Provincial Clinical Knowledge Topic
Gout, Adult – Inpatient
V 1.0

Revision History

Version	Date of Revision	Description of Revision	Revised By
1.0	December 2018	Completion of Topic	Paul MacMullan and Stephanie Kulhawy

Important Information Before You Begin

The recommendations contained in this knowledge topic have been provincially adjudicated and are based on best practice and available evidence. Clinicians applying these recommendations should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care. This knowledge topic will be reviewed periodically and updated as best practice evidence and practice change.

The information in this topic strives to adhere to Institute for Safe Medication Practices (ISMP) safety standards and align with Quality and Safety initiatives and accreditation requirements such as the Required Organizational Practices. Some examples of these initiatives or groups are: Health Quality Council Alberta (HQCA), Choosing Wisely campaign, Safer Healthcare Now campaign etc.

Guidelines

This Clinical Knowledge Topic is based on the following guideline(s):

- 2016 Updated EULAR Evidence-Based Recommendations for the Management of Gout[1]
- 2015 Gout Classification Criteria: An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative[2]
- 2012 American College of Rheumatology Guidelines for Management of Gout Part I: Systematic Non-pharmacologic and Pharmacologic Therapeutic Approaches to Hyperuricemia[3]
- The British Society for Rheumatology Guideline for the Management of Gout 2017[4]
- Development of the American College of Rheumatology Electronic Clinical Quality Measures for Gout[5]
- Enhanced Primary Care Pathway: Gout developed as a collaborative effort with the Calgary Zone Primary Care Networks, the Division of Rheumatology, and Alberta Health Services[6]
- See References for additional references used

Keywords

- Allopurinol
- Gout
- Colchicine
- Indomethacin

Decision Making

Goals

Hospitalization is a risk factor for acute gout attacks[7]. This is driven by both acute illness and mismanagement of chronic gout sufferers such as holding or discontinuing of urate lowering therapy at the time of hospital admission. During an acute gout attack, diagnosis is often delayed or missed leading to further mismanagement, which may lead to poor outcomes. Both consultation by rheumatology as well as implementation of a gout management protocol have been shown to improve outcomes[8,9].

1. Reduce permanent or temporary discontinuation of urate lowering therapy and concurrent prophylaxis during admission (unless there is an absolute contraindication).
2. Reduce time from diagnosis to treatment of acute gout attacks in hospitalized patients to reduce pain and improve patient outcomes related to acute attacks.
3. Initiate urate lowering therapy, if appropriate, with concurrent prophylaxis to reduce recurrent gout attacks.
4. Promote education on diet and lifestyle modifications for treatment of gout.

Decision Making Information

ADMISSION OF PATIENTS WITH A KNOWN HISTORY OF GOUT

1. Identify patients with a history of gout.
2. Perform medication reconciliation (see medication reconciliation)
3. Continue urate lowering therapy (ULT) and prophylaxis or consider initiating if appropriate.

ACUTE GOUT FLARE

1. Identify flares early using diagnostic tools (see Scoring and Assessment Tool section), look for red flags for septic arthritis (WBC, fever, signs of sepsis), perform arthrocentesis with synocial fluid analysis with or without a rheumatology consult if diagnosis unclear or septic arthritis suspected.
2. Initiate **most appropriate treatment** (based on comorbidities) as soon as possible.
3. Evaluate need for initiation of urate lowering therapy or continue current ULT if already taking.
4. Arrange for appropriate follow up with family doctor or rheumatology.
5. Provide patient education and resources (see Patient Resources) for diet and lifestyle management.

