Group A Streptococcal Pharyngitis Treatment Protocol

I. Purpose

The purpose of this standing order is to reduce morbidity and mortality in Arkansas by allowing Arkansas-licensed pharmacists to initiate therapy including ordering and/or dispensing treatment medications, along with any necessary supplies for administration, to eligible persons who are GAS pharyngitis positive.

II. Authority

This standing order is issued pursuant to Act 503 of 2021 (HB 1246) (Arkansas Code § 17-92-101) to authorize licensed pharmacists in Arkansas to order and/or dispense GAS treatment medications according to the provisions of Arkansas Code § 17-92-101 and the requirements of this standing order.

III. Screening and Assessment

The Board of Pharmacy will adopt screening assessment and questionnaire (Appendix A) to be used by pharmacists throughout the state. When a patient requests point-of-care testing services, or when a pharmacist, in his or her professional judgement, decides to initiate point-of-care testing and treatment, the patient will be assessed for presenting signs and symptoms that warrant GAS testing, parental consent for individuals under the age of 18, and if appropriate, administer a rapid GAS point-of-care test.

IV. Dispensing Guidelines

A. Eligibility Criteria

Inclusion:

- Age 3 years and older
- Centor Score ≥ 2
- Positive GAS result via CLIA-waived point-of-care RADT

Exclusion:

- Immunocompromised as defined
    - Been receiving active cancer treatment for tumors or cancers of the blood
    - Received an organ transplant and are taking medicine to suppress the immune system
    - Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
    - Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
    - Advanced or untreated HIV infection

    - Active treatment with high-dose corticosteroids (20mg prednisone daily for >2 weeks) or other drugs that may suppress your immune response
- Pregnant
- Antibiotic therapy prescribed for sore throat or upper respiratory infection with in previous 30 days
- Clinically unstable based on the clinical judgement of the pharmacist or any of the following criteria:
    - Systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg
        - For age 3-9 years: Systolic blood pressure <70 + (age in years × 2)
    - Tachypnea (>25 breaths/min adult or >20 breaths/min <18 y/o)
    - Oxygen saturation (SpO_2) <90% via pulse oximetry

B. Contraindications

Do not administer amoxicillin to an individual with a known hypersensitivity to penicillin or any component of the formulation

Do not administer cephalexin to an individual with a known hypersensitivity to cephalexin, other cephalosporins, or any component of the formulation

Do not administer azithromycin to an individual with a known hypersensitivity to azithromycin, erythromycin, other macrolide (e.g., azalide or ketolide) antibiotics, or any component of the formulation.

Do not administer azithromycin to an individual with a history of cholestatic jaundice/hepatic dysfunction associated with prior azithromycin use

C. Product Availability

Streptococcal pharyngitis treatment products that may be dispensed/provided under this standing order. Following dosing below, pharmacist can dispense any commercially available product form (tablet, capsule, suspension) based on availability and patient preference.

1st line Treatment

- Amoxicillin
    - Adults: 1000mg by mouth once daily for 10 days
    - Children <20kg: 50mg/kg by mouth once daily for 10 days
- Penicillin V, oral
    - Adults: 500mg twice daily for 10 days
    - Children: 250 mg twice daily for 10 days

2nd Line Treatment or PCN allergy alternative

- Cephalexin
    - Adults: 500 mg by mouth twice daily for 10 days
    - Children <25kg: 20mg/kg/dose twice daily for 10 days

3rd Line Treatment if PCN allergy or equivalent exclusions to first or second line treatment options

- Azithromycin 500 mg by mouth Day 1 and 250 mg by mouth Days 2-5
- Children <40kg: Azithromycin 12mg/kg per day for 5 days

Over-the-Counter Adjunctive Treatment

- Recommend adjunctive treatment as needed for symptom relief and use of weight-based dosing for children.
    - Acetaminophen 650 mg Q4-6H PRN (MAX 3250 mg/day)
    - Ibuprofen 200 mg Q4-6H PRN X10D for pain or X3D for fever
      Can titrate to 400 mg if needed (MAX 1200 mg/day)

D. Warnings/Precautions

1. Amoxicillin
    - *Concerns related to adverse effects:*
        - Anaphylactic/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy, including amoxicillin, especially with a history of beta-lactam hypersensitivity (including severe reactions with cephalosporins) and/or a history of sensitivity to multiple allergens.
        - Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months post antibiotic treatment.
    - *Disease-related concerns:*
        - Infectious mononucleosis: A high percentage of patients with infectious mononucleosis develop an erythematous rash during amoxicillin therapy; avoid use in these patients.
        - Renal impairment: Use with caution in patients with renal impairment; dosage adjustment recommended in patients with GFR <30 mL/minute. Avoid extended release 775 mg tablet and immediate release 875 mg tablet in patients with GFR <30 mL/minute or patients requiring hemodialysis.
    - *Dosage form specific issues:*
        - Benzyl alcohol and derivatives: Some dosage forms may contain sodium benzoate/benzoic acid; benzoic acid (benzoate) is a metabolite of benzyl

alcohol; large amounts of benzyl alcohol (≥99 mg/kg/day) have been associated with a potentially fatal toxicity ("gasping syndrome") in neonates; the "gasping syndrome" consists of metabolic acidosis, respiratory distress, gasping respirations, CNS dysfunction (including convulsions, intracranial hemorrhage), hypotension, and cardiovascular collapse (AAP ["Inactive" 1997]; CDC 1982); some data suggests that benzoate displaces bilirubin from protein binding sites (Ahlfors 2001); avoid or use dosage forms containing benzyl alcohol derivative with caution in neonates. See manufacturer's labeling.

