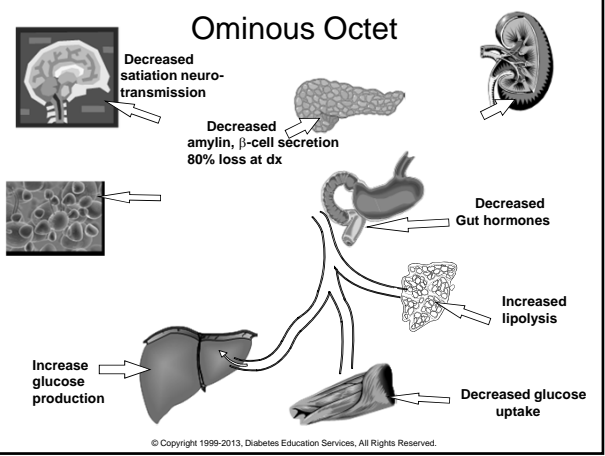
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## Ominous Octet



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## Ominous Octet



### Increased

1. liver production of glucose
2. free fatty acid circulation
3. alpha cell secretion of glucagon
4. glucose reabsorption from the kidney

### Decreased

5. insulin/ amylin secretion (80% of beta cells lost at dx)
6. muscle absorption of glucose
7. gut hormones GLP-1 and GIP
8. neurotransmitter function from the brain (affects appetite control)

From the Triumvirate to the Ominous Octet – a new paradigm for the treatment of T2DM. DeFronzo at the 2008 Banting Lecture.




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## Resources for Medications

- Partnership for Prescription Assistance
  - [www.pparx.org](http://www.pparx.org)
- NeedyMeds.org
- [www.rxassist.org](http://www.rxassist.org)



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## Action/Classes of Type 2 Meds

- |                        |  |
|------------------------|--|
| 1. Suppressor          | Biguanide – Metformin                                    |
| 2. Squirter            | Sulfonylureas<br>Meglitinides                            |
| 3. Satiators           | AmylinoMimetics<br>Incretin Mimetics<br>DPP-4 Inhibitors |
| 4. Sensitizer          | Thiazolidinediones (TZD)                                 |
| 5. Glucoretics         | SGLT2 Inhibitors   |
| 6. Circadian Switchers | Dopamine Receptor Agonists                               |
| 7. Slower              | Alpha-glucosidase inhibitors                             |

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## Diabetes Agents Considerations

- Diabetes medications can be used as monotherapy, in combo or with insulin
- Combining agents from different classes has additive effect
- Most reduce A1c 0.5 – 2.0%
- Not to be used during preconception, pregnancy or when breastfeeding

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### Patient-Centered Approach – Meds Part 2

*“...providing care that is respectful of and responsive to individual patient preferences, needs, and values - ensuring that patient values guide all clinical decisions.”*

- Gauge patient’s preferred level of involvement.
- Explore, where possible, therapeutic choices.
- Utilize decision aids.
- Shared decision making – final decisions re: lifestyle choices ultimately lie with the patient.



Diabetes Care 2013;35:1364-1379  
Diabetologia 2013;55:1577-1596

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### Ideal Diabetes Med -



- No hypoglycemia
- No weight gain
- Affordable
- Lowers CV risk
- Most people can tolerate /use?

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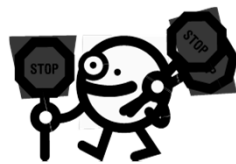
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### Biguanides – Suppressor Metformin (Glucophage®)

- Action: suppresses release of glycogen from the liver
- Who?
  - Fasting hyperglycemia
  - Dysmetabolic Syndrome
  - For pediatrics starting age 10
    - (XR age 17)



Glycogen Stopper

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## Biguanides - Metformin

- **Action:** decrease hepatic glucose (glycogen)
- **Names:**
  - Metformin (Glucophage)
    - Starting dose: 500 BID, max 2500mg daily
  - Metformin extended release (3 different versions)
    - Starting dose 500mg at dinner, max dose 2000 to 2500 mg daily
  - **Efficacy:**
    - Decrease fasting plasma glucose 60-70 mg/dl
    - Reduce A1C 1.0-2.0%

