Chronic Kidney Disease in Diabetes Mellitus 2 (CKD in DM2) Primary Care [Team] Pathway for Optimizing Kidney and Cardiovascular Outcomes:

For use in Stable Ambulatory Patients over 18 years of age

Quick links: Glossary | Expanded details | Provider resources | Patient resources

Adult with type 2 diabetes → Appropriate counselling/use of lifestyle therapies

Change in clinical status or review of diabetes targets

Required Therapy and Targets

- **Metformin** - if indicated
- Ensure optimal cardiorenal protection:
  1. **ACE/ARB**: Prescribe if HTN (BP target < 130/80)
  2. **Statin**: Prescribe as per guidelines
  3. Medication reconciliation and relevant de-prescribing
     e.g., Sulfonylureas

No red flags

If Red Flags present

Immediate initiation of insulin therapy or transfer to Urgent Care **recommended** if evidence of Metabolic Decompensation, defined as one of more of the following:

1. Unintentional severe weight loss due to diabetes **OR**
2. Marked or symptomatic hyperglycemia **OR**
3. Diabetic Ketoacidosis/Hyperosmotic Syndrome

Consider based on history and current visit

Kidney Protection

Prioritize CKD in DM2 with ACR > 3

Note: If intolerant to any medication category, other medication categories for kidney protection may still be used

Should be used in conjunction with the CKD Pathway

Optimal kidney protection. Confirm **ACE/ARB** is prescribed to max tolerated dose
- BP target < 130/80

GFR ≥ 20 (mL/min/1.73m^2)?

Yes → **SGLT2is**: Prescribe for cardiorenal protection
- Prescribe if ACR < 3; consider if GFR < 45

Safe use: SGLT2is (Sick Day Meds)

No → Consult Nephrology prior to initiating SGLT2i

Additional Foundational Kidney Protection

Finerenone: Prescribe if GFR ≥ 25 and ACR > 3

Avoid initiation if K^+ > 5.0

- If K^+ ≥ 4.8 measure electrolytes and creatinine **within 4 weeks**
- If K^+ 4.9 - 5.0 measure electrolytes and creatinine **more frequently** as per monograph

Heart (CV) Protection

Cardiovascular disease?

Atherosclerotic Cardiovascular Disease (ASCVD) and Multiple Risk Factor (MRF)

Optimal CV protection. Confirm **ACE/ARB** and **Statin** to max tolerated dose

Heart Failure predominates
Ensure optimal guideline directed medical therapy for HF in addition to prescribing SGLT2i

Heart Failure Pathway

ASCVD/MRF predominates
History of stroke, TIA, heart disease, myocardial infarction, peripheral artery disease; evidence of atherosclerosis; angina

Consider prescribing in combination
1. SGLT2i
2. GLP-1
GLP-1RA may be preferred where blood sugar lowering/weight loss is priority

Review appropriate **GLP-1** for A1C Optimization

DO NOT use GLP-1 and DPP-4i together due to redundant mechanism of action

Reassess patient regularly as per guidelines

Prescribe appropriate **SGLT2is** for cardiorenal organ protection or A1C optimization

A1C Optimization

Target: A1C ≤ 7.0% or individual target

Insulin may be indicated on patients who remain above target despite optimal therapy or in those who have metabolic complications of hyperglycemia

Consider most appropriate care stream based on patient goal(s). Goals listed below.

Reduce weight

Minimize hypoglycemia risk

Multiple possible agents **GLP1-RA, SGLT2i, DPP4i**
Refer to Diabetes Canada Guidelines

Reduce blood glucose

Consider other agents. See Diabetes Canada User's Guide

Consider Endocrinology referral

Safe use: SGLT2is (Sick Day Meds)

Continue monitoring patient per guidelines
Medication reconciliation and relevant de-prescribing

Consider using specialist tele-advice or continue on pathway depending on clinical situation or concern

Pathway Primer

The Chronic Kidney Disease in Diabetes Mellitus 2 (CKD in DM2) Primary Care Team Pathway for Optimizing Kidney and Cardiovascular Outcomes is intended to provide evidence-based guidance to support primary care providers and clinical pharmacists in providing guideline concordant therapy in caring for patients over the age of 18 years-old who are living with diabetes and kidney and/or heart disease within the medical home.

Originally envisioned as a treatment pathway to improve the care and treatment of persons living with kidney disease, it became evident the pathway needed to expand to address treatment of persons living with cardiovascular disease and those requiring Hemoglobin A1C control. The pathway also aims to improve the rate of SGLT2i (sodium/glucose cotransporter-2 inhibitor) prescriptions for appropriate patients.

The provincial working group who developed this pathway includes physician representation from

- Cardiology
- Endocrinology
- General Internal Medicine
- Nephrology
- Primary Care

The Working Group also included Pharmacists working in Diabetes and Kidney Care along with representatives from

- The Kidney Health Section, Medicine Strategic Clinical Network
- The University of Calgary and the University of Alberta Physician Learning Programs
- The Health Quality Council of Alberta
- Members from the University of Calgary's Chronic Kidney Disease (CKD) Pathway team

