The background features a large, semi-transparent 'V' on the left and a play button icon on the right, both in light green. At the bottom, there is a light green rectangular area containing the word 'Vizle' in white. The text 'Drugs Used to Treat Diabetes Mellitus' is centered over these graphics.

Drugs Used to Treat Diabetes Mellitus

Vizle



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- In UKPDS study, patients initially intensively treated with sulfonylurea or insulin had reductions in MI (15%) and death of any cause (13%), while metformin was accompanied with greater reductions in MI (33%) and death of any cause (27%).
- **Other uses:**
- **Polycystic ovary disease:** the ability of metformin to lower insulin resistance in these women can result in ovulation and, possibly, pregnancy.
- **Metformin decreases the risk of diabetes in high risk patients (prediabetic persons).**
- **Metformin is also emerging as a therapy that may reduce cancer risk,** possibly attributable to its activation of AMPK, which can suppress tumor formation.

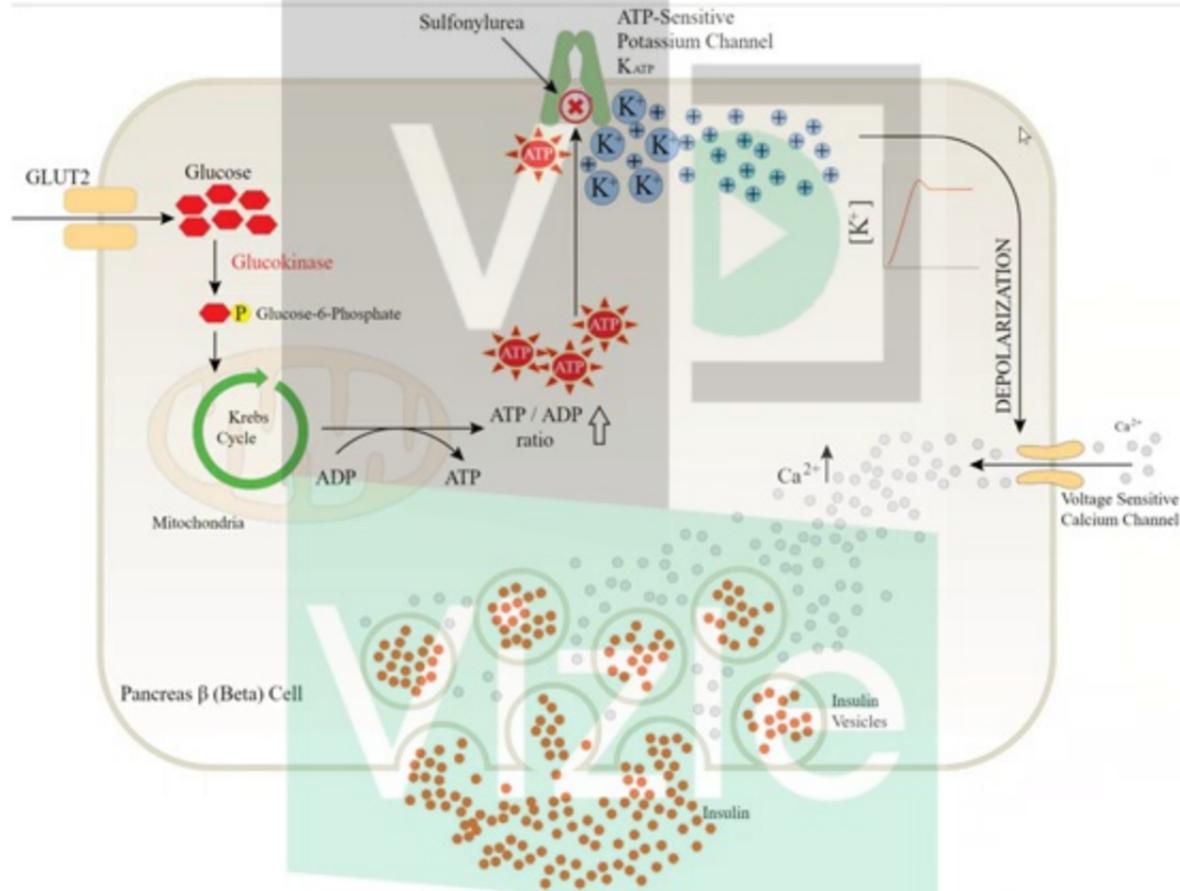
Pharmacokinetics:

- Metformin is not bound to serum proteins, not metabolized. Excretion is via the urine.

Dosing:

- **Metformin immediate-release:** Start at 500 mg orally twice daily with the largest meals and increase by 500 mg weekly as tolerated until reaching glycemic goals or **2500 mg/day**.
- Metformin 850 mg can be dosed once daily and then increased every 2 weeks to maximum 850 mg three times daily (**2550 mg/day**).
- The 750 mg tablets can be titrated weekly to maximum dose of **2250 mg/day**.
- *Notice that metformin immediate-release is taken with meals.*
- **Metformin extended-release** (Glucophage XR): Start with 500 mg orally with the evening meal and increase by 500 mg weekly as tolerated to maximum single evening dose of **2000 mg/day**.
- Administration two or three times daily may reduce GI side effects and improve glycemic control.

Mechanism of action of sulfonylureas



3. Short-acting Insulin Secretagogues (Meglitinides, Glinides)

- *Repaglinide & nateglinide.*

Mechanism of action: they bind to a distinct site on the sulfonylurea receptor of ATP-sensitive potassium channels, thereby initiating a series of reactions culminating in the release of insulin.

- Categorized as postprandial glucose regulators.
- **Average A1C reduction is 0.8% to 1%.**
- They have a faster onset & shorter duration of action than sulfonylureas.
- Combined with metformin or the glitazones.
- Should not be combined with sulfonylureas.

Side effects of glinides:

- Hypoglycemic risk appears to be less with meglitinides than with sulfonylureas.



Side Effects of glitazones :

1. Increased Weight.
 2. Fluid Retention, which presents as mild anemia and peripheral edema (4%) and may increase the risk of heart failure.
 3. Heart failure.
 4. Increase LDL (Rosiglitazone).
 5. ↑ Myocardial infarction with rosiglitazone.
 6. Female patients taking thiazolidinediones appear to have an increased risk of bone fractures.
- Rosiglitazone is less safe than pioglitazone and is associated with more mortality than pioglitazone.
 - The original thiazolidinedione (troglitazone) was removed from the market in several countries because of hepatotoxicity. Rosiglitazone and pioglitazone have not been linked to serious liver dysfunction but still require routine monitoring of liver function.



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