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## Biguanides - Metformin

- **Side effects**
  - Diarrhea and abdominal discomfort
  - Lactic acidosis if improperly prescribed
  - Decrease LDL cholesterol and triglycerides
  - No weight gain, with possible modest weight loss
  - Watch for B12 deficiency
- Hold prior to IV contrast dye studies and use caution during acute illness. Resume when kidney function adequate

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## Considerations

### Biguanide - Metformin (Glucophage®)

- **Contraindications due to lactic acidosis:**
  - creatinine >1.4 females, >1.5 males
  - liver disease
  - alcohol abuse
  - over 80 years old
  - risk of acidosis
  - during IV dye study
  - CHF requiring meds



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## Metformin – How does it rate?

Question	Answer
■ Cause hypoglycemia?	No
■ Cause weight gain?	No
■ Affordable?	Yes
■ Lowers CV risk?	Yes
■ Can most tolerate /use?	Yes/No



(GI, creat)

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## What questions would you ask?

35 yr old, BMI 28, A1c 6.7% x 2. LDL 154, enjoys “occasional” beer.



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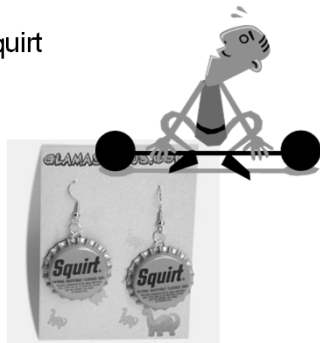
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## Sulfonylureas –

- Action: tells pancreas to squirt insulin all day
- Who?
  - Lean type 2



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## Sulfonylureas - Squirts

- Action: Increase endogenous insulin secretion
- Efficacy:
  - Decrease FPG 60-70 mg/dl
  - Reduce A1C by 1.0-2.0%
- Primary failures: about 20% no response
  - R/O glucose toxicity or low beta cell function
- Secondary failures: 5-10% shortly after initial response, many more later
  - Usually after 5 or more years of therapy due to natural history of DM 2

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## Sulfonylureas: 1st Generation

<u>Trade</u>	<u>Generic</u>	<u>Duration</u>
■ Diabinese*	Chlorpropamide	72 hr
■ Tolinase	Tolazamide	10-14 hrs
■ Orinase	Tolbutamide	6-12 hrs

\*Longest duration. Use with caution in elderly and those with renal disease. Can cause flushing reaction with alcohol.

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## Sulfonylureas: 2nd Generation

<u>Generic</u>	<u>Trade</u>	<u>Duration</u>
■ Glyburide	Diabeta, Micronase, Glynase Prestabs	12-24 hrs
■ Glipizide*	Glucotrol, Glucotrol XI	12-24 hrs
■ Glimepiride	Amaryl	16-24 hrs

\*take short acting product on empty stomach

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## Sulfonylureas

- Other Effects
  - Hypoglycemia
  - Weight gain
  - Cleared by kidney, use caution for pts with kidney problems
  - Generally the least expensive class of medication



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## Indication for “Fast Acting” Insulin Secretagogues- Meglitinides

- Action: tells pancreas to squirt insulin with meals
- Who?
  - Targets post-prandial hyperglycemia



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## Meglitinides - Squirts

- **Action:** stimulate insulin secretion (rapid and short duration) when glucose present
- **Names:**
  - repaglinide (Prandin)
    - **Dosing:** 0.5 to 4 mg a.c. Max dose 16mg
    - Metabolized by liver and mostly excreted in feces (some renally).
  - nateglinide (Starlix)
    - **Dosing:** 120 mg tid with meals
    - Metabolized by liver, excreted by kidney
- **Efficacy:**
  - Decreases peak postprandial glucose
  - Decreases plasma glucose 60-70 mg/dl
  - Reduce A1C 1.0-2.0%

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## Meglitinides

- Other Effects
  - Hypoglycemia (less than with sulfonylureas if patient has a variable eating schedule)
  - Minimal weight gain
  - No significant effect on plasma lipid levels
  - Safe at higher levels of serum Cr than sulfonylureas



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## Squirters – How does they rate?

Question	Answer
■ Cause hypoglycemia?	Yes
■ Cause weight gain?	Yes
■ Affordable?	Yes
■ Lowers CV risk?	No
■ Can most tolerate /use?	Yes/No



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## What questions?