EXPANDED DETAILS

1. Glossary of Terms

ACEi – angiotensin converting enzyme inhibitor

ACR > 3 – albumin creatinine ratio > 3

ARB – angiotensin receptor blocker

BP – blood pressure

CKD – chronic kidney disease

CV – cardiovascular

CVD – cardiovascular disease

DM2 – type 2 diabetes

DPP 4 – dipeptidyl peptidase-4 inhibitors

GFR – glomerular filtration rate

GLP1- RA – glucagon-like peptide 1 receptor agonists

A1C – hemoglobin A1C

HTN – hypertension

SGLT2i – sodium glucose luminal transport inhibitors

2. Definitions

CKD (chronic kidney disease) – is defined as GFR <60 or ACR > 3
CKD and DM2 (chronic kidney disease and type 2 diabetes) – is defined as an ACR > 3
DM2 – is defined as pre-treatment/historical HgbA1C ≥ 6.5%

3. Medications

Metformin

Metformin Product Monograph	Normal dose range	eGFR (mL/min/1.73m^2)		
		≥ 60	≥ 30 to < 60	< 30
	1000mg bid or 850mg tid	No dose adjustment required	• If initiating, start at 250 – 500mg daily • Titrate based on patient effect • Maximum dose: 1000mg bid • NOTE: eGFR closer to 30, consider lowering dose • If already on Metformin, maintain current dose	• Consider discontinuing • May consult Nephrology

SGLT2 Inhibitors

- Dapagliflozin and Empagliflozin are indicated by Health Canada to prevent progression of kidney disease in patients with, and without, Type 2 Diabetes.
- Canagliflozin is indicated by Health Canada to prevent of progression of kidney disease in patients with Type 2 Diabetes

Canagliflozin (Invokana ®) Product Monograph	**Normal dose range**: 100 to 300mg PO OD depending on clinical indication		**eGFR (mL/min/1.73m^2)**		
	Organ protection	**A1C optimization**	**≥ 60**	**≥ 30 to < 60**	**< 30**
	100mg PO daily for organ protection	Starting dose 100mg PO daily. May increase up to 300mg PO daily for additional A1C control	No dose adjustment required	100mg PO daily is the recommended dose for patients with a GFR< 60	• Do not initiate at GFR <30; but may continue 100mg PO daily for CKD or Heart Failure. • Consider Nephrology consult • Discontinue once on dialysis
Dapagliflozin (Forxiga ®) Product Monograph	**Normal dose range**: 5 to 10mg PO OD depending on clinical indication		**eGFR (mL/min/1.73m^2)**		
	Organ protection	**A1C optimization**	**≥ 60**	**≥ 25 to < 60**	**< 25**
	10mg PO daily for organ protection	Starting dose 5mg PO daily. May increase up to10 mg daily for additional A1C control	No dose adjustment required	• No dose adjustment required • May continue for heart failure or CKD	• Do not initiate at GFR <25; but may continue 10mg PO daily for CKD or Heart Failure • Consider Nephrology consult • Discontinue once on dialysis
Clinical Note: **As of September 1, 2023, Dapagliflozin is listed as a regular benefit in Alberta.**					
Empagliflozin (Jardiance ®) Product Monograph	**Normal dose range**: 10 to 25mg PO OD depending on clinical indication		**eGFR (mL/min/1.73m^2)**		
	Organ protection	**A1C optimization**	**≥ 30**	**≥ 20 to < 30**	**< 20**
	10mg PO daily for organ protection	Starting dose 10mg PO daily. May increase to 25mg PO daily for additional A1C control	No dose adjustment required	10mg PO daily is the recommended dose for patients with a GFR< 30	• Do not initiate at GFR <20; but may continue 10mg PO daily for CKD or Heart Failure • Consider Nephrology consult • May continue on dialysis, but there is limited data

SGLT2i weight loss and hypoglycemia risk

Class	Medication	Hypoglycemia		Weight Loss	ABC Formulary	Cardiovascular Outcomes	Renal Outcomes
		Monotherapy	Combo therapy[1]				
SGLT-2 Inhibitors	Dapagliflozin	N/A	Min-mod[1]	1 – 3 kg	Yes	Yes	Yes
	Empagliflozin	Rare	Min-mod[1]	1 – 3 kg	Yes	Yes	Yes
	Canagliflozin	Rare	Rare	1 – 3 kg	Yes	Yes	Yes

[1]min-mod (minimum- moderate). Depending on the nature of combination therapy. May be elevated if patient is already well controlled on insulin or a secretagogue.

Legend
Rare hypoglycemia
Considering lowering insulin of SU dose

Alberta Blue Cross

DPP-4 / SGLT2 Inhibitors / GLP-1 Receptors Agonists

Special Authorization Request Form:

https://idbl.ab.bluecross.ca/idbl/DBL/60012.pdf

As of September 1, 2023, Dapagliflozin is listed as a regular benefit.

Data source for hypoglycemia

Diabetes Canada Guidelines

https://guidelines.diabetes.ca/cpg/chapter13

Mineralocorticoid Receptor Antagonists

Finerenone (Kerendia®) Product Monograph	**Initiation dose**	**eGFR (mL/min/1.73m2)**		
		≥ 60	**≥ 25 to < 60**	**<25**
	• 10mg to 20mg PO daily • Target dose is 20mg PO daily	Starting dose 20mg PO daily	Starting dose 10mg PO daily	• Do not initiate at eGFR <25, but may continue until eGFR reaches 15 or dialysis • Consider Nephrology consult
Potassium (K^+) Warning: • If **K^+ > 5.0 do not initiate**; may maintain on Finerenone if K^+ > 5.0 (If currently on therapy and K^+ > 5.0 see adjustment table below) • If K^+ ≤ 4.8 recommend measuring electrolytes and creatinine at 4 weeks • If K^+ 4.9 – 5.0 measuring electrolytes and creatinine more frequently as per product monograph Clinical Note: • Finerenone can be prescribed in addition to ACE/ARB and/or SGLT2i for patients with **GFR ≥ 25 and ACR > 3 and K^+ ≤ 5.0 (see K^+ note above).** • If eGFR has decreased by > 30% compared to previous measurement, investigate for causes of Acute Kidney Injury (AKI) and consider holding or dose-reducing finerenone • Ensure full medication assessment completed prior to initiation to consider potential drug interactions				
Alberta Blue Cross Finerenone Special Authorization Request Form: https://idbl.ab.bluecross.ca/idbl/DBL/60111.pdf				