CHRONIC GOUT

1. Medication reconciliation (see medication reconciliation)
    a. Medication that may trigger attacks
    b. Continue ULT (do not hold on admission)
    c. Appropriate plan for treatment of flares
2. Prevent flares in hospital by continuing ULT, encourage ambulation, and diet orders.
3. Provide education and resources (see Patient Resrouces) and arrange follow up

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Most Appropriate Treatment:

Corticosteroids	<u>Systemic</u> • Includes oral or intramuscular therapy • Can be used safely in chronic kidney disease • Safer than NSAIDs or colchicine in the elderly • Caution in patients with diabetes <u>Intra-articular</u> • Useful in treatment of 1 or 2 involved joints • Sometimes more effective than oral corticosteroids • Aspirating excess synovial fluid prior to injection of steroid has therapeutic benefit • Synovial fluid aspirate should be sent to lab for cell count, culture, and crystals
Oral colchicine	• Use with caution if severe renal (GFR less than 30 mL/minute) or hepatic insufficiency • Do not use old regimens with frequent doses until patient has diarrhea • More effective if started within the first 36 hours of an attack
Nonsteroidal anti-inflammatory drug (NSAIDs)	• Often contraindicated due to comorbidities • Other NSAIDs (full dose) may be as effective as indomethacin • Consider gastroprotection • Monitor renal function especially in the elderly or chronic kidney disease (CKD)
IL-1 receptor Antagonist	• This is only used at the direction of a rheumatologist • Non-formulary in the hospital. • Not covered by Alberta Blue Cross. STEDT coverage is usually required. • Off-label indication.

Medication Reconciliation

- *Some medications may trigger gout attacks. Use this opportunity to eliminate non-essential medications or change to an alternative, less exacerbating option.*
- *Medications that can trigger gout flares:*
    - *Diuretics (especially thiazide diuretics)*
    - *Niacin*
    - *Calcineurin inhibitors*
    - *Low dose ASA; however, this should not be stopped in patients who have a good indication for ASA such as coronary artery disease.*
    - *Levodopa; again, this is not an indication to stop this medication in patients with Parkinson Disease.*
- *Take note of patients on azathioprine (Imuran ®) and 6-mercaptopurine (Purinethol ®), as this is a contraindication to ULT.*
- *Do not routinely hold allopurinol on admission (even in the case of an AKI). Acute medical illness increases the risk of precipitating flares and can prolong hospitalization. In the case of an AKI with eGFR less than 30 mL/minute consider using renal dosing of Allopurinol, reduce dose by 50%. If you do this, make a plan to resume full home dose as renal function improves.*

Scoring and Assessment Tools

ACR-EULAR Gout Classification Criteria - Provides formal diagnostic criteria for gout
https://www.mdcalc.com/acr-eular-gout-classification-criteria

Acute Gout Diagnosis Rule - Risk stratifies for gout vs non-gout arthritis and helps determine which patients benefit most from joint aspiration.
https://www.mdcalc.com/acute-gout-diagnosis-rule

Nutrition Screening – Use Canadian Nutrition Screening Tool (CNST). Refer to Registered Dietitian if CNST score equals 2 Yes responses.

Acute and Chronic Gout Adult Inpatient Order Set

Order Set Keywords: gout, colchicine, indomethacin, allopurinol
Order Set Requirements: weight, creatinine/eGFR

Diet and Nutrition
Therapeutic diet as appropriate given patients comorbidities

- ☐ Regular Diet
  Therapeutic Diet
  - ☐ Diabetic
  - ☐ Heart Healthy
  - ☐ Renal
  - ☐ Low sodium

Patient Care

Activity

- ☐ Elevate extremity, rest, and apply ice to acutely flaring joints

Point of Care Testing Glucose
Consider more frequent monitoring if corticosteroids are being used for management of gout

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~Start of Point of Care Testing (POCT) Glucose Order Panel~

- ☐ Blood Glucose Monitoring – POCT 4 times per day 15 to 30 minutes before scheduled meals and at bedtime, AND PRN for suspected hypoglycemia
- ☐ Blood Glucose Monitoring – POCT at 0200 hours for _____ days
- ☐ Blood Glucose Monitoring – POCT 2 hours after meal time
- ☐ Blood Glucose Monitoring – POCT other (specify) _____