    - Chewable tablets: May contain phenylalanine; see manufacturer's labeling.

2. Penicillin V
    - *Concerns related to adverse effects:*
        - Anaphylactic/hypersensitivity reactions: Serious and occasionally severe or fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy, especially with a history of beta-lactam hypersensitivity or history of sensitivity to multiple allergens.). Use with caution in asthmatic patients. If a serious reaction occurs, treatment with supportive care measures and airway protection should be instituted immediately.
        - Superinfection: Prolonged use may result in fungal or bacterial superinfection, including C. difficile-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months postantibiotic treatment.
    - *Disease-related concerns:*
        - Renal impairment: Use with caution in patients with severe renal impairment.
        - Seizure disorders: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures.
    - *Other warnings/precautions*
        - Prolonged use: Extended duration of therapy or use associated with high serum concentrations (eg, in renal insufficiency) may be associated with an increased risk for some adverse reactions (neutropenia, hemolytic anemia, serum sickness).
3. Cephalexin
    - *Concerns related to adverse effects:*
        - Hypersensitivity: Allergic reactions (e.g., rash, urticaria, angioedema, anaphylaxis, erythema multiforme, Stevens-Johnson syndrome, toxic

epidermal necrolysis [TEN]) have been reported. If an allergic reaction occurs, discontinue immediately and institute appropriate treatment.

- Elevated INR: May be associated with increased INR, especially in nutritionally deficient patients, prolonged treatment, hepatic, or renal disease.
- Penicillin allergy: Use with caution in patients with a history of penicillin allergy, especially IgE-mediated reactions (e.g., anaphylaxis, angioedema, urticaria).
- Seizure disorder: Use with caution in patients with a history of seizure disorder; high levels, particularly in the presence of renal impairment, may increase risk of seizures.
- Superinfection: Prolonged use may result in fungal or bacterial superinfection, including *C. difficile*-associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months post antibiotic treatment.

- *Disease-related concerns:*
  - Renal impairment: Use with caution in patients with renal impairment; modify dosage in severe impairment.
- *Other warnings/precautions:*
  - Direct Coombs tests: Positive direct Coombs tests and acute intravascular hemolysis has been reported. If anemia develops during or after therapy, discontinue use and work up for drug-induced hemolytic anemia.

4. Azithromycin
   - *Concerns related to adverse effects:*
     - Superinfection: Prolonged use may result in fungal superinfection.
   - *Disease-related concerns:*
     - Bronchiolitis obliterans: When studied to prevent bronchiolitis obliterans syndrome in patients with hematologic malignancy who underwent allogeneic hematopoietic cell transplantation, rates of cancer relapse and mortality were increased among patients receiving long-term azithromycin, leading to early trial termination (Bergeron 2017; FDA Drug Safety Communication 2018).
     - Gonorrhea/syphilis: May mask or delay symptoms of incubating gonorrhea or syphilis, so appropriate culture and susceptibility tests should be performed prior to initiating a treatment regimen.
     - Myasthenia gravis: Use with caution in patients with myasthenia gravis; exacerbation and new onset of symptoms have occurred.

- *Special populations:*
    - Infants: Use of azithromycin in neonates and infants <6 weeks of age has been associated with infantile hypertrophic pyloric stenosis (IHPS); the strongest association occurred with exposure during the first 2 weeks of life; observe for nonbilious vomiting or irritability with feeding (Eberly 2015). The risks and benefits of azithromycin use should be carefully considered in neonates; some experts recommend avoidance except for in the treatment of pertussis or *C. trachomatis* pneumonia; specific risk-benefit ratio should be considered before use for *Ureaplasma* spp. eradication (Meyers 2020).
- *Dosage form specific issues:*
    - Oral suspensions: Immediate release and extended-release suspensions are not interchangeable.

E. Documentation

Patient records must be furnished to a health care practitioner designated by the patient upon the request of the patient. Documentation may include, but is not limited to presenting signs and symptoms that warrant strep testing, parental consent for individuals under the age of 18, and results of rapid diagnostic test(s). Maintain records of all patients receiving services for two (2) years.

APPENDIX A.