Finerenone Maintenance Dose Adjustment (applicable only to GFR > 60; where GFR < 60, dose should not be titrated)

Current serum potassium (mmol/L)	**Current Finerenone dose**	
	10mg PO daily	**20mg PO daily**
≤4.8	Increase to 20mg PO daily	Continue 20mg PO daily
>4.8 to ≤5.5	Continue 10mg PO daily	Continue 20mg PO daily
>5.5	Hold therapy. May consider restarting at 10mg PO daily when serum potassium ≤5mmol/L.	Hold therapy. Restart at 10mg PO daily when serum potassium ≤5mmol/L.
Clinical Note: If eGFR has decreased by > 30% compared to previous measurement, investigate for causes of Acute Kidney Injury (AKI) and consider holding or dose-reducing finerenone.		

GLP-1 Receptor Antagonists

	Normal dose range	eGFR (mL/min/1.73m^2)		
		> 60	**30 to 60**	**< 30**
Dulaglutide (Trulicity ®) Product Monograph	• Initiating dose: 0.75mg SC once weekly • For additional glycemic control, dose may be increased by 1.5mg/week at 4-week intervals up to 4.5mg SC weekly	No dose adjustment required	No dose adjustment required	• No dose adjustment required • Use with caution at < 15mL/min • Monitor renal function for transient decline in patients with renal impairment reporting severe gastrointestinal reactions which may worsen the renal function
Liraglutide (Victoza ®) Product Monograph	Initiating dose: 0.6mg SC daily for 1 week, then 1.2mg SC daily (max 1.8 mg/day SC)	No dose adjustment required	No dose adjustment required	• No dose adjustment required; use not recommended < 15mL/min due to limited clinical experience • Monitor renal function for transient decline in patients with renal impairment reporting severe gastrointestinal reactions which may worsen the renal function
Semaglutide (Ozempic ®) Product Monograph	• Initiating dose: 0.25mg SC weekly for 4 weeks, then 0.5mg SC weekly. • For additional glycemic control may increase by 0.5mg/week at 4-week intervals up to 2mg SC weekly (reference: https://guidelines.diabetes.ca/cpg/chapter13)	No dose adjustment required	No dose adjustment required	• No dose adjustment required • Use with caution < 30mL/min and use not recommended in patients with end- stage renal disease • Consult Nephrology if considering initiation

GLP-1 weight loss and hypoglycemia risk

Class	Medication	Hypoglycemia		Weight Loss	ABC Formulary	Cardiovascular Outcomes	Renal Outcomes
		Monotherapy	Combo therapy[1]				
GLP 1 Agonists	Semaglutide inj	Rare	Min-mod[1]	>3 kg	Yes	Yes	Yes[2]
	Semaglutide po	Rare	Min-mod[1]	>3 kg	No	No	No
	Dulaglutide	Rare	Min-mod[1]	Monotherapy: 0 – 1 kg	No	Yes	Yes[3]
		Rare	Min-mod[1]	Combo therapy with SGLT2i or metformin: 1 – 3 kg			
	Liraglutide	Rare	Min-mod[1]	1 – 3 kg	No	Yes	Yes[3]

[1]min-mod (minimum- moderate). Depending on the nature of combination therapy. May be elevated if patient is already well controlled on insulin or a secretagogue

[2]based on outcomes and evidence from the FLOW trial (https://www.nejm.org/doi/full/10.1056/NEJMoa2403347)

[3]Based on secondary outcomes from cardiovascular trials

Legend

Rare hypoglycemia

Considering lowering insulin of SU dose

Alberta Blue Cross	**Data source for hypoglycemia**
DPP-4 / SGLT2 Inhibitors / GLP-1 Receptors Agonists	Diabetes Canada Guidelines
Special Authorization Request Form:	https://guidelines.diabetes.ca/cpg/chapter13
https://idbl.ab.bluecross.ca/idbl/DBL/60012.pdf	

DPP – 4 Inhibitors

	Normal dose range	eGFR (mL/min/1.73m^2)		
		> 60	**30 to 60**	**< 30**
Linagliptin (Trajenta ®) Product Monograph	5mg PO daily	No dose adjustment required	No dose adjustment required	No dose adjustment required Use with caution at ≤ 15mL/min
Sitagliptin (Januvia ®) Product Monograph	100mg PO daily	No dose adjustment required	50mg PO daily at GFR < 45mL/min	25mg PO daily

DPP – 4 weight loss and hypoglycemia risk

Class	Medication	Hypoglycemia		Weight Loss	ABC Formulary	Cardiovascular Outcomes	Renal Outcomes
		Monotherapy	Combo therapy[1]				
DPP-4 Inhibitors	Sitagliptin	Rare	Rare	±	Yes	No	Yes[2]
	Linagliptin	Rare	Min-mod	0 – 1 kg	Yes	No	Yes[2]

