ANTI DIABETIC MEDICATIONS

BENEFITS, COSTS AND ADVERSE EFFECTS

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No disclosure

Objectives

- Recognize all available medical treatment options for diabetes
- Individualize treatment and glycemic target based on patient factors
- Should be able to switch to more affordable treatment regimens when cost is an issue

Case

- 74 y/o male of medical history of osteoporosis, HTN, CKD
- T2DM for more than 15 years
- Admitted to hospital with hyperglycemia and urinary incontinence
- Patient reports that he has not been taking his medication for about 3 weeks because of the cost
- On admission his RBG was 520 mg/dl and A1C 11.6

Home medications

Tresiba 70 units daily

Tradjenta 5 mg daily

Actos 45 mg daily

patient was previously on Levemir , then switched to Tresiba, he recalls that he was switched from metformin but to Tradjenta because its safer for kidneys. He also reports that he was on glimepiride long time ago but not sure why was discontinued. No hx of severe hypoglycemia

NKDA

Hospital course

Patient was mentally alert, was found to have UTI, admitted for IV antibiotics and rehydration, oral medication were discontinued, started on lantus 30 units and Novolog 6 units before meals in addition to correction

After 2 days patient is stable and ready for discharge

His BG was well controlled on the current insulin regimen

BMP: BG 148, BUN 26, Cr 1.5 eGFR 45

What would be the most appropriate discharge regimen

1. Continue Tresiba, Tradjenta and Actos and ask the patient to see his PCP ASAP
2. d/c Tresiba, but continue Tradjenta and Actos
3. d/c Tresiba, Tradjenta and Actos, start Novolog SS
4. d/c Tresiba, Tradjenta and Actos, start Novolin N and metformin
5. d/c Tresiba, Tradjenta and Actos, start Novolin mix 70/30 and glimepiride

The Staggering Costs of Diabetes

GROWING EPIDEMIC

Diabetes affects
30 million
children and adults
in the U.S.

That's
1 in 11
Americans.

84 million Americans
have prediabetes and are at risk
for developing type 2 diabetes.

**90% of them don't know
they have it.**

Every **21 seconds**
someone in the
U.S. is diagnosed
with diabetes.

HUMAN COSTS

African Americans and
Hispanics are over
50%
more likely to have diabetes
than non-Hispanic whites.

People with diabetes are at higher risk of serious health complications:

STROKE | BLINDNESS | KIDNEY DISEASE | HEART DISEASE | LOSS OF TOES, FEET, OR LEGS

ECONOMIC COSTS

The total cost of diabetes
and prediabetes in the U.S. is
$322 billion.

The average price of
insulin increased nearly
between 2002 and 2013. **3x**

People with diabetes have
health care costs
2.3x greater
than those
without diabetes.

Learn more at **diabetes.org**

American Diabetes Association.