- 72 yr old, thin, lives alone, A1c 7.3%. History of MI, stroke. DM for 12 yrs, “diet controlled”. Creat 1.6



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## Indications for Amylin Mimetics Incretin Mimetics DPP-4 Inhibitors

- **Action: Satiates**
- **Who?**
  - Target post-prandial hyperglycemia
  - Avoid hypoglycemia, wt gain
  - For type 2s only, except Amylin Mimetics used in type 1 and 2.



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## Amylin Mimetic Pramlintide (Symlin) 2005

- **Action:**
  - prevents post-meal rise in glucagon
  - slowing gastric emptying
  - Increases satiety
- **Efficacy:** Decreases A1c by 0.7%, wt by 3lbs
- **Dosing:**
  - Type 2 – max 120 mcg, BID before meals
  - Type 1 – max 60 mcg ac meals (meal = 30 gms carbs)
- **Other:** approved only as adjunct to insulin therapy – can't mix in same syringe with insulin

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## Pramlintide (Symlin) Considerations



**WARNING**  
SYMLIN is used with insulin and has been associated with an increased risk of insulin-induced severe hypoglycemia, particularly in patients with type 1 diabetes. When severe hypoglycemia associated with SYMLIN use occurs, it is seen within 3 hours following a SYMLIN injection.

- Sub-Q injection in abd or thigh prior to meal
- Reduce insulin by 50% when starting pramlintide
- Side effects include **hypoglycemia**, nausea, loss of appetite, redness, swelling at inject site
- Don't use in pts with gastroparesis, hypoglycemia unawareness
- Store unopened vials in refrig, toss after 28 days  
Cost: \$100 for 5 ml vial

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## Amylin Mimetic– How does it rate?

Question	Answer
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- |                           |    |
|---------------------------|----|
| ■ Cause hypoglycemia?     | No |
| ■ Cause weight gain?      | No |
| ■ Affordable?             | No |
| ■ Lowers CV risk?         | No |
| ■ Can most tolerate /use? | No |



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## Great time to Take a Break



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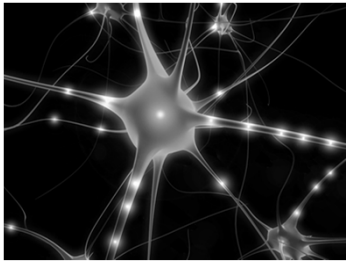
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## Incretin Mimetics – “Gut Hormones” DPP-IV Inhibitors

- How do they work?



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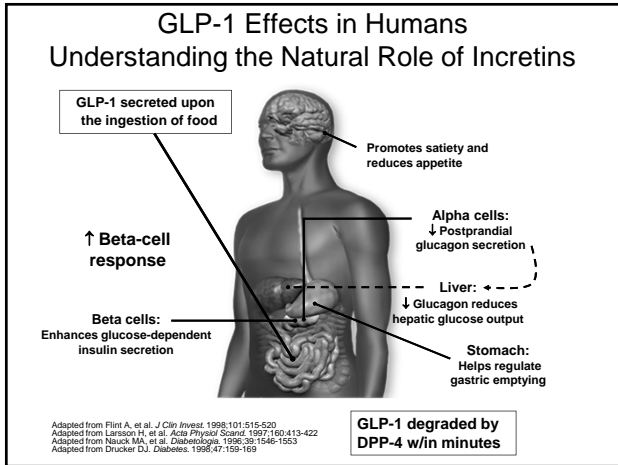
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### Incretin Mimetics

Exenatide (Byetta), Liraglutide (Victoza)

- **Action:**
  - Insulin release in response to meal
  - Slows gastric emptying
  - Causes Satiety
- **Exenatide Dosing:** - 5-10 mcg ac break, dinner
  - Long acting version in pipeline (LAR)
- **Efficacy:** Decreases A1c by 0.7%, wt by 3lbs
- **Indication:** For type 2s only - mono or in combo
- **Other:** In prefilled pens in 5 or 10 mcg doses

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### Incretin Mimetics — Exenatide XR - Bydureon

- **Once a Week Dosing:** 2mg
- **Efficacy:** Decreases A1c by 1.6%, wt by ~6lbs
- **Indication:** For type 2s only
- **Other:** Pt will need to mix powdered form and inject
- **Caution:** not indicated for those with history of medullary thyroid tumor - pancreatitis warning

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\$323.44 for four doses, or about \$4,200 a year.