[1]min-mod (minimum- moderate). Depending on the nature of combination therapy. May be elevated if patient is already well controlled on insulin or a secretagogue

[2] Based on intermediate secondary outcomes (e.g., albuminuria reduction) seen in cardiovascular outcome trials, only use when others have not worked

Legend

Rare hypoglycemia

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Alberta Blue Cross

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Data source for hypoglycemia

Diabetes Canada Guidelines

https://guidelines.diabetes.ca/cpg/chapter13

4. Medication Reconciliation and Relevant De-prescribing

Canadian Medication Appropriateness and Deprescribing Network website

Key pages:

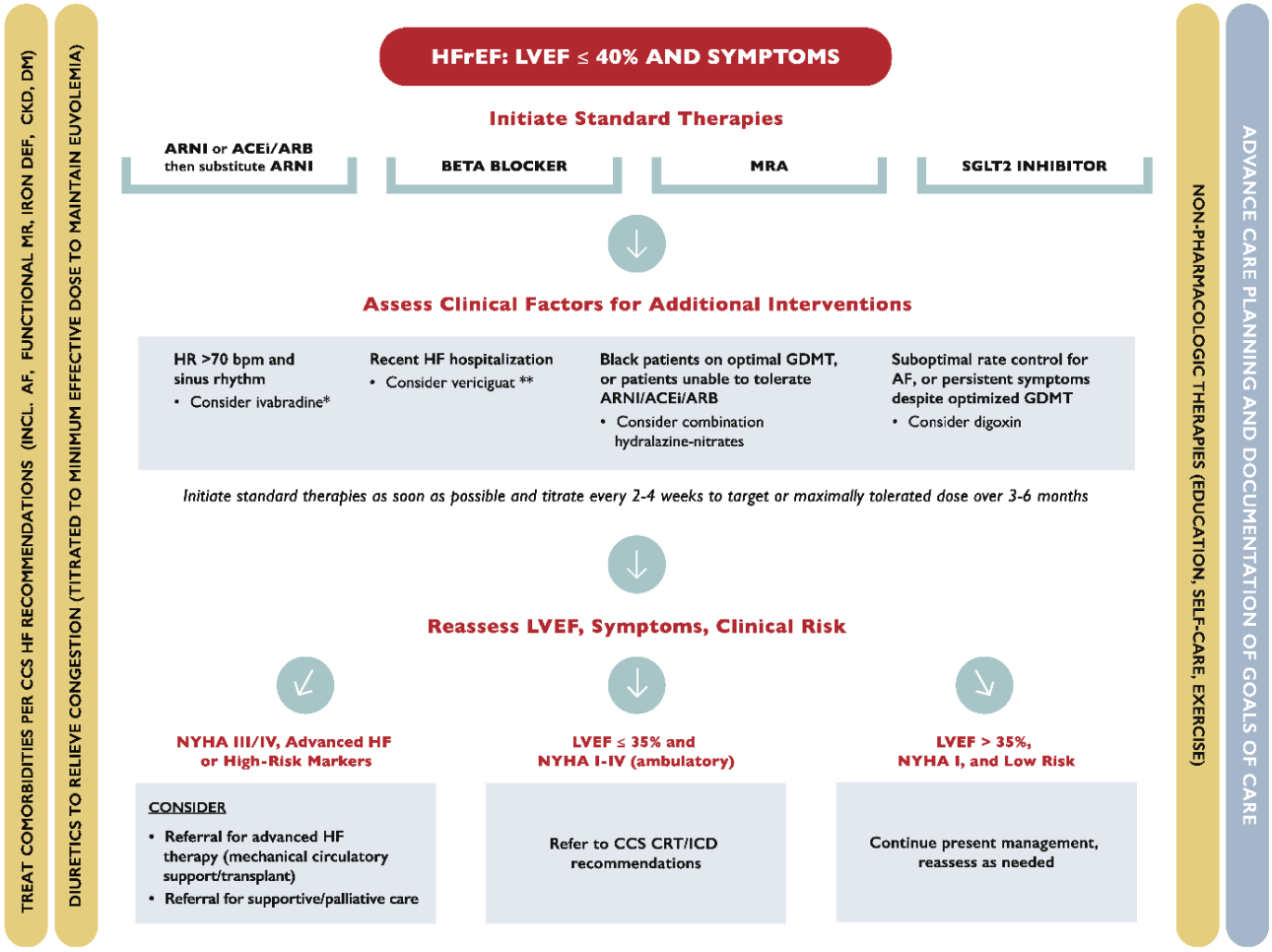
- Do I still need this medication? Is deprescribing for you?
- Other resources for clinicians – Do I still need this medication? Is deprescribing for you?

MedStopper

MedStopper is a deprescribing web-based tool developed by a team of health professionals to help doctors and their patients look at a list of medications to decide if some should be stopped or changed.