Classes of medications

Metformin

Sulfonylureas SU

Meglitinides GLN

Thiazolidindions TZD

Alfa glucosidase inhibitors AG-i

GLP-1 agonist

DPP-4 inhibitors

SGLT-2 inhibitors

Bromocriptin

Colesevelam

Insulin

Pramlintide

Glycemic Recommendations for Nonpregnant Adults with Diabetes

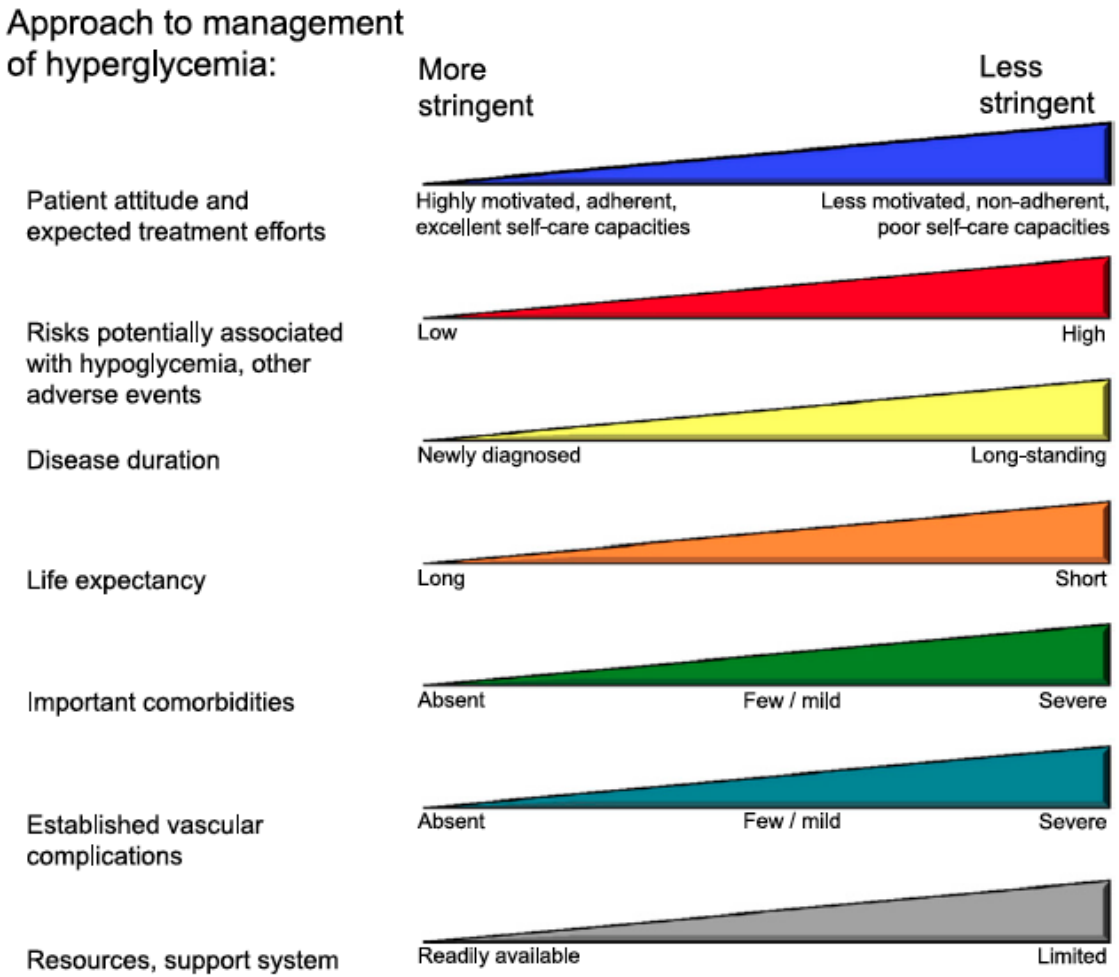
A1C	**<7.0%* (<53 mmol/mol)**
Preprandial capillary plasma glucose	**80–130 mg/dL* (4.4–7.2 mmol/L)**
Peak postprandial capillary plasma glucose†	**<180 mg/dL* (<10.0 mmol/L)**

* Goals should be individualized.

† Postprandial glucose measurements should be made 1–2 hours after the beginning of the meal.

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

Target individualization



American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56

Metformin

- The first choice for oral treatment of type 2 diabetes.
- Glycemic efficacy: 1-1.5%
- Cost: ($)
- No hypoglycemia or weight gain
- Gastrointestinal side effects with initiation and high doses
- B12 deficiency is often overlooked
- Lactic acidosis is exceedingly rare
- Contraindications: GFR<30, decompensated CHF, critical illness

Lu WR et al, Ann Pharmacother. 2013 Nov;47(11):1488-97. Epub 2013 Oct 10

Sulfonylureas

- Long acting: Glimepiride and Glyburide and Short acting: glipizide
- Glycemic efficacy: 1-2%
- Cost: ($)
- Side effects includes hypoglycemia and weight gain
- Hypoglycemia risk higher with long acting
- Gliclazide or Glimipride do not appear to be associated with increased CV risk

Monami M et al, Diabetes Obes Metab. 2013 Oct;15(10):938-53. Epub 2013 May 13.

