Warfarin Management – Adult – Ambulatory: Primary and Specialty Care - Clinical Practice Guideline

A. Scope: (disease/condition, treatment, clinical specialty)

1. Conditions: Conditions requiring anticoagulation with oral vitamin K antagonist (warfarin) therapy
2. Objectives:
   2.1. To standardize warfarin management (dosing, monitoring, patient assessment) for adult patients across UW Health
3. Target population: adult ambulatory patients whose warfarin is managed by a UW Health primary care clinic, specialty clinic or anticoagulation clinic

B. Methodology:

1. A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1.) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.[1]

Figure 1. Quality of Evidence and Strength of Recommendation Grading Matrix

SIZE OF TREATMENT EFFECT →

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	CLASS I *Benefit >>> Risk* Procedure/Treatment **SHOULD** be performed/ administered	CLASS IIa *Benefit >> Risk* *Additional studies with focused objectives needed* **IT IS REASONABLE** to perform procedure/administer treatment	CLASS IIb *Benefit ≥ Risk* *Additional studies with broad objectives needed; additional registry data would be helpful* Procedure/Treatment **MAY BE CONSIDERED**	CLASS III *Risk ≥ Benefit* Procedure/Treatment should **NOT** be performed/administered **SINCE IT IS NOT HELPFUL AND MAY BE HARMFUL**
LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses	■ Recommendation that procedure or treatment is useful/effective ■ Sufficient evidence from multiple randomized trials or meta-analyses	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from multiple randomized trials or meta-analyses	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Sufficient evidence from multiple randomized trials or meta-analyses
LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is useful/effective ■ Evidence from single randomized trial or nonrandomized studies	■ Recommendation in favor of treatment or procedure being useful/effective ■ Some conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation's usefulness/efficacy less well established ■ Greater conflicting evidence from single randomized trial or nonrandomized studies	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Evidence from single randomized trial or nonrandomized studies
LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care	■ Recommendation that procedure or treatment is useful/effective ■ Only expert opinion, case studies, or standard of care	■ Recommendation in favor of treatment or procedure being useful/effective ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation's usefulness/efficacy less well established ■ Only diverging expert opinion, case studies, or standard of care	■ Recommendation that procedure or treatment is not useful/effective and may be harmful ■ Only expert opinion, case studies, or standard of care
Suggested phrases for writing recommendations†	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	is not recommended is not indicated should not is not useful/effective/beneficial may be harmful

C. Definitions:

Warfarin[2]

1. Mechanism of action
   - 1.1 Inhibits reduction of vitamin K epoxide; limiting activation of vitamin K dependant clotting factors: II, VII, IX and X
   - 1.2 Inhibits synthesis of anticoagulant proteins C, S and Z (potential procoagulant effects)

2. Pharmacokinetics and pharmacodynamics
   - 2.1 Oral administration
     - 2.1.1 Absorption: rapidly and completely absorbed
     - 2.1.2 Distribution: primarily intravascular and highly protein bound
     - 2.1.3 Half life: 36-42 hours
     - 2.1.4 Metabolism: primarily metabolized by the cytochrome P450 (CYP) enzyme 2C9, 1A2 and 3A4
   - 2.2 Half-lives of clotting factors (Note: effects of warfarin may be seen within the first 24 hours due to inhibition of factor VII, but peak effect is not seen for 72-96 hours with factor II inhibition)
     - 2.2.1 Factor II: 60 – 72 hours
     - 2.2.2 Factor VII: 6 hours
     - 2.2.3 Factor IX: 24 hours
     - 2.2.4 Factor X: 40 hours

D. Introduction:

1. This guideline outlines the evidence for managing anticoagulation therapy with oral vitamin K antagonist (warfarin). Evidence is based on recommendations from the Antithrombotic Therapy and Prevention of Thrombosis, 9th edition: American College of Chest Physicians Clinical Practice Guidelines.