5. Heart Failure Guidelines

Canadian Cardiovascular Society Heart Failure (HF) guidelines (2021)



https://pubmed.ncbi.nlm.nih.gov/33827756/

6. Holistic Approach for improving outcomes in patients with diabetes and chronic kidney disease

KDIGO 2024 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease

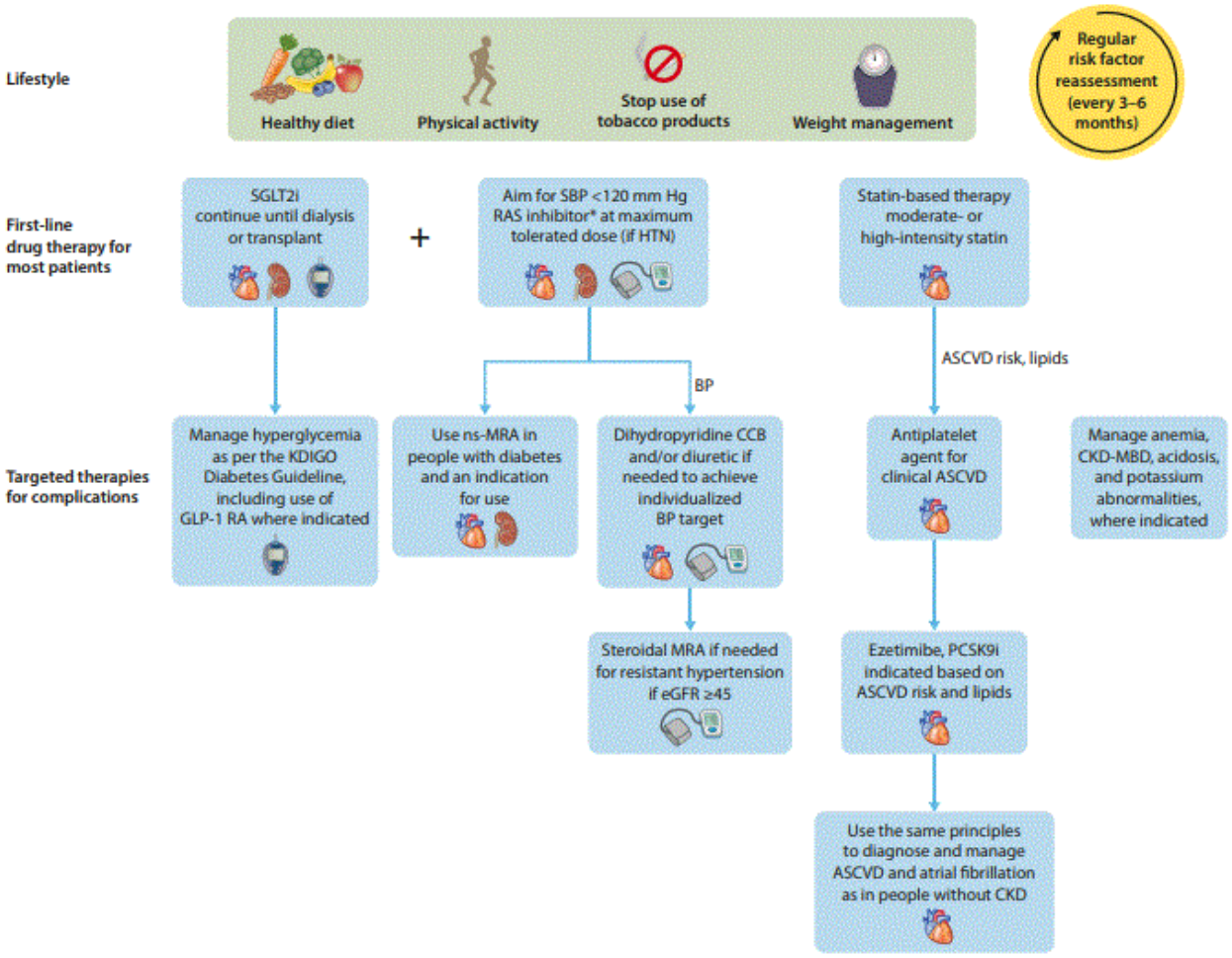


Figure 18 | Holistic approach to chronic kidney disease (CKD) treatment and risk modification. *Angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker should be first-line therapy for blood pressure (BP) control when albuminuria is present; otherwise dihydropyridine calcium channel blocker (CCB) or diuretic can also be considered. All 3 classes are often needed to attain BP targets. Icons presented indicate the following benefits: blood pressure cuff = blood pressure–lowering; glucometer = glucose-lowering; heart = heart protection; kidney = kidney protection; scale = weight management. ASCVD, atherosclerotic cardiovascular disease; CKD-MBD, chronic kidney disease-mineral and bone disorder; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HTN, hypertension; KDIGO, Kidney Disease: Improving Global Outcomes; MRA, mineralocorticoid receptor antagonist; ns-MRA, nonsteroidal mineralocorticoid receptor antagonist; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; RAS, renin-angiotensin system; SBP, systolic blood pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitor. Modified from Kidney Disease: Improving Global Outcomes Diabetes Work Group. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022;102:S1–S127.[23]

https://doi.org/10.1016/j.kint.2022.06.008

7. Managing Type 2 Diabetes

For more details on Type 2 Diabetes management consult https://guidelines.diabetes.ca/

8. A1C Optimization Goals

- Consult Diabetes Canada | Clinical Practice Guidelines – A1C Target 2018 for guidance on individualizing your patients A1C targets.