Meglitinides

- Repaglinide (Prandin) and nateglinide (Starlix) are short-acting hypoglycemics
- Glycemic efficacy: 0.6-2.1%
- Cost ($$)
- Mechanism of action is similar to the sulfonylureas but Less risk of hypoglycemia.
- Useful for patient with allergy to SFU
- Repaglinide is principally metabolized by the liver

Huang Y et al, Diabetes Complications. 2015 Mar;29(2):196-202. Epub 2014 Dec 2.

Thiazolidinediones

- Rosiglitazone (avandia) and pioglitazone (Actos)
- Glycemic efficacy: 0.5-1.4 %
- Cost ($$)
- Side effect: Fluid retention: prominent with concomitant insulin therapy
- Rosiglitazone might be associated with increased CV risk
- Contraindicated in NYHA III CHF
- Concerns: Macular edema, Osteoporosis, bladder cancer

Dormandy JA et al, Lancet. 2005;366(9493):1279.

Alpha-glucosidase inhibitors

- Acarbose and miglitol
- Glycemic efficacy: 0.4-0.9%
- Cost ($$)
- No hypoglycemia
- Side effects : flatulence and diarrhea

Chiasson JL et al, Ann Intern Med. 1994;121(12):928.

GLP-1 agonists

- Injectable Liraglutide (Victoza), Exenatide (Bydureon), dulaglutide (Trulicity), Lixisenatide (soliqua)
- Glycemic efficacy: 1%
- Cost ($$$)
- Benefits: weight reduction (approximately 1.5 to 2.5 kg over 30 week)
- (Liraglutide) appears to decrease macrovascular and microvascular complications
- Side effect: Nausea, vomiting and diarrhea
- Contraindications: h/o pancreatitis, medullary thyroid cancer, gastroparesis
- Semaglutide : CV benefits

Mann JFE et al, N Engl J Med. 2017;377(9):839.

DPP-4 inhibitors

- Sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina)
- Glycemic efficacy: 0.4-0.8%
- Cost ($$$)
- No weight gain or hypoglycemia
- Well tolerated
- ? Acute pancreatitis
- Cases of hepatic dysfunction (liver enzyme elevations, hepatitis) with alogliptin
- Linagliptin metabolized by liver

Amori RE et al, JAMA. 2007;298(2):194.

SGLT2-inhibitors

- Dapagliflozin (Farxiga), canagliflozin (Invokana) and emagliflozin (Jardiance)
- Glycemic efficacy: 0.4-1.1%
- Cost ($$$)
- Benefits: Lowers systolic BP, Weight loss, No hypoglycemia
- Empagliflozin and canagliflozin appear to improve CV outcome
- Sotagloflozin for ? T1DM
- Side effect: Increased incidence of vulvovaginal candidiasis, genital infection and UTI
- Risks: Euglycemic DKA, risk of amputation with canagliflozin

Neal B et al N Engl J Med. 2017;377(7):644. Epub 2017 Jun 12.

