

	Ranexa Profile for Chronic Angina (current indication)	Hypothetical Ranexa Diabetes Profile
<b>Indications and Usage</b>	<ul style="list-style-type: none"> <li>Ranexa is indicated for the treatment of chronic angina</li> <li>Ranexa may be used with beta-blockers, nitrates, calcium channel blockers, anti-platelet therapy, lipid-lowering therapy, ACE inhibitors, and angiotensin receptor blockers</li> </ul>	<ul style="list-style-type: none"> <li>Ranexa is indicated for the treatment of Type 2 diabetes alone or in combination with existing anti-diabetic medications (similar indication statement to januvia / actos)</li> </ul>
<b>Efficacy</b>	<ul style="list-style-type: none"> <li>Ranexa, on top of standard of care, reduces angina frequency and nitroglycerin use with improvements in exercise duration and time to 1 mm ST-depression</li> <li>The anti-ischemic and antianginal effects of Ranexa do not depend upon reductions in heart rate or blood pressure, although the mechanism of Ranexa's antianginal effects is undetermined</li> </ul>	<p>Efficacy supporting this approval:</p> <ol style="list-style-type: none"> <li>325 person placebo controlled trial in type 2 diabetics with average baseline HbA1c of 8.5% - Ranexa in monotherapy vs. placebo. (26 weeks)</li> <li>500 person placebo controlled trial in type 2 diabetics with average baseline HbA1c of 8.0% - Metformin + Ranexa vs. Metformin + placebo. (26 weeks)</li> <li>500 person placebo controlled trial in type 2 diabetics with average baseline HbA1c of 8.0% - Metformin + Actos + Ranexa vs. Metformin + Actos + placebo (26 weeks)</li> </ol> <p>Combination trials showed:</p> <ol style="list-style-type: none"> <li>similar efficacy than Januvia, or approximately 0.8% reduction in HbA1c (placebo corrected), on top of baseline meds</li> </ol>
<b>Safety and Tolerability</b>	<ul style="list-style-type: none"> <li>Ranexa has a proven safety profile in high-risk populations including patients with CHF, diabetes, renal impairment, and challenging coronary anatomies</li> <li>Ranexa produced no pro-arrhythmic effects</li> <li>Ranexa is not associated with tolerance or rebound</li> <li>The most common adverse reactions (&gt; 4% and more common than with placebo) during treatment with Ranexa are dizziness, headache, constipation, and nausea</li> <li>Ranexa produced small reductions in A1C in patients with co-morbid diabetes, the clinical significance of which is unknown. Ranexa should not be considered a treatment for diabetes.</li> </ul>	<ul style="list-style-type: none"> <li>Ranexa shows corresponding reductions in post-prandial glucose (PPG) and fasting-plasma glucose (FPG)</li> <li>Ranexa also shows evidence of beta cell preservation by HOMA-B assay</li> <li>There were no instances of hypoglycemia observed (compared to placebo)</li> </ul> <p>CV Safety data supporting approval</p> <ul style="list-style-type: none"> <li>Ranexa has previously been studied in a 6500 person outcomes trial in patients presenting in the ER with acute myocardial infarction. Of these patients, 2,200 had type 2 diabetes and ~20% had CHF. Drug was added by IV for 24-48 hours, and patients were discharged on oral treatment with an average treatment duration of 1 year. No adverse trends in death, MI or other cardiac events were observed. Safety results were similar for the diabetic subpopulation and general population.</li> </ul>
<b>Contraindications</b>	<ul style="list-style-type: none"> <li>Ranexa is contraindicated in patients taking strong inhibitors of CYP3A (eg, ketoconazole, clarithromycin, nelfinavir); patients taking inducers of CYP3A (eg, rifampin, phenobarbital); and with clinically significant hepatic impairment</li> </ul>	
<b>Dosing</b>	<ul style="list-style-type: none"> <li>Patients should begin treatment with 500 mg twice daily and can be increased to the maximum recommended dose of 1000 mg twice daily, based on clinical symptoms</li> <li>Limit the dose of Ranexa to 500 mg twice daily in patients on moderate CYP3A inhibitors, including diltiazem and verapamil</li> </ul>	
<b>MOA</b>	<ul style="list-style-type: none"> <li>Ranexa at therapeutic levels can inhibit the cardiac late sodium current. However, the relationship of this inhibition to angina symptoms is uncertain</li> </ul>	<ul style="list-style-type: none"> <li>Mechanism has been defined as glucose-stimulated insulin secretion – additional insulin is secreted from beta-islets cells, but only in the presence of high levels of glucose.</li> </ul>