Refer to AHS Glycemic Management Policy

- ☐ If blood glucose less than 4.0 mmol/L initiate Hypoglycemia Procedure. Do not hold Insulin without prescriber order
- ☐ If blood glucose is greater than 18.0 mmol/L initiate Hyperglycemia Procedure and call prescriber

~End of Point of Care Testing (POCT) Glucose Order Panel~
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Laboratory Investigations Routine

If septic joint suspected a joint aspiration is mandatory. If low suspicion for infection, this calculator can help to determine if arthrocentesis is appropriate: https://www.mdcalc.com/acute-gout-diagnosis-rule

If Arthrocentesis is required - See Arthrocentesis Order Panel

Basic lab investigations should be collected (if not already done) at onset of flare or prior to initiating urate lowering therapy:

Hematology

☐ Complete Blood Count with differential

Chemistry

☐ Creatinine
☐ ALT
☐ Glucose Random

Utility of Urate limited in systemic illness, but is required in diagnostic aids / calculators

☐ Urate

*HLA-B*58:01 TESTING FOR ETHNIC GROUPS AT RISK FOR HYPERSENSITIVITY REACTIONS. Chinese, Thai and Korean patients are at risk for life-threatening allopurinol hypersensitivity reactions. HLA-B*5801 screening should be considered in these patients before starting allopurinol, and if positive allopurinol should not be used. This genetic test can be ordered through CLS. High-risk individuals should be treated with febuxostat instead.*

☐ *HLA-B*58:01 TESTING FOR ETHNIC GROUPS AT RISK OF HYPERSENSITIVITY REACTIONS*

Diagnostic Imaging

General Radiology

Consider ordering an x-ray of the affected joint, especially if diagnosis unclear and no previous recent x- ray or other imaging studies of affected joint.

☐ X-ray (GR of affected joint). Specify anatomical area to be imaged: _____

VTE Prophylaxis

Consider opening and merging VTE Prophylaxis order set (Placeholder - Provincial VTE Prophylaxis order set to be signed off)

Medication

Medications for Acute Gout

Analgesics and Antipyretics

NSAIDs may be contraindicated due to comorbidities. Consider temporary gastroprotection such as a proton pump inhibitor for patients at high risk of GI bleed. Recommend to taper as symptoms beging to resolve. For example, start with full dose until symptoms improve, then half dose until symptoms resolve, then discontinue.

For indomethacin, recommended dosage is 25 to 50 mg. Other NSAIDs (full dose) may be as effective as indomethacin (see below).

☐ indomethacin___mg PO TID

OR

For naproxen, recommended dosage is 250 to 500 mg

☐ naproxen___mg PO BID

Corticosteroids

Choose ONE of systemic or Intra-articular therapy

Can be used safely in chronic kidney disease, safer than NSAIDs or Colchicine in elderly. Requires closer blood glucose monitoring in patients with diabetes.

Systemic Therapy (choose ONE):

- ☐ predniSONE 30 mg PO daily for 3 to 5 days, then consider dropping to prophylaxis dosing (predniSONE 20 mg daily, taper by 5mg every 5days) if planning to initiate ULT

For triamcinolone acetonide (Kenalog®) and methylprednisolone acetate (Depo-medrol ®), recommended dosage is 80 mg or 1mg/kg up to 120mg

- ☐ triamcinolone acetonide (Kenalog®)___mg IM ONCE into gluteal muscle, use a 22 G x 1.5 inch needle
- ☐ methylprednisolone acetate (Depo-medrol®)____mg IM ONCE into gluteal muscle, use a 22 G x 1.5 inch needle

OR

Intra-articular Therapy- Use Arthrocentesis Order Panel.

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~Start of Arthocentesis Order Panel~

Refer to Procedure Guidance for Arthrocentesis

Laboratory Investigations

For body fluid investigations

Hematology

- ☐ Cell Count, Body Fluid
- ☐ Differential
- ☐ Crystals

Microbiology

- ☐ Fluid Culture (includes Gram stain)

Medications

Corticosteroids

For Intra-articular Injection:
Do not administer intra-articular steroids if septic joint is suspected. Wait until preliminary fluid results (cell count and gram stain) are back prior to administering intra-articular corticosteroids.