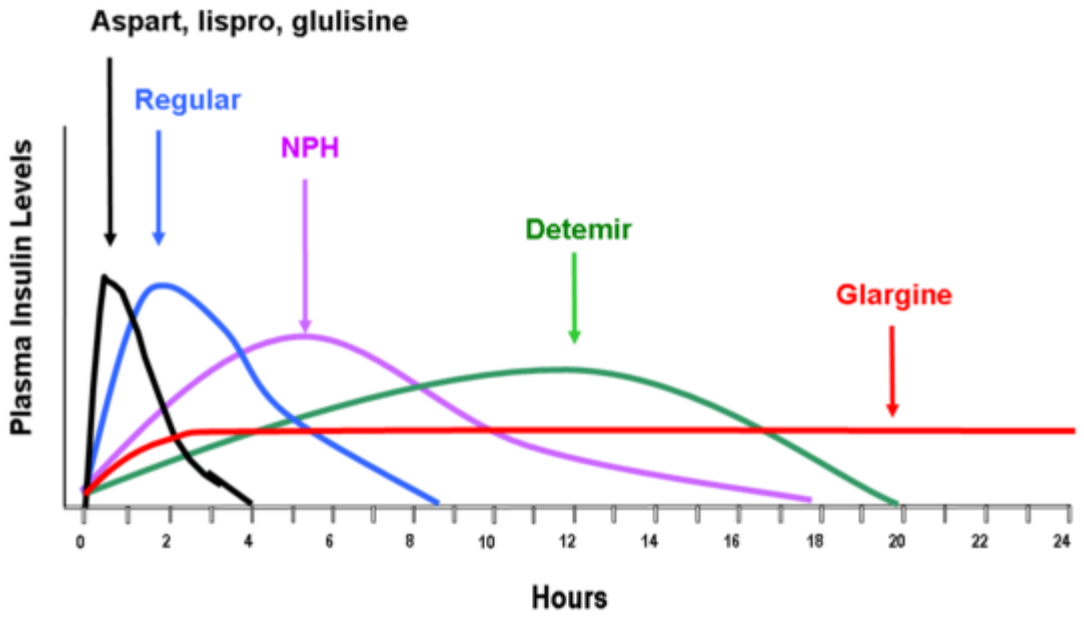
Colesevelam

- Welchol is bile acid sequestrant that lowers (LDL)
- Glycemic efficacy: 0.5%
- Cost ($$$$)
- Mechanism to improve glycemic control is uncertain.
- Side effects can include constipation, nausea, and dyspepsia.

Bromocriptine

- (Cycloset) short acting bromocriptine
- Glycemic efficacy: 0.5%
- Cost ($$$$)
- The mechanism of action in reducing blood sugar is unknown.
- Common side effects include nausea, vomiting, dizziness, and headache.

Insulin preparations



Basal INSULIN

- T1DM: TDD 0.5 units/kg/day, 40% basal, 60% prandial
- T2DM: Add on therapy or starting, 10 U or 0.1-0.2 U/kg administered at bedtime to be titrated
- ($$$) Analog long glargine (Lantus, Basaglar), detemir (Levemir), degludec (Tresiba) lower risk of hypoglycemia
- ($) Human Intermediate (NPH) Novolin N : twice daily, hypoglycemia

BOLUS INSULIN

- T1DM: TDD 0.5 units/kg/day, 40% basal, 60% prandial
- T2DM: Add on therapy or starting, 6 units before 1-3 meals to be titrated
- $$$ Analog rapid aspart (Novolog), lispro (Humalog), glulisine (Apidra) : 5-10 mins before meals.
- $ Human Short regular (Novolin R) : 30 mins before meals
- Ultra Rapid analog Fiasp

Premixed insulin

- Not recommended for T1DM
- Convenient with less injections per day
- Difficult to titrate and needs consistent meal plan and timing
- Premixed insulin may be administered at the largest meal once daily or at the 2 largest meals twice daily.
- ($$$) Analog Intermediate (NPL, NPA) + rapid lispro (Humalog mix), aspart(Novolog mix) different 70/30, 75/25, 50/50
- ($) Human Intermediate NPH + regular 70/30 Novolin mix
- Analog long Degludec + rapid aspart (Ryzodeg)
- Switching from basal use 1:1 ratio, from basal/bolus decrease TTD by 20% , then split 50/50 vs 70/30 with breakfast and dinner to be titrated separately

U-500

- Concentrated
- Available in vials and pens
- Cost ($$)
- Severe insulin resistance: > 200 units per day or 3 U/kg/day
- TTD 60/40 before breakfast and dinner
- > 300 U/day = 40/30/30 before meals

