

Tolbutamide

Why should I use this medication?

- You should only take this medication if you are unable to take any other medication available for diabetes or if you are having frequent episodes of low blood sugar on other sulfonylureas such as glyburide. Tolbutamide is one of the original medications developed in a class called sulfonylureas and it is rarely used anymore because of questionable side effects (possibly increased chance for heart-related events) and the availability of better medications.
- Taking this medication will decrease your blood sugars, make you feel better, and decrease your risk of complications.
- Taking tolbutamide and/or other medications is only one part of a 3 point plan in the battle against diabetes. You should also make positive lifestyle changes and manage stress.

How will it make my life better?

- In the first month or two, it will be a trade-off. If you are going to have side-effects, it tends to happen in the beginning. After a while, you will experience fewer side-effects. Where tolbutamide really pays off is in the long run since decreasing blood sugar with this medication can reduce the risk of eye, kidney and/or nerve problems by approximately 25%.

How do I know it's working?

This medication should start to work right away but you may not see its full effect for a couple weeks.

You can tell if the drug is working by:

1. Checking your blood sugar on a regular basis. If the drug is working, you should start to see the numbers come down. This medication can lower your blood sugar by up to 4 units (mmol/l), but typically around 1-2 units. Your own results depend on many things so it's not possible to say for sure how well this drug will work for you.

Example: If your blood sugar in the morning is usually around 11 mmol/l, you may see a decrease to 7-9 mmol/l.

2. You start to feel better. Once your blood sugars come down, you'll feel less tired and not so thirsty all the time. You'll also stop going to the bathroom so often.

Your doctor or healthcare provider can tell if the drug is working by:

1. Reviewing your day to day blood sugars with you (it is very helpful if you can jot down your numbers regularly and bring them with you to the clinic).
2. Ordering a blood test called your Hemoglobin A1C. Your A1C is the best "big picture" test for your blood sugar control. It looks at your blood sugar control over the last 2 to 3 months. Tolbutamide can typically decrease this number by 1-2 %.

Dr. Mike's Key Points

- Your body without diabetes does an amazing job of balancing insulin and sugar in your bloodstream. When you skip a meal and your sugar goes down, the body reduces insulin output to keep the balance. Tolbutamide is a sulfonylurea and it works by continually stimulating your pancreas to make more insulin. So you can run into trouble if you skip a meal as tolbutamide is still pushing out the insulin and therefore your blood sugar goes too far down. The bottom line is, as Dr. Christine points out, that you need to put more of an emphasis on eating regularly when you take tolbutamide or you will end up with blood sugar levels that are too low.

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Is there any reason why I shouldn't take this drug?

You should not use this drug if you are allergic to it or to other similar drugs called sulfonylureas (e.g. chlorpropamide, gliclazide, glimepiride, glyburide). This drug should not be used and will not work if you have type-1 diabetes. Before taking this medication, tell your doctor specifically if you have or have ever had:

- kidney disease or lactic acidosis
- an allergic reaction to sulfa-like drugs (e.g. Septra, sulfamethoxazole) – you may have an increased risk to an allergic reaction but overall, your risk is likely minimal.
- low blood sugar (hypoglycemia)
- difficulty eating 2-3 meals per day
- problems with the liver
- porphyria, a group of disorders that result in accumulation of certain body chemicals
- thyroid problems

What about possible side effects?

The most common side effects to tolbutamide are low blood sugar (hypoglycemia) and weight gain. Low blood sugar can usually be seen in up to 5% of patients and some form of weight gain usually occurs in the majority of those who take tolbutamide.

Both side effects are related to the dose but the frequency and severity of low blood sugar is often dependent on other factors such as age, diet, exercise, alcohol and other drugs or medical conditions.

Talk to your doctor or pharmacist about whether you have any risk factors that may make you more sensitive to low blood sugar.

Other side effects that occur less often are:

- Rash (less than 2% of people)
- Increased sensitivity to the sun
- Nausea and heartburn (less than 2% of people – usually related to higher doses and should go away over time.)
- Rare cases (under 0.1% of people) of hepatitis (inflammation of the liver) and jaundice (yellowing of skin and eyes) have been reported. Call your doctor if you experience unexplained nausea, vomiting, stomach pain, fatigue, loss of appetite, dark urine, yellowing of the skin and/or eyes, low sodium in the blood (rare)

- low white blood cells in the blood (rare)
- high insulin levels in the blood and a possible increased risk for heart-related events (one study showed that tolbutamide might have a higher risk for death due to heart disease; however there is debate over “how true” the study results may be)

This is not a complete list of side effects. If you are concerned about these or other unusual symptoms while taking this medication, ask your doctor and/or pharmacist for more information and advice.