Intra-articular corticosteroids: Useful in treatment of 1 or 2 involved joints, sometimes more effective than oral corticosteroids. Aspirating excess synovial fluid prior to injection of steroid has therapeutic benefit[10]

For larger joints, recommended dosage is 40 to 80 mg
For smaller joints or bursae, recommended dosage is 10 to 20 mg

- ☐ triamcinolone acetonide (Kenalog®)__mg intraarticular once
- ☐ methylprednisolone acetate (DepoMedrol ®)__mg intraarticular once

~End of Arthocentesis Order Panel~

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Other

Colchicine *is most effective if started within the first 36 hour of an attack. Use with caution in severe renal (GFR less than 30 mL/minute) or hepatic insufficiency; in these circumstances of reduced colchicine clearance bone marrow suppression can be an issue and this requires monitoring with CBCs.*

Choose ONE:

☐ colchicine 0.6 mg PO BID

If GFR less than 50 mL/minute but greater than 30 mL/minute

☐ colchicine 0.3 mg PO BID

If GFR less than 50 mL/minute but greater than 30 mL/minute and if BID dosing is not tolerated

☐ colchicine 0.3 mg PO daily

If GFR less than 30 mL/minute

☐ colchicine 0.3 mg PO daily

IL-1 Receptor Antagonist – Anakinra (Kineret®) *used only at the direction of a rheumatologist. This is non-formulary in hospital and not covered by ADBL. STEDT coverage is usually required. For reference, dosing is: Anakinra (Kineret®) 100 mg subcutaneously daily for 3 days*.

Medications

Medications for Chronic Gout and Urate Lowering Therapy

Indications for lifelong urate lowering therapy:

- *More than 2 or 3 acute attacks of gout within 1 to 2 years (or unremitting gouty inflammation)*
- *Radiographic evidence of joint damage due to gout*
- *Presence of tophi*
- *Established gout with chronic kidney disease stage 2 or worse (GFR less than 90 mL/min)*
- *Renal stones (urate)*

Note that ULT can be initiated even in an acute flare, as long as prophylaxis is maintained after treatment of acute flare. This works especially well in the setting of the use of corticosteroids used for treatment of flare.

Urate Lowering Therapy

Before initiation of ULT consider contraindications and screening.

<u>Contraindications and Reasons to Stop ULT</u>

1. *Allopurinol and febuxostat should not be used in patients on azathioprine (Imuran®) or 6-mercaptopurine (Purinethol ®) due to the risk of bone marrow failure (refer to rheumatology).*
2. *Patients with allopurinol hypersensitivity (rash, fever, thrombocytopenia, abnormal liver enzymes) should stop immediately and never take this drug again.*

Pharmacogenomic Screening

*See Laboratory orders. High-risk individuals should be treated with febuxostat (Uloric ®) instead. Note that HLA- B*58:01 positivity is an indication for febuxostat (Uloric ®) use as first line; however, this alone is often not enough to qualify for coverage by drug insurance plans such as Alberta Blue Cross. Many plans require failure or contraindication to sulfinpyrazone in addition to allopurinol before covering febuxostat (Uloric ®). Contraindications for sulfinpyrazone include concurrent anticoagulation, eGFR less than 60mL/min, high bleeding risk or sulfa allergy.*

Febuxostat (Uloric ®) can also be considered in patients with stage 4 or 5 CKD (GFR less than 30 mL/minute), or other contraindications to allopurinol. Insurance plans such as Alberta Blue Cross requires a special authorization, but most private insurers do not. ***NOTE:*** *This is non-formulary in the hospital.*

Initiation of ULT

Target: serum urate less than 360 umol/L; less than 300 umol/L if tophi. Allopurinol 300 mg PO daily can be started in patients on prophylaxis with steroids or colchicine. Contrary to historical belief, an acute gout attack is not a contraindication to initiating ULT and as this is already a point of medical contact it provides an excellent opportunity to initiate ULT. Acute flare treatment can be stepped down to prophylaxis dosing once the symptoms of the acute flare have subsided.