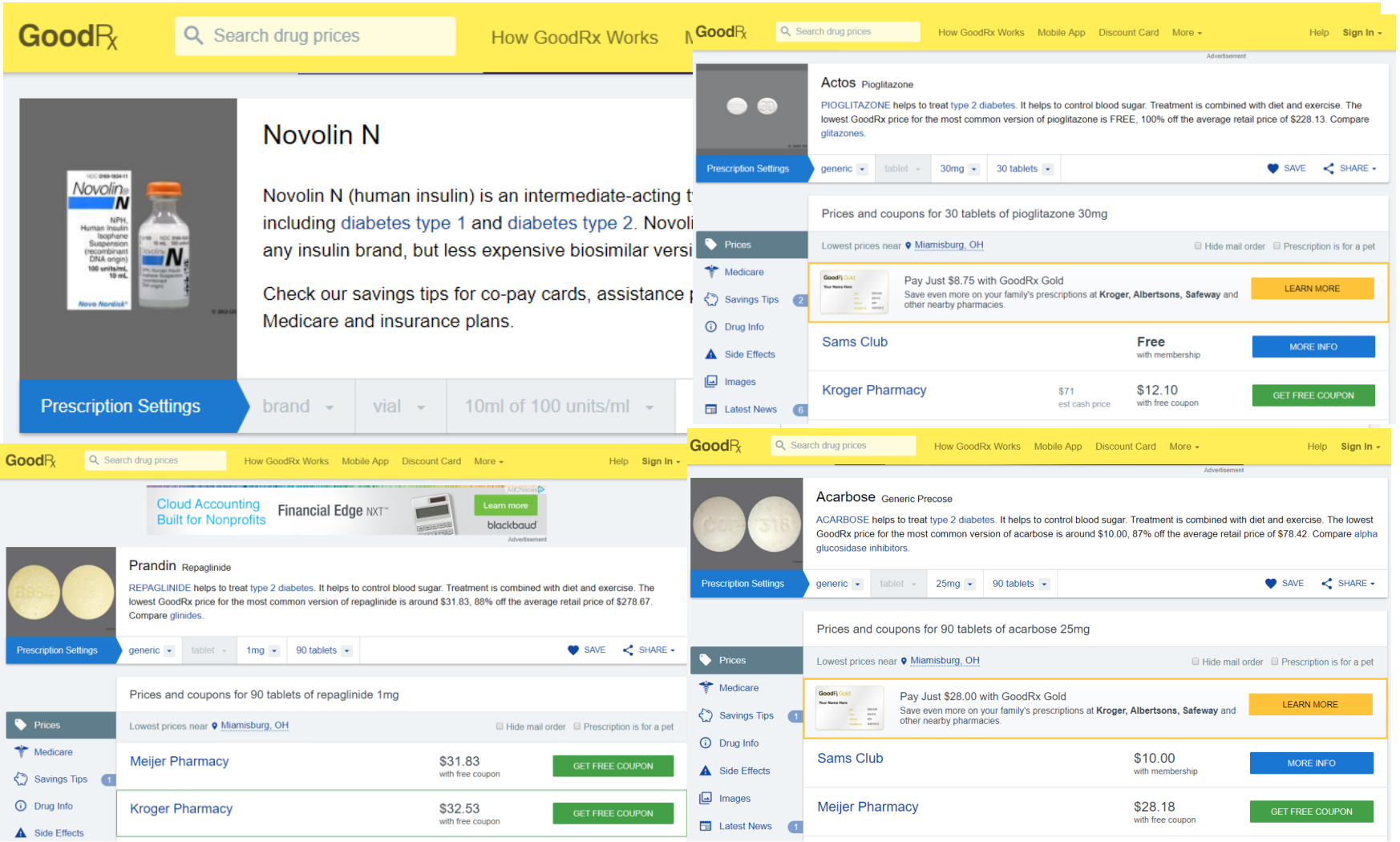
Inhaled insulin

- Ultra rapid Afrezza
- benefits: Needle phobia
- Cost ($$$)
- Side effects includes cough and reactive airway disease
- Contraindicated in chronic lung diseases and in smokers
- Needs PFT monitoring