What if I am taking other drugs?

Although there are potential interactions with other medications, many of these may not be significant and can be managed by closer monitoring of your blood sugar and discussing any changes with your healthcare provider.

Always provide your doctor with a list of all other drugs you are taking (including over-the-counter medications and herbal/natural products) as they may interact and may change the safety or effectiveness of either drug. Tell your doctor specifically if you are taking any of these drugs as he/she may need to make changes or check you more closely:

- Prednisone, dexamethasone, cortisone, high dose hydrochlorothiazide (greater than 25mg), albuterol, pseudoephedrine, olanzapine, risperidone, niacin. (These drugs may increase your blood sugar and decrease how well chlorpropamide can work).
- Warfarin
- Other diabetes medications (metformin, insulin, rosiglitazone, pioglitazone, repaglinide, nateglinide, acarbose)
- Rifampin: may decrease how well chlorpropamide works
- Sulfamethoxazole (e.g. Septra)
- ASA & other anti-inflammatories (e.g. ibuprofen, voltaren, diclofenac)
- Gemfibrozil (may increase effect of glyburide)
- Cimetidine
- Fenugreek, licorice, bitter melon, eucalyptus, ginseng, St. John's Wort
- Ciprofloxacin or other similar quinolone antibiotics
- Atenolol, metoprolol, propranolol and other beta-blockers. (May decrease your ability to recognize symptoms of low blood sugar)

This is not a complete list of drug interactions. Ask your doctor or pharmacist to review your list of medications.

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Dr. Christine's Pharmacist Tips:

- If you are given a prescription for this medication, you should ask yourself if you have tried all other medications first or if you are having problems with low blood sugar with other sulfonylureas. If the answer is "no", then you should talk to your doctor about a different medication since this one is rarely used anymore.
- Do not drink alcohol while taking this medication as it may cause side effects such as nausea, vomiting, flushing, sweating, headache, heart palpitations
- It is very important to eat 2-3 meals per day while taking this medication. If you don't eat, you may have a greater chance of having low blood sugars. If you find it difficult to maintain a steady intake of food, talk to your doctor or pharmacist as there are other medications that may be better suited for your lifestyle.
- Many people suggest that this medication should be taken 30 minutes before a meal. Although you can do this, the most important thing with this medication is that it is taken around the same time every day.
- Since your skin may burn more easily while taking this medication, you should use sunblock and protective clothing to protect yourself
- If you do develop symptoms of low blood sugar (shaking hands, fast heartbeat, sweating, confusion, dizziness, feeling hungry, feeling tired and drowsy) then take any of the following:
 - 3 glucose tablets, 6 life-savers, 3 teaspoons or packets of tablet sugar in water, 3/4 cup juice
 - Recheck your blood sugar again in 15 minutes, if it is still $< 4\text{mmol/l}$ then repeat the above.
 - Once the blood sugar is normalized (and not too high), you should have a small snack or a meal if it is around that time. This will help prevent another low blood sugar episode.
- This medication may not work as well if you are sick or you may have a greater chance for low blood sugar if you have diarrhea, vomiting or can't eat because of illness. It is best to check your blood sugars more frequently when you are sick. Call your doctor or pharmacist if you have any questions.
- The maximum amount of this medication is usually 500 mg per day. If you have not seen an improvement in your blood sugars after a month of being at your current dose, then you should go see your doctor. He/she may need to make changes.

Dr. Mike's Key Points

- We tend to especially use this type of drug in people who are lean.
- If you are like most of my patients, you don't really like taking medications. Taking pills is easier when you can see an immediate benefit. For example, if you take a pill for arthritis, you feel better within an hour. Taking tolbutamide lowers your overall blood sugar levels (and therefore your A1C) but you may not feel all that different. But make no mistake; lowering your A1C is critical for your long term quality of life.
- Think of taking medications to lower your blood sugar like an investment: it requires some effort and commitment but it will provide large returns in the long run.