2. It is recommended for dosing and monitoring of maintenance warfarin therapy that standardized and validated decision support tools be used for most patients. Evidence has shown improved time in therapeutic INR range and clinical outcomes in patients managed by trained staff using standardized procedures and dosing decision support tools.[3] ***(Grade 2C)***

3. All patients whose warfarin therapy is managed within the UW Health System will have warfarin management information accessible in the electronic medical record. All warfarin related indications, INR goal, progress notes, INR results, and dosing information is located:
   - 3.1. Chart review 7 Epis (Episodes) 7 Anticoagulation Episode
   - 3.2. Flowsheets: Anticoagulation Monitoring OP

E. Recommendations:

1. Indications for warfarin therapy and target INR ranges

Table 1. Indications for Use and Target INR Range

Indication	INR (Range)	Duration	Comments
Thrombophilia with Thromboembolic Event[3]			
Antiphospholipid Syndrome	2.5 (2-3)	Chronic	
Homozygous Factor V Leiden	2.5 (2-3)	Chronic	
Deficiency of Protein C, S or Anti-Thrombin	2.5 (2-3)	Chronic	
Atrial Fibrillation (AF)/ Atrial Flutter[4]			
$CHADS_2$ = 0; Low stroke risk	None		May choose aspirin 75-325 mg daily
$CHADS_2$ = 1; Intermediate stroke risk	2.5 (2-3)	Chronic	CI anticoagulation: aspirin 75-325 mg and clopidogrel 75 mg daily
$CHADS_2 \geq 2$; High stroke risk	2.5 (2-3)	Chronic	CI anticoagulation: aspirin 75-325 mg and clopidogrel 75 mg daily
With mitral stenosis	2.5 (2-3)	Chronic	CI anticoagulation: aspirin 75-325 mg and clopidogrel 75 mg daily
With stable CAD	2.5 (2-3)	Chronic	No aspirin needed
Pre-cardioversion (AF or flutter >48 hours)	2.5 (2-3)	3 weeks	
Post-cardioversion (in NSR)	2.5 (2-3)	4 weeks	
Ischemic Stroke[5]			
Non-cardioembolic stroke or TIA	None	Chronic	Use antiplatelet therapy
Cardioembolic stroke or TIA			
-With warfarin CI	None	Chronic	Aspirin 81-325 mg daily
-With cerebral venous sinus thrombosis	2.5 (2-3)	3-6 months	
- With patent foramen ovale	None	Chronic	Use antiplatelet therapy
- With other indication for anticoagulation (VTE, AF)	2.5 (2-3)	Chronic	
Thromboembolism (DVT, PE) symptomatic or asymptomatic[6]			
Provoked VTE event	2.5 (2-3)	3 months	
Unprovoked: 1st VTE event			
- Proximal or Distal DVT	2.5 (2-3)	3 months	After 3 months evaluate risk-benefit for extended therapy
- PE (low bleed risk)	2.5 (2-3)	> 3 months	After 3 months evaluate risk-benefit for extended therapy
- PE (high bleed risk)	2.5 (2-3)	3 months	
Unprovoked: 2nd VTE event			
- DVT or PE (low bleed risk)	2.5 (2-3)	> 3 months	Consider chronic
- DVT or PE (high bleed risk)	2.5 (2-3)	3 months	
With malignancy	2.5 (2-3)	> 3 months	LMWH preferred over warfarin Consider chronic
Acute Upper Extremity DVT			
- Associated with central venous catheter that was removed	2.5 (2-3)	3 months	
- Associated with central venous catheter that was NOT removed	2.5 (2-3)	Extended	Continue anticoagulation until catheter removed