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### Incretin Mimetics – GLP-1 Analog Liraglutide (Victoza)

**Liraglutide Dosing:** 1x daily, time not critical

- 0.6 x 1 week – if tolerated (nausea), go to >
- 1.2 x 1 week – if tolerated go to >
- 1.8 mg daily

- **Efficacy:** lowers; A1c by 1%, body wt by ~ 2.5kg
- **Indication:** Monotherapy or in combo . Type 2 only
- **Other:** In pen, with preset dosing
- **Black box**–thyroid tumor warning (avoid if family hx, notify MD of hoarseness, lump).

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### Incretin Mimetics Considerations Exenatide, Liraglutide

- Store pens in refrig, toss after 30 days
- Sub-Q Injection in abd, thigh, upper arm
- To prevent hypoglycemia , reduce sulfonylurea/insulin dose when starting
- Side effects include nausea, diarrhea
- Pancreatitis warning (instruct pt to report abd pain, vomiting)
- Don't use w/ gastroparesis, severe renal disease
- Exenatide Cost : \$150-175 for month supply of pen devices

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## Incretin Mimetics – How do they rate?

Question	Answer
■ Cause hypoglycemia?	No
■ Cause weight gain?	No
■ Affordable?	No
■ Lowers CV risk?	No
■ Can most tolerate /use?	Yes/No (GI)



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## DPP-4 Inhibitors – “Incretin Enhancers”

Januvia (sitagliptin) – Tradjenta (linagliptin)  
Onglyza (saxagliptin) - Nesina (alogliptin)

- **Action:**
  - Increase insulin release w/ meals
  - Suppress glucagon
- **Dosing:** Januvia – 100mg a day  
Onglyza – up to 5mg a day  
Tradjenta – 5mg a day  
Nesina – 25 mg a day
- **Efficacy:** Decreases A1c by 0.6 -0.8%
- **Indication:** For type 2s

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## DPP-4 Inhibitors – “Incretin Enhancers”

Januvia (sitagliptin) – Tradjenta (linagliptin)  
Onglyza (saxagliptin) Nesina (alogliptin)

- Januvia, Onglyza eliminated via kidney, lower dose needed
- Tradjenta reduced efficacy in combo w/ CYP 3A4 inducer (e.g., rifampin).
- Do not cause wt gain or hypoglycemia
- Side effects – headache, runny nose, sore throat - watch for pancreatitis
- Cost \$100 - \$150 mo

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## DPP-IV Inhibitors – How do they rate?

Question	Answer
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- |                           |     |
|---------------------------|-----|
| ■ Cause hypoglycemia?     | No  |
| ■ Cause weight gain?      | No  |
| ■ Affordable?             | No  |
| ■ Lowers CV risk?         | No  |
| ■ Can most tolerate /use? | Yes |



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## For all the Previous GLP-1 Enhancers

- **Pancreatitis Warning**
  - Please tell all patients to report signs right away and discontinue meds
  - Signs include:
    - Sudden abdominal pain, nausea and vomiting
- May also be associated w/ increased risk of pancreatic cancer? Studies ongoing.

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## What questions?

- 69 year old male, BMI 25, on Metformin 1000mg BID and Exenatide 5mcg before breakfast and dinner. AM glucose 120s, A1c 8.1%. Creat 1.4



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## Indications for Insulin Sensitizers

Rosiglitazone (Avandia®), Pioglitazone (Actos®)

- Action: **Sensitizers**
- Who?
  - Insulin resistant patient
  - Dysmetabolic syndrome



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## Thiazolidinediones – TZD's

- **Action:** decrease insulin resistance by making muscle and adipose cells more sensitive to insulin. Decrease free fatty acids
- **Names:**
  - pioglitazone (Actos)
    - Dosing: 15-45 mg daily
  - rosiglitazone (Avandia) - restricted
    - Dosing: 4-8 mg daily
- **Efficacy:**
  - Decrease fasting plasma glucose ~35-40 mg/dl
  - Reduce A1C ~0.5-1.0%
  - 6 weeks for maximum effect
  - \$30 a month