Weight loss and hypoglycemia risk

Class	Medication	Hypoglycemia		Weight Loss	ABC Formulary	Cardiovascular Outcomes	Renal outcomes
		Monotherapy	Combo therapy[1]				
SGLT-2 Inhibitors	Dapagliflozin	N/A	Min-mod	1 – 3 kg	Yes	Yes	Yes
	Empagliflozin	Rare	Min-mod	1 – 3 kg	Yes	Yes	Yes
	Canagliflozin	Rare	Rare	1 – 3 kg	Yes	Yes	Yes
GLP 1 Agonists	Semaglutide inj	Rare	Min-mod	>3 kg	Yes	Yes	Yes[2]
	Semaglutide po	Rare	Min-mod	>3 kg	No	No	No
	Dulaglutide	Rare	Min-mod	Monotherapy 0 – 1 kg	No	Yes	Yes[3]
		Rare	Min-mod	Combo therapy with SGLT2i or metformin 1 – 3 kg			
	Liraglutide	Rare	Min-mod	1 – 3 kg	No	Yes	Yes[3]
DPP-4 Inhibitors	Sitagliptin	Rare	Rare	±	Yes	No	Yes[4]
	Linagliptin	Rare	Min-mod	0 – 1 kg	Yes	No	Yes[4]

[1]min-mod (minimum- moderate). Depending on the nature of combination therapy. May be elevated if patient is already well controlled on insulin or a secretagogue

[2]based on outcomes and evidence from the FLOW trial (https://www.nejm.org/doi/full/10.1056/NEJMoa2403347)

[3]Based on secondary outcomes from cardiovascular trials

[4]Based on intermediate secondary outcomes (e.g., albuminuria reduction) seen in cardiovascular outcome trials, only use when others have not worked

Legend
Rare hypoglycemia
Considering lowering insulin of SU dose

9. Specialist Referral

- Specialist Link

  https://www.specialistlink.ca/

- ConnectMD

  https://pcnconnectmd.com/

- Provincial Pathways Unit – Integration and Innovation, Primary Health Care Hub

  www.albertapathways.ca

Cardiology

- Specialist link Heart Failure Pathway

  https://www.specialistlink.ca/assets/pdf/CZ_HeartFailure_Pathway.pdf

Endocrinology

- Calgary

  Primary Care Access to Endocrinology

- Edmonton

  Diabetes Program Information and Referral for Health Professionals (Edmonton)

Nephrology

- Provincial Nephrology Referral Quick Reference

  https://www.albertahealthservices.ca/assets/info/hp/arp/if-hp-arp-nephrology-qr.pdf

10. Other Resources

- SGLT-2 Inhibitors, Insulin and Diabetic Ketoacidosis (DKA) (albertahealthervices.ca) https://www.albertahealthservices.ca/assets/mha/diabetes/mha-diabetes-sglt-2-inhibitors-insulin-diabetic-ketoacidosis.pdf
- Diabetes Information - Diabetes Educators Calgary https://www.diabeteseducatorscalgary.ca/
- Diabetes Canada – Clinical Practice Guidelines https://guidelines.diabetes.ca/
- CKD Pathway https://ckdpathway.ca/

11. Safe Use of SGLT2is

- Additional resource: https://guidelines.diabetes.ca/appendices/appendix8
- Type 2 Diabetes and Sick Days Medications to Pause document. This file is used with permission from the SADMANS-RX.pdf (rxfiles.ca) (contact: RXFiles Info info@rxfiles.ca)

Click to print sick days medications hand-out

This handout is in general accordance with 2018 Diabetes Canada Guidelines.

TYPE 2 DIABETES and SICK DAYS
MEDICATIONS to PAUSE

Name: _____ **Date:** _____

When you are sick, it is easy to become dehydrated from throwing up, diarrhea, and/or a fever.

If you become dehydrated, your kidneys may be stressed. This can make certain medications cause problems.

This means that **some** medications should be PAUSED when you are sick to prevent side effects or kidney problems.

These medications can then be STARTED AGAIN once you have recovered from being sick.

SIGNS OF DEHYDRATION

thirst
unusual tiredness
dry mouth
headache
lightheadedness
dry/cool skin
irritability
confusion
less peeing

MY PLAN

If I have been throwing up, and/or having diarrhea, and/or a fever and I am worried that I am dehydrated because I cannot keep "anything down", I will PAUSE (temporarily stop) the following medicine(s):

	Type of Medication		Your Medication
S	sulfonylureas, other secretagogues	☐	
A	ACE inhibitors	☐	
D	diuretics*, direct renin inhibitor	☐	
M	metformin	☐	
A	angiotensin receptor blockers	☐	
N	nonsteroidal anti-inflammatory drugs	☐	
S	SGLT2 inhibitors, or "flozins"	☐	

For over-the-counter cough, cold & flu products, please check with your pharmacist first.
Do not take any products that contain nonsteroidal anti-inflammatory drugs such as ibuprofen (ADVIL/MOTRIN) or naproxen (ALEVE).

* If using diuretics for heart failure, please contact your physician or health care team for detailed instruction before stopping.

ACE=angiotensin converting enzyme SGLT2=sodium-glucose cotransporter-2

I will START these medications again at my usual dose when I am feeling well and my body has recovered from the illness.

I will increase the number of times I RECORD (check) my blood glucose levels when I am sick. If they are too high or too low, I will contact my health care provider.

If you are using insulin, you may need to increase or decrease the amount of insulin you inject. For example, you may need to also PAUSE your meal time, short-acting insulin if not eating while sick.

WHEN YOU ARE SICK IT IS OK TO STOP THESE PARTICULAR MEDICINES FOR A FEW DAYS.