- ☐ allopurinol 300 mg PO daily

OR

Alternatively, allopurinol can be started at 100 mg daily and slowly up titrated to minimize the risk of gout attacks. This is the recommended dosing for patients with renal disease (eGFR less than 50 mL/minute), but can be used in patient with normal renal function asl well.

- ☐ allopurinol 100 mg daily and slowly increase dosage every 2 to 4 weeks as per below:
  - allopurinol 100 mg PO daily x ___ weeks
  - allopurinol 200 mg PO daily x ___ weeks
  - allopurinol 300 mg PO daily thereafter (300 mg is sufficient for most)
  - allopurinol dose may be further increased if serum urate level remains above target
  - Consult Rheumatology if not responding

Gout Prophylaxis Options

Gout Prophylaxis (mandatory while initiating urate lowering therapy)

- *Continue colchicine prophylaxis for:*
  - *3 months after achieving the serum uric acid goal in patients without tophi, OR*
  - *6 months after achieving the serum uric acid goal in patients with 1 or more tophi, OR*
  - *continue prophylaxis for longer if acute gout flares persist*
- *It is common practice to treat with BOTH corticosteroids (single IM dose or short course PO) AND colchicine when initiating urate lowering therapy.*

1. ***For Colchicine*** *- Choose ONE dose according to renal function*

   If GFR greater than 50 mL/minute

   - ☐ colchicine 0.6 mg PO daily
   - ☐ colchicine 0.6 mg PO BID

If GFR 30-50 mL/minute or elderly

- ☐ colchicine 0.3 mg PO daily
- ☐ colchicine 0.3 mg PO BID

If GFR less than 30 mL/minute - use corticosteroids instead- see orders below

Analgesics and Antipyretics

2. ***For NSAIDs*** *- To be used with caution in elderly and GFR less than 30 mL/minute. Avoid concurrent treatment with corticosteroids for additional risk of gastrointestinal (GI) bleed.*

For naproxen, recommended dosage is 250 to 500 mg

- ☐ naproxen_____mg PO BID

Gastrointestinal Agents

Proton pump inhibitor (PPI) for GI protection

- ☐ pantoprazole 40 mg PO daily (or any fomulary PPI)

Corticosteroids

3. ***For Corticosteroids*** *- Preferred in patients with GFR less than 30 mL/minute or elderly. Caution in patients with diabetes*

For triamcinolone acetonide (Kenalog®) and methylprednisolone acetate (Depo-medrol ®), recommended dosage is 80 mg or 1 mg/kg to a maximum of 120mg.

- ☐ triamcinolone acetonide (Kenalog®)_____mg IM ONCE into deep gluteal muscle
  OR
- ☐ methylprednisolone acetate (Depo-medrol ®)_____mg IM ONCE into deep gluteal muscle
  OR
- ☐ prednisone 20 mg PO daily, taper by 5 mg every 5 day

Consults/Referrals

Inpatient Specialty Consults

Consider Consult Rheumtology for the following:

- *Diagnostic dilemma*
- *Not responding to treatment*
- *Contraindications for treatment*
- *Stage 4 or 5 CKD (eGFR less than 30 mL/minute)*
- *On immunosuppression for organ transplant*
  - ☐ Consult Rheumatology (inpatient or outpatient)

Inpatient Allied Health Consults

- ☐ Physiotherapy Referral to encourage mobility in patients with chronic gout
- ☐ Inpatient consult to Registered Dietitian. Reason for consult:
  - CNST score equals 2 Yes responses
  - Discharge Instructions: Nutrition plan after discharge for patients assessed to be malnourished.
  - For diet instructions for patients with gout

Discharge

Discharge Referral

- ☐ Ambulatory referral to Registered Dietitian. Reason for referral: Patient assessed to be malnourished; other reasons) Internal Referral, Post Discharge