Pramlintide

- Pramlintide (Symlin) is a synthetic analog of amylin that reduces postprandial blood glucose by slowing gastric emptying and promoting satiety
- Pramlintide is only approved for use in patients also taking prandial insulin to control weight
- Cost ($$$$$)

	$4, 30-day Supply	$10, 90-day Supply	Other
Glimepiride 1mg	30 tablets	90 tablets	–
Glimepiride 2mg	30 tablets	90 tablets	–
Glimepiride 4mg	30 tablets	90 tablets	–
Glipizide 5mg	30 tablets	90 tablets	–
Glipizide 10mg*	60 tablets	180 tablets	–
Glyburide 2.5mg	30 tablets	90 tablets	–
Glyburide 5mg (blue)	30 tablets	90 tablets	–
Glyburide 5mg (green)	30 tablets	90 tablets	–
Glyburide, micronized 3mg	30 tablets	90 tablets	–
Glyburide, micronized 6mg	30 tablets	90 tablets	–
Metformin 500mg	60 tablets	180 tablets	–
Metformin 850mg	60 tablets	180 tablets	–
Metformin 1000mg*	60 tablets	180 tablets	–
Metformin 500mg ER*	60 tablets	180 tablets	–


GoodRx
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Novolin N
Novolin N (human insulin) is an intermediate-acting t
including diabetes type 1 and diabetes type 2. Novoli
any insulin brand, but less expensive biosimilar versi
Check our savings tips for co-pay cards, assistance p
Medicare and insurance plans.
Prescription Settings
brand
vial
10ml of 100 units/ml
GoodRx
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How GoodRx Works
Mobile App
Discount Card
More
Help
Sign In
Actos Pioglitazone
PIOGLITAZONE helps to treat type 2 diabetes. It helps to control blood sugar. Treatment is combined with diet and exercise. The lowest GoodRx price for the most common version of pioglitazone is FREE, 100% off the average retail price of $228.13. Compare glitazones.
Prescription Settings
generic
tablet
30mg
30 tablets
SAVE
SHARE
Prices and coupons for 30 tablets of pioglitazone 30mg
Prices
Medicare
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Drug Info
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How GoodRx Works
Mobile App
Discount Card
More
Help
Sign In
Cloud Accounting
Built for Nonprofits
Financial Edge NXT
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Prandin Repaglinide
REPAGLINIDE helps to treat type 2 diabetes. It helps to control blood sugar. Treatment is combined with diet and exercise. The lowest GoodRx price for the most common version of repaglinide is around $31.83, 88% off the average retail price of $278.67. Compare glinides.
Prescription Settings
generic
tablet
1mg
90 tablets
SAVE
SHARE
Prices and coupons for 90 tablets of repaglinide 1mg
Prices
Medicare
Savings Tips
Drug Info
Side Effects
Lowest prices near Miamisburg, OH
Hide mail order
Prescription is for a pet
Meijer Pharmacy
$31.83
with free coupon
GET FREE COUPON
Kroger Pharmacy
$32.53
with free coupon
GET FREE COUPON
GoodRx
Search drug prices
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Mobile App
Discount Card
More
Help
Sign In
Acarbose Generic Precose
ACARBOSE helps to treat type 2 diabetes. It helps to control blood sugar. Treatment is combined with diet and exercise. The lowest GoodRx price for the most common version of acarbose is around $10.00, 87% off the average retail price of $78.42. Compare alpha glucosidase inhibitors.
Prescription Settings
generic
tablet
25mg
90 tablets
SAVE
SHARE
Prices and coupons for 90 tablets of acarbose 25mg
Prices
Medicare
Savings Tips
Drug Info
Side Effects
Images
Latest News
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MORE INFO
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$28.18
with free coupon
GET FREE COUPON

Start with Monotherapy unless:

A1C is greater than or equal to 9%, **consider Dual Therapy.**

A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 8.2).

