

Ozempic for Treatment of Diabetes DRUG SHORTAGE QUICK GUIDE

All formats of Ozempic are in short supply due to global supply constraints and increased demand. Supply is available intermittently but is unpredictable, insufficient to meet current demand, and not expected to stabilize until at least **March 31, 2024**.

For more details and references, see medSask full guidance document.

Options

Continue Ozempic with Available Supply

- As supply permits, use a lower dose (e.g., 0.5 mg instead of 1 mg once weekly).
- Use Ozempic intermittently/with extended dosing interval.
 - Depending on duration between doses, may expect:
 - AIC and weight increases
 - t gastrointestinal adverse effects at next dose; may need lower dose and re-titration if 3 or more doses are missed
 - unknown effects on cardiorenal outcomes

Discontinue Ozempic and Switch

Switch to a Different Antihyperglycemic Agent (different MOA)

- The following do not have the same degree of glucose lowering and weight loss as Ozempic, but may be options:
 - SGLT-2 inhibitors, especially if established or high-risk for cardiorenal disease
 - DPP-4 inhibitors as they may decrease postprandial hyperglycemia
 - Basal (+/- prandial) insulin, especially if glycemic control is a significant concern

Switch to an Alternative GLP-1a or GIP-GLP-1a (same/similar MOA)

- Allows for similar glycemic control as Ozempic; weight and cardiorenal benefits are similar but vary depending on the specific agent.
- Consider cost and coverage (several are not covered by SK Drug Plan or NIHB).
- Drug shortages of these agents may occur. See medSask Drug Shortages.

See the <u>RxFiles Outcomes Comparison Summary Table</u> for considerations

Discontinue Ozempic

• It may be possible for some patients to maintain control without Ozempic. See <u>full document</u>.



Considerations for Choosing Alternative Agents

Unless otherwise specified, all agents in a class are included.

AIC Lowering

- insulin, GIP-GLP-1a MOST
 - GLP-1a, metformin, SU
 - repaglinide, TZD
- LEAST SGLT-2i, DPP-4i

Risk of Hypoglycemia

- intensive insulin (multiple daily doses) MOST
 - less intensive insulin (e.g., once daily basal), SU (glyburide)
 - repaglinide, SU (gliclazide, glimepiride) TZD (rosiglitazone)
 - DPP-4i, GLP-1a, GIP-GLP-1a, SGLT-2i, TZD (pioglitazone)
- LEAST | metformin

Weight Changes

Gain	• insulin, TZD	
$\mathbf{\uparrow}$	 repaglinide, SU 	
Neutral	• DPP-4i	
$\mathbf{+}$	• SGLT-2i, metformin (or neutral)	
Loss	• GIP-GLP-1a, GLP-1a	

Use in Chronic Kidney Disease

Reduced risk of progression	SGLT-2i if eGFR >20 ml/min

See Diabetes Canada Appendix 7 for dosage adjustments/precautions in renal impairment

Formulary Status	Saskatchewan Drug Plan	NIHB
Open Benefit	 insulin* metformin repaglinide SU (gliclazide MR, glyburide) 	 DPP-4i (linagliptin, saxagliptin, sitagliptin[‡]) insulin GLP-1a/insulin (lixisenatide/insulin glargine) metformin repaglinide SGLT-2i (canagliflozin[‡], dapagliflozin, empagliflozin) SU (gliclazide, glyburide) TZD (pioglitazone)
EDS/LUB	 DPP-4i (linagliptin, saxagliptin, sitagliptin) GLP-1a/insulin (lixisenatide/insulin glargine) SGLT-2i TZD 	
Not covered	 DPP-4i (alogliptin) GIP-GLP-1a GLP-1a (dulaglutide, liraglutide, PO semaglutide) GLP-1a/insulin (liraglutide/insulin degludec) metformin XR SU (glimepiride) 	 DPP-4i (alogliptin) GIP-GLP-1a^ GLP-1a (dulaglutide, liraglutide, PO semaglutide) GLP-1a/insulin (liraglutide/insulin degludec) metformin XR SU (glimepiride) TZD (rosiglitazone)

*Novorapid for use in insulin pumps is EDS [‡]LUB status has been lifted temporarily during the Ozempic shortage ^ Formulary status under review

Cardiovascular Outcomes

GLP-1a (subcut), SGLT-2i (canagliflozin, empagliflozin), metformin (potential), TZD (pioglitazone [potential]) **Improved MACE** SGLT-2i, metformin (potential) **Improved HF** SGLT-2i **Improved CKD** DPP-4i (alogliptin, linagliptin, sitagliptin), GLP-1a (PO), GIP-GLP-1a, insulin, repaglinide, SU Neutral/Unknown DPP-4i (saxagliptin [potential]), TZD CV Harm (HF)



Switching from Ozempic

• to GLP-1a or GIP-GLP-1a:

- Choose a dose (see <u>full document</u> for considerations).
- Administer the dose 7 days after the last Ozempic dose.
- Oral semaglutide can be administered within 7 days of the last Ozempic dose. For maximum absorption, oral semaglutide must be taken on an empty stomach with minimal water and nothing else for at least 30 minutes.

• to agents from a different antihyperglycemic class:

- In general, use the starting dose of the new agent.
- Consider current glycemic control, renal function, and drug interactions.
- Start the new agent 7 days after the last Ozempic dose.



Optimizing Treatment

- In some cases, doses of existing antihyperglycemic agents may have room to be increased if the current dose is the usual starting dose.
- Be mindful of renal function and increased risk of hypoglycemia.
- Note that SGLT-2 inhibitors are **not** associated with additional AIC lowering or cardiorenal benefit at higher therapeutic doses.
- When increasing basal insulin doses, be aware of overbasalization. See <u>full document</u>.

Ensure patient is educated on:

- When to start new medication
- How to administer new medication
- Side effects including signs and symptoms of hyper/ hypoglycemia
- How to store new medication
- What to expect from new medication

Abbreviations

AIC=glycated hemoglobin CKD=chronic kidney disease EDS=Exception Drug Status eGFR=estimated glomerular filtration rate HF=heart failure LUB=Limited Use Benefit MACE=major adverse cardiovascular events MOA=mechanism of action MR=modified release NIHB=Non-Insured Health Benefits PO=oral subcut=subcutaneous XR = extended release

Drug Class Abbreviations and Agents Included

DPP-4i=dipeptidyl peptidase-4 inhibitor and includes: alogliptin, linagliptin, saxagliptin, sitagliptin

GIP-GLP-1a=glucose-dependent insulinotropic polypeptide - glycoprotein-like peptide-1 agonist and includes: tirzepatide GLP-1a=glycoprotein-like peptide-1 agonist and includes: subcutaneous formulations (dulaglutide, liraglutide, semaglutide [Ozempic]) and oral (semaglutide) GLP-1a/insulin includes: liraglutide/insulin degludec, lixisenatide/insulin glargine Insulin includes regular and analogues

SGLT-2i=sodium glucose transporter-2 inhibitor and includes: canagliflozin, dapagliflozin, empagliflozin **SU**=sulfonylureas and includes: gliclazide, glimepiride, glyburide

 $\textbf{TZD}\mbox{=} thiazolidine diones and includes: pioglitazone, rosiglitazone$