Admission/Transfer/Discharge Planning

Outpatient Follow Up

- Follow-up with family doctor and/or with rheumatology
- Continuation or consideration of urate lowering therapy
- Repeat labs every 3 months until urate stable at target, then every 6 to 12 months
    - Hematology
        - Complete Blood Count with differential
    - Chemistry
        - Creatinine
        - Urate
        - CRP
        - ALT
        - Glucose

Patient and Caregiver Education and Discharge Instructions

- Patient Resources:
    - Diet and lifestyle modifications
        - www.rheuminfo.com/diseases/gout
        - www.gouteducation.org
        - http://www.albertahealthservices.ca/assets/info/nutrition/if-nfs-healthy-eating-for-managing-gout.pdf

Analytics

Analytics – Outcome Measure #1

Name of Measure	Inpatient Gout Rate
Definition	1. Target cohort: Patient with established gout in 5 years PTA 2. Outcome cohort: inpatient acute gout flare 3. Comparator cohort: Patient with established gout in 5 years PTA, no inpatient acute gout flare

Analytics – Outcome Measure #2

Name of Measure	Allopurinol Dosing
Definition	1. Allopurinol dosing in patients with kidney injury 2. Allopurinol dosing in patients without kidney injury 3. Changes in allopurinol dosing at admission
Notes for Interpretation	1. Target cohort: Patients with Established Gout and Kidney injury who have their dose lowered or held. 2. Comparator cohort: Patients with Established Gout Kidney Injury who don't have their dose lowered 3. Outcome: Inpatient Gout flare

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Appendix A - Procedure Guidance for Arthrocentesis

Additional procedural guidance is available in the Gout Clinical Knowledge Topic. Recommended for review prior to procedure.

Arthrocentesis: Indications

- Evaluation of septic joint
- Confirm diagnosis of gout

Arthrocentesis: Contraindications

- Joint with prior instrumentation such as arthroplasty should be discussed with orthopedic surgery prior to arthrocentesis. Note: this should not delay arthrocentesis if a septic joint is suspected.
- Uncontrolled coagulopathy. Note: Arthrocentesis can still be performed while on anticoagulation[11]. Generally speaking this can be performed if the INR less than 4.

Consent

- Required for Arthrocentesis

Materials for Arthrocentesis:

- 20-22 gauge needle, may require larger needle if effusion is large.
- 10 mL syringe (or larger depending on effusion size,10ml syringes are easier to use and large effusions may require several syringes).
- Three chlorhexidine swabs, or other sterilizing material.
- Sterile gloves as the procedure is performed under sterile technique.
- Optional: local anesthetic.

Procedure:

For the purposes of this protocol the parapatellar approach to arthrocentesis of the knee is described[12]. Arthrocentesis technique varies by approach and joint. This should be performed by someone who is comfortable with the procedure. Ultrasound guidance can be used as well. Aspirating excess synovial fluids prior to injection of steroid has therapeutic benefit[10]. Note: the presence of gout does not rule out a concomitant infection.

1. Prior to sterilizing the site, position the patient's knee at 15 degrees of flexion using a rolled up towel for support. Palpate and mark the site using a hard object such a pen or needle cap. For the parapatellar approach, mark at the lateral or medial midpoint of the patella.
2. Sterile preparation: Shaving is not required (and can actually predispose to infection), cutting of longer hairs may be helpful. Three sterile spirals, starting inside and working your way outwards. Allow to dry and then drape.
3. Local anesthetic can be used, this is considered optional.
4. Using a 18-20 gauge needle attached to a 10mL syringe (or larger depending on effusion size, 10ml syringes are easier to use and large effusions may require several syringes). Enter the joint space perpendicular to the long axis of the femur and directing the needle behind the patella. Pull back on the syringe while advancing the needle.

Once you have entered the joint space, fluid will enter the syringe. Milk the effusion in order to remove as much fluid as possible.

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Thank you to all provincial stakeholders who participated in the review process for this topic. Your time spent reviewing the knowledge topics and providing valuable feedback is appreciated.

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