- Not associated with a central venous catheter	2.5 (2-3)	3 months	
Spontaneous superficial vein thrombosis	None	45 days	Prophylaxis LMWH or Fondaparinux
Valvular Disease[7]			
Rheumatic mitral valve disease			
- Left atrial diameter < 55 mm	None		
- With AF, left atrial thrombus, or left atrial diameter > 55 mm	2.5 (2-3)	Chronic	
Valve Repair			
Aortic	None		Aspirin 81 mg daily
Mitral	None	3 months	Antiplatelet therapy
Valve Replacement - Bioprosthetic			
Aortic	None		Aspirin 81 mg daily
Mitral	2.5 (2-3)	3 months	Followed by aspirin 81 mg daily
* If other indication for anticoagulation exist – see specific indication for therapy recommendations			
Valve Replacement - Mechanical			
Aortic	2.5 (2-3)	Chronic	Low bleed risk: add aspirin 81 mg
Mitral	3 (2.5-3.5)	Chronic	Low bleed risk: add aspirin 81 mg
Dual Aortic and Mitral Valve	3 (2.5 -3.5)	Chronic	Low bleed risk: add aspirin 81 mg
Orthopedic Surgery[8]			
Total Knee or Hip Arthroplasty	1.8-2.2	10-14 days	INR goal per UWHC Orthopedics
Hip Fracture Surgery	1.8-2.2	10-14 days	INR goal per UWHC Orthopedics
Trauma Surgery	2.5 (2-3)	35 days	

AF- atrial fibrillation; CAD – coronary artery disease; CI- contraindications; DVT- deep vein thrombosis; LMWH- low molecular weight heparin, NSR- normal sinus rhythm; PE- pulmonary embolism; TIA- transient ischemic attack; VTE – venous thromboembolism

1.1 Stroke risk stratification schemes use risk factors to assess stroke risk in patient with non-rheumatic atrial fibrillation[4]

1.2 The most validated risk score is $CHADS_2$[4]

1.3 A new risk score $CHADS_2$-VASc combines $CHADS_2$ with additional moderate risk factors[4]

1.4 The predictive ability for stroke of $CHADS_2$-VASc is similar to $CHADS_2$[4]

Table 2. Calculating a $CHADS_2$ Score[4]

C	Congestive Heart Failure	1 point
H	Hypertension	1 point
A	Age ≥ 75	1 point
D	Diabetes	1 point
S	Secondary prevention in patients with prior ischemic stroke, TIA, or systemic thromboembolic event	2 points

V	Vascular Disease	1 point
A	Age 64-75	1 point
Sc	(Sex Category) - Female	1 point
Scoring: 0 point – Low Risk 1 point – Intermediate Risk ≥ 2 points – High Risk		

2. Initial Patient Assessment
   2.1 Table 3 identifies conditions that may increase a patient's sensitivity to warfarin[2]
   2.2 Patients with multiple high sensitivity risk factors may require a lower initiation dose and reduced maintenance doses ***(Grade 2C)***

Table 3. Factors for Identifying Warfarin Sensitive Patients

High Sensitivity Warfarin	Low Sensitivity Warfarin
Baseline INR ≥ 1.5	Baseline INR < 1.5
Age > 65	Age ≤ 65
Actual body weight < 45 kg or actual < ideal	No other risk factors
Malnourished/ NPO >3 days	
Hypoalbuminemia <2 g/dl	
Chronic diarrhea	
Significant drug interactions (see Table 9)	
Decompensated heart failure	
Cancer	
Current antiplatelet therapy	
Thrombocytopenia: platelet <75 K/uL	
Alcohol abuse history	
Significant hepatic disease: cirrhosis or total bilirubin.>2.4 mg/dl	
End stage renal disease	
GI bleed within past 30 days	
Surgery within past 2 weeks	
Intracranial bleed within past 30 days	

3. Initial Warfarin Dosing
   3.1 Initial dosing should be tailored based on patient bleed risk, potential sensitivity to warfarin, indication for anticoagulation, goal INR range and if potential drug interactions are present[2]
   3.2 Table 4 provides recommendations for adjusting warfarin doses to a goal INR of 2-3 within the first week of therapy
   3.3 A dose larger than the anticipated maintenance dose (loading dose) of warfarin is inappropriate and should not be used in most patients ***(Grade 2C)***
      3.3.1 In healthy patients with either a PE or DVT warfarin 10 mg for the first 2 days may be considered followed by dosing based on INR measurements[3] ***(Grade 2C)***
   3.4 If appropriate, patients should received another form of anticoagulation such as LMWH for at least 5 days and until they are therapeutic on warfarin for 24-48 hours[2,6] ***(Grade 1B)***