REMEMBER TO:

hydrate

try to drink plenty of fluids with minimal sugar, limit caffeine, and consider electrolyte replacement solutions

consult

your health care provider if you have questions about what to do when you are sick or **if you do not feel better after about 3 days**

Supplementary Information

SADMANS: COMMON medications to temporarily stop with dehydration from throwing up, diarrhea, sweating, etc...				Comments
S	Sulfonylureas, other Secretagogues	gliclazide	DIAMICRON MR	- hold due to reduced clearance of the drug by the kidneys and increased risk of low blood sugars or hypoglycemia
		glimepiride	AMARYL	
		glyburide	DIABETA	
		repaglinide	GLUCONORM	
A	ACE Inhibitors	benazepril	LOTENSIN	- hold due to increased risk for decline in kidney function - note: combination medication products not listed
		captopril	CAPOTEN	
		cilazapril	INHIBACE	
		enalapril	VASOTEC	
		fosinopril	MONOPRIL	
		lisinopril	ZESTRIL	
		perindopril	COVERSYL	
		quinapril	ACCUPRIL	
		ramipril	ALTACE	
		trandolapril	MAVIK	
D	Diuretics	chlorthalidone		- hold due to increased risk for decline in kidney function - special consideration - whether or not to hold diuretics (especially furosemide) in heart failure with short-term illness depends on heart failure and fluid retention status - note: combination medication products not listed
		eplerenone	INSPRA	
		furosemide	LASIX	
		hydrochlorothiazide	HCTZ	
		indapamide	LOZIDE	
		metolazone	ZAROXOLYN	
		Spironolactone[1]	ALDACTONE	
	Direct Renin Inhibitor	aliskiren	RASILEZ	
M	Metformin	metformin	GLUCOPHAGE GLUMETZA	- hold due to reduced clearance of the drug by the kidneys and increased risk for adverse effects (e.g. more stomach upset) - consider restarting at a lower dose if ongoing nausea and/or diarrhea - note: combination medication products not listed
A	Angiotensin receptor blockers	candesartan	ATACAND	- hold due to increased risk for decline in kidney function - note: combination medication products not listed
		eprosartan	TEVETEN	
		irbesartan	AVAPRO	
		losartan	COZAAR	
		olmesartan	OLMETEC	
		telmisartan	MICARDIS	
		valsartan	DIOVAN	
N	Non-steroidal anti-inflammatory drugs & COXIBS	acetylsalicylic acid (ASA)	ASPIRIN ENTROPHEN	- hold due to increased risk for decline in kidney function - in most situations, it is recommended to continue with low dose ASA during short-term illness - note: combination medication products not listed; as well, over-the-counter cough, cold & flu products that contain these medications are not listed
		celecoxib	CELEBREX	
		diclofenac	VOLTAREN	
		ibuprofen	ADVIL / MOTRIN	
		indomethacin	INDOCID	
		ketorolac	TORADOL	
		naproxen	NAPROSYN / ALEVE	
S	SGLT2 inhibitors or "*flozins*"	canagliflozin	INVOKANA	- hold due to increased risk for decline in kidney function - note: combination medication products not listed
		dapagliflozin	FORXIGA	
		empagliflozin	JARDIANCE	
		ertugliflozin	STEGLATRO	

ACE=angiotensin converting enzyme SGLT2=sodium-glucose cotransporter

Disclosures: No conflicts of interest are reported.

[1]**Finerenone is included under diuretics spironolactone/aldactone**

BACKGROUND

About this pathway

The Chronic Kidney Disease in Diabetes Mellitus 2 (CKD in DM2) Primary Care [Team] Pathway for Optimizing Kidney and Cardiovascular Outcomes pathway is for use in stable ambulatory patients over 18 years of age.

Originally envisioned as a treatment pathway to improve the care and treatment of persons with kidney disease, it became evident that the pathway needed to address cardiovascular and endocrinology treatment as well as kidney treatment.

The provincial DKD/SGLT2i working group who developed this pathway includes physician representation (e.g., Cardiology, Endocrinology, General Internal Medicine, Nephrology, Primary Care), representation from the Kidney Health Section, Medicine SCN, the University of Calgary and the University of Alberta Physician Learning Programs, the Health Quality Council of Alberta, Clinical Pharmacists, and members from the CKD Pathway team.

The DKD pathway is intended to provide evidence-based guidance to support primary care providers and clinical pharmacists in providing guideline concordant therapy in caring for patients with diabetes and kidney and/or heart disease within the medical home.

Authors and conflict of interest declaration

- This pathway was reviewed and revised under the auspices of the Kidney Health Section, Medicine SCN in 2023 by a multi-disciplinary team led by nephrologists, cardiologists, general internists, family physicians, endocrinologists, and pharmacists.
- For more information, contact the Kidney Health Section, Medicine SCN at MedicineSCN@ahs.ca.
- Pathway Feedback and Review Process Primary care pathways undergo scheduled review every three years, or earlier if there is a clinically significant change in knowledge or practice. The next scheduled review is April 2026; however, we welcome feedback at any time. Click on the Provide Feedback button to provide your feedback.

Provide Feedback

Pathway review process, timelines

- Created and approved August 2023
- Revised June 2024 to add Finerenone
- Next review April 2026

Copyright information

DISCLAIMER

This pathway represents evidence-based best practice but does not override the individual responsibility of health care professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.