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## rosiglitazone (Avandia) Warning

- Avandia FDA Restricted.  
NO new pts can start. Mail order only. Not in pharmacies
  - Associated w/ increase risk of Myocardial Infarction
- Restriction includes combo meds
  - Avandamet
  - Avandaryl

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## Pioglitazone (Actos) Warning

### Bladder Cancer Risk

- Risk increased with increasing dose and duration
- France has pulled Actos, Germany restricted access
- FDA Recommends
  - Do not use in pts with active bladder cancer.
  - Use with caution in pts w/ prior history of bladder CA
  - "Benefits of BG control should be weighed against the unknown risks for cancer recurrence"
- Patient Instructions
  - Report symptoms of bladder cancer: blood or red color in urine; urgent need to urinate or pain while urinating; pain in back or lower abdomen.

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## TZD Actos– How does it rate?

Question	Answer
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- |                           |     |
|---------------------------|-----|
| ■ Cause hypoglycemia?     | No  |
| ■ Cause weight gain?      | Yes |
| ■ Affordable?             | Yes |
| ■ Lowers CV risk?         | No  |
| ■ Can most tolerate /use? | ??  |



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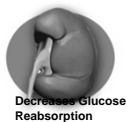
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## SGLT2 Inhibitor-

- **Action:** "Glucoretic" decreases renal reabsorption in the proximal tubule of the kidneys (reset renal threshold and increase glucosuria)
- **Name:**
  - Canagliflozin (Invokana)
  - Dosing: 100 – 300 mg once daily ac first meal
    - If eGFR 45-60: do not exceed 100mg a day
    - If eGFR <45, do not use
- **Efficacy:**
  - Weight loss of 1-3 lbs
  - Reduce A1C ~0.7-1.0%



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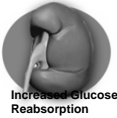
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## SGLT2 Inhibitors – Considerations



- Monitor B/P, K+ & renal function.
- Side effects: hypotension, UTI, increased urination, genital yeast infections.
- Improves beta cell function?
  - Reverses glucoses toxicity by increasing GLUT4 transport in muscle
  - Increase liver sensitivity to insulin and decreases gluconeogenesis.
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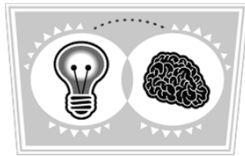
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## “Circadian Switchers” Dopamine Receptor Agonist bromocriptine mesylate QR “Quick Release”

- Action: Increases dopamine levels
  - Decreases insulin resistance
  - Decreases dyslipidemia
  - No weight gain



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## “Circadian Switchers” Increased Dopamine Levels =

### Decreased:

- Insulin resistance
- Hepatic Glucose Output
- Lipolysis / FFA
- Lipogenesis / TG
- Vascular pathology

### Increased:

- Glucose tolerance
- Insulin Sensitivity



DeFronzo R A Dia Care  
2011;34:789-794

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## Dopamine Agonists – Circadian Re-Setters

- **Action:** Increase am dopamine levels
- **Name:** bromocriptine mesylate QR (Cycloset)
  - **Dosing:** 1.6 to 4.8 mg per day
  - Each tab 0.8 mg, start at one tab a day, increase one tab a week
  - Give w/in 2 hrs of waking (before food)
- **Efficacy:**
  - Reduces A1C 0.6 – 0.9%
  - Reduces death from CV events
- **Side Effects:**
  - Nausea, vomiting, headaches, fatigue (watch for syncope)

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## “Circadian Switchers” bromocriptine mesylate QR

- **Other considerations:**
  - Avoid in patients:
    - With syncopal migraines
    - With psychotic disorders
    - Who are breastfeeding (stops lactation)
  - Eval for somnolence
  - Watch for drug/drug interaction w/ meds that affect CYP450 isoenzyme



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## Cycloset– How does it rate?

Question	Answer
■ Cause hypoglycemia?	No
■ Cause weight gain?	No
■ Affordable?	No
■ Lowers CV risk?	Yes
■ Can most tolerate /use?	??