Table 4. Warfarin Initiation (Week 1) with INR Goal 2-3

Day Therapy	INR Value	Dose Adjustment
Day 1		5 mg daily (2.5 mg daily if high sensitivity to warfarin identified)
In 2-3 days after initiation	< 1.5 1.5-1.9 2.0-2.5 2.5-3.0 > 3.0	5 – 7.5 mg daily 2.5 - 5 mg daily 2.5 mg daily 0-2.5 mg daily Hold and recheck INR next day
In additional 2-3 days after last INR check	< 1.5 1.5-1.9 2.0-3.0 > 3.0	7.5 – 10 mg daily 5 – 10 mg daily 2.5 – 5 mg daily Hold warfarin, recheck in 1-2 days

4. Maintenance Warfarin Dosing
   - 4.1 Warfarin should be adjusted based on INR measurements ***(Grade 1A***)
   - 4.2 Prior to making a dose adjustment assess for any missed doses, changes in diet, potential drug interaction or other changes that may affect INR level (Appendix A. Patient Assessment Tool) ***(Grade 1C)***
   - 4.3 Tables 5, 6, and 7 provide recommendations for adjusting warfarin based on goal INR range
     - 4.3.1 For INRs minimally above or below therapeutic range by ≤ 0.5 in patients previously stable or if there is a specific reason for the INR to be out of range (ex. missed dose), no dosing change may be needed. Recommend to continue current dose and test INR in 1-2 weeks.[3]
   - 4.4 Daily low dose vitamin K supplement should not be used to improve INR control[3] ***(Grade 2C)***

Table 5. Warfarin Maintenance Dosing Protocol with INR Goal 1.5-2.0

INR ≤ 1.2	INR 1.3 -1.4[ŧ]	INR 1.5 - 2.0	INR 2.1 – 3.0[ŧ]	INR 3.1 - 4.0*	INR 4.1-5.0*	INR 5.1-9.0*	INR > 9.0
Increase weekly dose 10%	Increase weekly dose 5%	No change	Decrease weekly dose 5%	Consider half dose x 1 and Decrease weekly dose 10%	Hold 1 dose Decrease weekly dose by 10-20%	**MD order required** Consider: Hold 2 doses Decrease weekly dose 10-20% Check Hct	Contact MD for urgent patient evaluation

Table 6. Warfarin Maintenance Dosing Protocol with INR Goal 2-3

INR < 1.5	INR 1.5 - 1.9[ŧ]	INR 2.0 - 3.0	INR 3.1- 4.0*[ŧ]	INR 4.1-5.0*	INR 5.1- 9.0*	INR > 9.0
Extra Dose Increase weekly dose 10-20%	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Hold 1 dose Decrease weekly dose 10%	**MD order required** Consider: Hold 2 doses Decrease weekly dose 10-20% Check Hct	Contact MD for urgent patient evaluation

Table 7. Warfarin Maintenance Dosing Protocol with INR Goal 2.5-3.5

INR < 1.9	INR 1.9 - 2.4[ŧ]	INR 2.5 - 3.5	INR 3.6 - 4.5*[ŧ]	INR 4.6-5.0*	INR 5.1- 9.0*	INR > 9.0
Extra Dose Increase weekly dose 10-20%	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Hold 1 dose Decrease weekly dose 10%	**MD order required** Consider: Hold 2 doses Decrease weekly dose 10-20% Check Hct	Contact MD for urgent patient evaluation

* If the INR is above the specified range for accuracy per POC device, a repeat venipuncture is required to verify INR

5. Laboratory Monitoring[2,3]
    5.1 A baseline INR must be reported prior to the first dose of warfarin ***(Grade 1A)***
        5.1.1 A baseline INR can be within past 30 days prior to initiating first dose warfarin
    5.2 Upon discharge from the hospital an INR should be obtained within 2-3 days ***(Grade 1C)***
    5.3 CBC with platelet, ALT, total bilirubin, and creatinine within preceding 3 months and periodically thereafter per physician discretion ***(Grade 2C)***
    5.4 For women of child bearing age a pregnancy test is recommended before initiating warfarin ***(Grade 1C)***
    5.5 Follow up INR monitoring per recommendations in table #8 and table #9