PROVIDER RESOURCES

Clinical Practice Guidelines

Description	Website
Canadian Cardiovascular Society Guideline for Use of GLP-1 Receptor Agonists and SGLT2 Inhibitors for Cardiorenal Risk Reduction in Adults	https://www.sciencedirect.com/science/article/abs/pii/S0828282X2200335X?via%3Dihub
Canadian Cardiovascular Society heart failure (HF) guidelines (2021)	https://pubmed.ncbi.nlm.nih.gov/33827756/
Diabetes Canada Clinical Practice Guidelines Expert Committee. Chronic Kidney Disease in Diabetes. McFarlane, P. et al (2018).	http://guidelines.diabetes.ca/cpg/chapter29
Diabetes Canada Clinical Practice Guidelines Quick Reference Guide (Updated 2024)	https://guidelines.diabetes.ca/cpgrefguide
Guidelines Diabetes Canada	http://guidelines.diabetes.ca/cpg
KDIGO 2024 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease	https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf
Top 10 Takeaways on Management for Primary Care Physicians from the KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease	https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline-Top-10-Takeaways-for-PCPs-Management.pdf

Resources

Description	Website
Advance Care planning	https://www.albertahealthservices.ca/info/Page9099.aspx
Atrial Fibrillation	https://www.specialistlink.ca/assets/pdf/Cardiology_AFIB_Pathway.pdf
Canadian Medication Appropriateness and Deprescribing Network website	https://www.deprescribingnetwork.ca/algorithms
Heart Failure	https://www.specialistlink.ca/assets/pdf/CZ_HeartFailure_Pathway.pdf
My Kidneys My Health	https://mykidneysmyhealth.com/
Primary Care Access to Endocrinology	https://www.specialistlink.ca/assets/pdf/endocrinology/Endocrinology_AccessPathway.pdf
Provincial Nephrology Referral Quick Reference	https://www.albertahealthservices.ca/assets/info/hp/arp/if-hp-arp-nephrology-qr.pdf
SADMANS	https://www.rxfiles.ca/RxFiles/uploads/documents/SADMANS-Rx.pdf
Updates to the Alberta Drug Benefit List (September 1, 2023)	https://idbl.ab.bluecross.ca/idbl/DBL/sep_dblupdate.pdf?_gl=1*pht0mf*_%0bga*MTQ5NjIwMjg2OC4xNjIyNTY0MTY4*_ga_L344K4V4H4*MTY5MzI1%0bNTk5Mi40MC4xLjE2OTMyNTYzMjUuNTIuMC4w

References

Description	Website
2019 update to: Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia, 63, 221–228. Buse, J.B., et al (2019, December 19).	https://diabetesjournals.org/care/article/43/2/487/36098/2019-Update-to-Management-of-Hyperglycemia-in-Type
Cardiovascular Protection with Diabetes Quick Reference	https://www.diabetes.ca/DiabetesCanadaWebsite/media/Health-care-providers/2018%20Clinical%20Practice%20Guidelines/prescription-for-cardiovascular-protection-with-diabetes.pdf?ext=.pdf
Diabetes Canada Quick Reference Guide (updated regularly)	https://guidelines.diabetes.ca/cpg
Effects of Semaglutide on Chronic Kidney Disease in Patients with Type 2 Diabetes	https://www.nejm.org/doi/full/10.1056/NEJMoa2403347
Empagliflozin in Patients with Chronic Kidney Disease	https://www.nejm.org/doi/full/10.1056/NEJMoa2204233
KDIGO 2024 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease	https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf
My Diabetes Care	https://www.diabetes.ca/DiabetesCanadaWebsite/media/Managing-My-Diabetes/Tools%20and%20Resources/my-diabetes-care-not-just-about-blood-sugar.pdf?ext=.pdf
Outcomes With Finerenone in Patients With Chronic Kidney Disease and Type 2 Diabetes by Baseline Insulin Resistance | Diabetes Care | American Diabetes Association (diabetesjournals.org)	https://diabetesjournals.org/care/article/47/3/362/154043/Outcomes-With-Finerenone-in-Patients-With-Chronic
SGLT-2 inhibitors and GLP-1 receptor agonists for nephroprotection and cardioprotection in patients with diabetes mellitus and chronic kidney disease. A consensus statement by the EURECA-m and the DIABESITY working groups of the ERA-EDTA. Nephrol Dial Transplant, 34, 208–230. Sarafidis, P., et al (2019).	https://academic.oup.com/ndt/article/34/2/208/5307730?login=true

PATIENT RESOURCES

Information

Description	Website
Advance care planning	https://myhealth.alberta.ca/HealthTopics/Advance-Care-Planning
Alberta Healthy Living Program	https://www.albertahealthservices.ca/info/page13984.aspx
My Diabetes Care	https://www.diabetes.ca/DiabetesCanadaWebsite/media/Managing-My-Diabetes/Tools%20and%20Resources/my-diabetes-care-not-just-about-blood-sugar.pdf?ext=.pdf
My Health Alberta	https://myhealth.alberta.ca/
My Kidneys My Health	https://mykidneysmyhealth.com/
SADMANS	https://www.rxfiles.ca/RxFiles/uploads/documents/SADMANS-Rx.pdf

Services available

Description	Website
Referral to a registered Dietitian	• Visit Alberta Referral Directory and search for nutrition counselling. • To learn more about programs and services offered in your zone, visit Nutrition Services. • Health Link has Registered Dietitians available to answer nutrition questions. If a patient has nutrition-related questions, they can call 8-1-1 and ask to talk to a Dietitian.
Services for patients with chronic conditions (Alberta Healthy Living Program – AHS)	https://www.albertahealthservices.ca/info/page13984.aspx
Supports for working towards healthy lifestyle goals and weight management (Weight Management – AHS)	https://www.albertahealthservices.ca/info/Page15163.aspx