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Indications for Glucosidase Inhibitors  
Acarbose (Precose®), Miglitol (Glyset®)

Action: Slower

- Target post-prandial blood glucose
- Minimal systemic absorption



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Alpha-glucosidase Inhibitors

- **Action:** blocks enzymes that digest starches in the small intestine
- **Name:** acarbose (Precose)
  - Dosing: 75-300mg based on weight
- **Efficacy**
  - Decrease postprandial glucose 40-50 mg/dl
  - Decrease A1C 0.5-1.0%
- **Other Effects**
  - Flatulence or abdominal discomfort
  - Contraindicated in patients with inflammatory bowel disease or cirrhosis
- **Special Consideration**
  - In case of hypoglycemia, treat with glucose tabs or milk
  - (other starches are blocked by medication)

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Acarbose– How does it rate?

<u>Question</u>	<u>Answer</u>
■ Cause hypoglycemia?	No
■ Cause weight gain?	No
■ Affordable?	Yes
■ Lowers CV risk?	Yes
■ Can most tolerate /use?	No/Yes



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## Juvisync Januvia + Simvastatin

- Incretin Enhancer + Cholesterol Lowering
- 3 Doses:
  - 100 mg sitagliptin + 10 mg simvastatin
  - 100 mg sitagliptin + 20 mg simvastatin
  - 100 mg sitagliptin + 40 mg simvastatin
- Plan to develop 50 mg sitagliptin dose
- Observe precautions of each.
- Pancreatitis & muscle weakness/ soreness

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## Juvisync– How does it rate?

Question	Answer
■ Cause hypoglycemia?	No
■ Cause weight gain?	No
■ Affordable?	No
■ Lowers CV risk?	Yes
■ Can most tolerate /use?	Yes



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## Combo Pills for Type 2

### Sulfonylurea + Biguanide

Glyburide	+	Metformin	-	<b>Glucovance</b>
Glipizide	+	Metformin	-	<b>Metaglip</b>

### Thiazolidinedione + Biguanide

Pioglitazone	+	Metformin	-	<b>Actoplus Met</b>
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### Thiazolidinedione + Sulfonylurea

Actos	+	Amaryl	-	<b>Duetact</b>
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### DPP-4 Inhibitor + Biguanide

Januvia	+	Metformin	-	<b>Janumet</b>
Onglyza	+	Metformin XR	-	<b>Kombiglyze</b>

### DPP-4 Inhibitor + Statin

Januvia	+	Zocor	-	<b>Juvisync</b>
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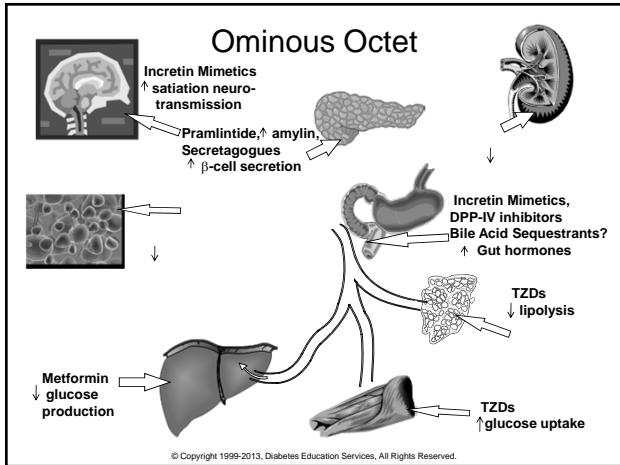
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**J. R.**

49 year old with type 2 diabetes for 9 years.  
 Weight – 370 lbs  
 A1c 13.9%  
 Creat 2.0  
 Gave up checking BG

Meds for past year:

- Januvia
- Byetta
- Determir 20units at hs




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Consider these Clinical Books as additional resources




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## Other Resources

- [Medications and Insulin Online Courses](#)
- [PocketCards](#)
- [Other Free Webinars](#)
- [Resource Page for Meds and Insulin](#)

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## Thank you for joining our Web Clinic



### Wrap up notes

1. You have 1 year to complete this program and take the post test to receive your CE credit (from time of purchase)
2. Complete the post test – click test button
3. Complete program survey – we appreciate your feedback
4. Now, your certificate is ready to print out
5. Join us on [FaceBook](#) for special events

**Keep in touch!**  
 Beverly Thomassian and  
 Lainey Koski




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