Table 8. Frequency of INR Monitoring After Initiation of Warfarin

INR Check	
Every 2 – 3 days	Until INR within therapeutic range on 2 consecutive INR checks
Then every week	Until INR within therapeutic range on 2 consecutive INR checks
Then every 2 weeks	Until INR within therapeutic range on 2 consecutive INR checks
Then every 4 weeks	When dose is stable check monthly

Table 9. Frequency of INR Monitoring for Maintenance of Warfarin

INR Check	
After 1 week	If start/stop interacting medication, change in diet, change in activity level or other change that could affect INR
Every 1-2 weeks	If dose needed adjustment by 5-10%
Every 4 weeks	If patient maintained on same stable dose < 6 months
Every 6-8 weeks	If patient maintained on same stable dose for at least 6 months

6. Symptomatic Monitoring ***(Grade 1C)***
    6.1 At each encounter for INR monitoring patients should be assessed for:
        6.1.1 Signs and symptoms of bleeding:
            - Significant blood in the urine, stool, sputum or emesis should be referred to a primary care provider or urgent care center/emergency department for evaluation.
        6.1.2 Sign and symptoms of clotting
            - Significant pain, swelling, redness, or heat in lower extremity or chest pain, shortness of breath, sweating, increased heart rate or coughing up blood should be referred to a primary care provider or urgent care center/emergency department for evaluation.
        6.1.3 Any missed doses, changes in diet or activity level, acute illness or medication changes
            - Changes may affect INR level and require warfarin dose adjustment

7. Drug Interactions[2,3]
    7.1 Most interactions with warfarin will start to have an effect within 3-5 days
        7.1.1 Amiodarone, carbamezapine and rifampin will start to have an effect within 7-14days
    7.2 An INR should be checked within 5-7 days of starting a medication, dietary supplement or food that has the potential to interact with warfarin ***(Grade 2C)***
    7.3 For some interactions a total weekly dose adjustment of 30% is needed
        7.3.1 For amiodarone and rifampin a total weekly dose adjustment of 50% is needed
    7.4 See Table 10 and 11 for medication, dietary supplements and food that have the potential to interact with warfarin. These tables are NOT all inclusive.

Table 10. Medications, dietary supplements and food that **INCREASE** INR or bleeding risk

Drug Class	Known Interaction	Probable Interaction	Possible Interaction	Unlikely Interaction
Anti-Infective	Ciprofloxacin Erythromycin **Fluconazole** Isoniazid **Metronidazole** Miconazole Miconazole Vaginal Suppository Moxifloxacin **Sulfamethoxazole** Voriconazole	Amoxicillin/clavulanate Azithromycin Clarithyomycin Itraconazole Ketoconazole Levofloxacin Ritonavir Tetracycline	Amoxicillin Chloramphenicol Darunavir Daptomycin Etravirine Ivermectin Miconazole topical gel Nitrofurantoin Norfloxacin Ofloxacin Saquinavir Telithromycin Terbinafine	Cefotetan Cefazolin Tigecycline
Cardiovascular	**Amiodarone*** Clofibrate Diltiazem Fenofibrate Propafenone Propranolol	Aspirin Fluvastatin Quinidine Ropinirole Simvastatin	Disopyramide Gemfibrozil Metolazone	Heparin
Analgesics, Anti-Inflammatory	Piroxicam	Acetaminophen Aspririn Celecoxib Tramadol	Indomethacin Propoxyphene Sulindac Tolmentin Topical Salicylates	Methylprednisolone Nabumetone
CNS Drugs	Alcohol Citalopram Entacapone Sertraline	Disulfiram Chloral hydrate Fluvoxamine Phenytoin	Felbamate	Diazepam Fluoxetine Quetiapine
GI Drugs and Food	Cimetidine Mango Omeprazole	Grapefruit	Orlistat	
Herbal Supplement	Fenugreek Feverfew Fish Oil Ginkgo Quilinggao	Dandelion Danshen Don Quai Lycium PC-SPES Red or Sweet Clover	Capsicum Forskolin Garlic Ginger Turmeric	
Other	Anabolic Steroids Capecitabine Zileuton	Fluorouracil Gemcitabine Levamisole Paclitaxel Tamoxifen Tolterodine	Acarbose Cyclophosphamide Danazol Iphosphamide Trastuzumab	Etoposide Carboplatin Levonorgestrel