Monotherapy — Metformin — Lifestyle Management

EFFICACY*	high
HYPO RISK	low risk
WEIGHT	neutral/loss
SIDE EFFECTS	GI/lactic acidosis
COSTS*	low

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Dual Therapy — Metformin + — Lifestyle Management

	Sulfonylurea	Thiazolidinedione	DPP-4 inhibitor	SGLT2 inhibitor	GLP-1 receptor agonist	Insulin (basal)
EFFICACY*	high	high	intermediate	intermediate	high	highest
HYPO RISK	moderate risk	low risk	low risk	low risk	low risk	high risk
WEIGHT	gain	gain	neutral	loss	loss	gain
SIDE EFFECTS	hypoglycemia	edema, HF, fxs	rare	GU, dehydration, fxs	GI	hypoglycemia
COSTS*	low	low	high	high	high	high

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

Triple Therapy — Metformin + — Lifestyle Management

Sulfonylurea +	Thiazolidinedione +	DPP-4 inhibitor +	SGLT2 inhibitor +	GLP-1 receptor agonist +	Insulin (basal) +
TZD	SU	SU	SU	SU	TZD
or DPP-4-i	or DPP-4-i	or TZD	or TZD	or TZD	or DPP-4-i
or SGLT2-i	or SGLT2-i	or SGLT2-i	or DPP-4-i	or SGLT2-i	or SGLT2-i
or GLP-1-RA	or GLP-1-RA	or Insulin[§]	or GLP-1-RA	or Insulin[§]	or GLP-1-RA
or Insulin[§]	or Insulin[§]		or Insulin[§]		

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

American Diabetes Association®

Combination Injectable Therapy (See Figure 8.2)

Glycemic Control Algorithm

LIFESTYLE MODIFICATION
(Including Medically Assisted Weight Loss)

Entry A1c < 7.5%

MONOTHERAPY*

- ✓ Metformin
- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ✓ AGi
- ⚠ TZD
- ⚠ SU/GLN

If not at goal in 3 months proceed to Double Therapy

Entry A1c ≥ 7.5%

DUAL THERAPY*

MET or other 1st-line agent +

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ✓ DPP-4i
- ⚠ TZD
- ⚠ Basal Insulin
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to Triple Therapy

TRIPLE THERAPY*

MET or other 1st-line agent + 2nd-line agent +

- ✓ GLP-1 RA
- ✓ SGLT-2i
- ⚠ TZD
- ⚠ Basal insulin
- ✓ DPP-4i
- ✓ Colesevelam
- ✓ Bromocriptine QR
- ✓ AGi
- ⚠ SU/GLN

If not at goal in 3 months proceed to or intensify insulin therapy

Entry A1c > 9.0%

SYMPTOMS

NO	YES
DUAL Therapy OR TRIPLE Therapy	INSULIN ± Other Agents

ADD OR INTENSIFY INSULIN
Refer to Insulin Algorithm

LEGEND
- ✓ Few adverse events or possible benefits
- ⚠ Use with caution

* Order of medications listed represents a suggested hierarchy of usage

PROGRESSION OF DISEASE

What would be the most appropriate discharge regimen

1. Continue Tresiba, Tradjenta and Actos and ask the patient to see his PCP ASAP
2. d/c Tresiba, but continue Tradjenta and Actos
3. d/c Tresiba, Tradjenta and Actos, start Novolg SS
4. d/c Tresiba, Tradjenta and Actos, start Novolin N and metformin
5. d/c Tresiba, Tradjenta and Actos, start Novolin mix 70/30 and glimepiride

Questions are guaranteed in life

Answers aren't