* See Section 7: Drug Interactions for further recommendations

Table 11. Medications, dietary supplements and food that **DECREASE** INR

Drug Class	Known Interaction	Probable Interaction	Possible Interaction	Unlikely Interaction
Anti-Infective	Griseofulvin Nafcillin Ribavirin **Rifampin***	Dicloxacillin Ritonovir Rifapentine	Terbinafine Nelfinavir Nevirapine	Cloxacillin Rifaximin Teicoplanin
Cardiovascular	Cholestyramine	Bosentan	Telmisartan	Furosemide
Analgesics, Anti-Inflammatory	Mesalamine	Azathioprine	Sulfasalazine	
CNS Drugs	Barbiturates Carbamazepine	Chlordiazepoxide		Propofol
GI Drugs and Food	High content vitamin K food Avocado	Soy milk Sucralfate	Sushi containing seaweed	
Herbal Supplement	Alfalfa	Ginseng Multivitamin St. John's Wort Parsley	Co-Enzyme Q10 Yarrow Licorice	Green Tea
Other	Mercaptopurine	Chelation Therapy Influenza vaccine Raloxifene	Cyclosporine Etretinate Ubidecarenone	

* See Section 7: Drug Interactions for further recommendations

8. Discontinuing Therapy[3]
   8.1 Warfarin may be abruptly discontinued. No tapering of warfarin is needed ***(Grade 2C)***

9. Warfarin Reversal
   9.1 See Anticoagulation Reversal **–** Adult – Clinical Practice Guideline *(in development)*

10. Periprocedural Anticoagulation (Bridging)[9]
    10.1 Evaluate patient's risk factor for thromboembolism
    10.2 Evaluate bleed risk for surgery/procedural
    10.3 Weigh the consequences of thromboembolism and bleeding for your individual patient
    10.4 **http://www.uwhealth.org/files/uwhealth/docs/anticoagulation/Periprocedural_Anticoagulation_Guideline.pdf**

F. References:

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9. Douketis J, Spyropoulos A, Spencer F, et al. Perioperative Management of Antithrombotic Therapy: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed. American College of Chest Physicians Evidence Based Clinical Practice Guidelines. *CHEST.* 2012;141: 326s-330s.

UW Health generated documents (e.g., policies, clinical references, protocols, order sets)

1. UW Health Protocol #7: Ambulatory initiation & management of warfarin for adults
2. Periprocedural Anticoagulation – Adult – Inpatient and Ambulatory – Clinical Practice Guideline

G. Benefits/Harms of Implementation –

1. Benefits:
   1.1. Guideline will standardize the management of warfarin therapy
2. Harms:
   2.1. These guidelines were designed to be used in the majority of patients on warfarin, however, not all patients may fit into these management guidelines, Clinical judgment should supersede the guidelines when clinically appropriate.

H. Implementation Strategy –

1. This guideline will be available electronically on both UConnect and Anticoagulation Website

I. Implementation Tools/Plan –

1. Health link will be used to implement the clinical practice guideline. The guideline will be hyperlinked to the anticoagulation episode of care.

2. Education
   2.1. Education packets will be provided to all primary care clinics and specialty clinics who manage warfarin therapy.
   2.2. Online training will include guideline recommendations
   2.3. Guideline will be highlighted in the Anticoagulation Newsletter
   2.4. Series of live training sessions will be offered to clinic staff

K. Disclaimer: Clinical practice guidelines are described to assist clinicians by providing a framework for evaluation and treatment of patients. The Clinical Practice Guideline outlines the preferred approach for most patients. It is not intended to replace a clinician's judgment. It is understood that some patients will not fit the clinical condition contemplated by a guideline and that a guideline will rarely establish the only appropriate approach to a problem.