Pharmacist Assessment, Evaluation and Prescribing Protocol Form: *Strep Throat*

PATIENT INFORMATION		
Name:	Date of Birth:	Age:
Address:	City/State/Zip:	
Email Address:	Phone:	
Primary Care Provider:		
Medication allergies?		
Current medications? (prescription, over-the-counter, herbals, topical medications, pain or allergy medication, and any supplements/vitamins)		
Treatments tried for the current condition (if none please indicate N/A):		

PATIENT ELIGIBILITY		
1. Are you 3 years of age and older?	❑ Yes	❑ No
2. Have you received antibiotics for sore throat or upper respiratory infection within the past 30 days?	❑ Yes	❑ No
3. Are you pregnant?	❑ Yes	❑ No
4. Have you ever been diagnosed with a weakened immune system? (e.g. cancer, transplant, or long term steroids)	❑ Yes* *Pharmacists refer to page 2, #4 for criteria	❑ No

When complete, please return the form to pharmacy staff along with insurance information

-- FOR PHARMACY STAFF ONLY--

Physical Assessment	**REFER TO PCP** if determined clinically unstable or any of the following criteria
❑ Blood pressure:_____ ❑ RR:_____ ❑ %Oxygen:_____ ❑ Temperature:_____	❑ Systolic blood pressure < 90 mmHg or diastolic blood pressure < 60 mmHg ❑ For age 3-9 years: Systolic blood pressure <70 + (age in years × 2) ❑ Tachypnea >25 breaths/min adult or >20 breaths/min <18 y/o ❑ Low oxygen <90% oxygen via pulse oximetry

Centor Score Assessment		**Interpretation**
Age	❑ 3-14 years: +1 ❑ 15-44: 0 ❑ ≥ 45 year: -1	Total Points: _____ ❑ If Score ≥ 2, proceed in using protocol ❑ If Score < 2, excluded from protocol
Exudate or swelling on tonsils	❑ No: 0 ❑ Yes: +1	
Tender/swollen anterior cervical lymph nodes	❑ No: 0 ❑ Yes: +1	
Temperature > 100.4°F	❑ No: 0 ❑ Yes: +1	
Cough	❑ Present: 0 ❑ Absent: +1	
CLIA-waived POCT Result		❑ Positive for GAS – continue ❑ Negative for GAS – refer to PCP + Symptomatic Treatment

Pharmacist Interpretation of qualifying questions and physical assessment; refer to PCP as appropriate. Exclusion criteria does not preclude from testing services. **Refer to PCP for treatment if:**

1. If younger than 3 years old **REFER TO PCP**
2. If patient has taken antibiotics for sore throat or URI in the last 30 days **REFER TO PCP**
3. If patient is pregnant **REFER TO PCP**
4. If patient is immunocompromised **REFER TO PCP**
    a. Been receiving active cancer treatment for tumors or cancers of the blood
    b. Received an organ transplant and are taking medicine to suppress the immune system
    c. Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
    d. Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
    e. Advanced or untreated HIV infection
    f. Active treatment with high-dose corticosteroids (20mg prednisone daily for >2 weeks) or other drugs that may suppress your immune response
5. CLIA-waived POCT result is negative for GAS **REFER TO PCP**

Treat using protocol if:

1. Age 3 years and older
2. Centor Score ≥ 2
3. Positive GAS result via CLIA-waived point-of-care RADT

Diagnosis of Patient:		
❑ Strep ADULT ≥18 year	❑ Strep CHILD/ADOLESCENT	❑ Refer to PCP

***the following can act as the prescription**

Treatment Options		
Streptococcal pharyngitis ADULT >18		
Strep first line treatment options:		
❑ Amoxicillin	Dispense: ❑ 500mg #20 ❑ 1000mg #10 No refills	Sig: 500mg by mouth twice daily for 10 days OR Sig: 1000mg by mouth daily for 10 days
❑ Penicillin VK	Dispense: ❑ 500mg #20 No refills	Sig: 500mg by mouth twice daily for 10 days
2nd Line Treatment or Penicillin allergy alternative		
❑ Cephalexin	Dispense ❑ 500mg #20 No refills	Sig: 500mg by mouth BID for 10 days
3rd Line Treatment for Penicillin allergy or equivalent		
❑ Azithromycin	Dispense ❑ 250mg #6 No refills	Sig: (500mg) by mouth on day 1, then (250 mg) po days 2-5
Symptomatic treatments (over the counter)		
❑ Acetaminophen regular strength (325mg) → 650 mg q4-6hr prn (MAX 3250 mg/day) ❑ Ibuprofen → 200mg q4-6h prn (400mg if no response to 200mg) (MAX 1200mg/day x10 days for pain or x 3 days for fever) ❑ Lozenges/drops containing menthol, dyclonine, benzocaine, or hexylresorcinol ❑ Throat spray containing phenol or benzocaine ❑ Hot/cold liquids or foods→ cold food provide hydration and numbing, hot foods feel good on sore throat. SOFT FOODS preferable to rough or hard foods ❑ Tea/honey → coats throat to provide relief of pain and irritation.		

Patient:_____ DOB:_____

Prescribed by:_____

Signature:_____Date:_____

***the following can act as the prescription**

Treatment Options		
Streptococcal pharyngitis CHILDREN AND ADOLESCENTS age 3-17 **Patient weight in kg:_____**		
First line treatment option		
❑ Amoxicillin	Dispense: ❑ _____mg (50mg/kg) #10 doses No refills	***MAX daily dose 1,000mg/day*** Sig: 50mg/kg by mouth Daily x10 days
❑ Penicillin VK	Dispense ❑ 250mg #20 doses No refills	Sig: 250mg by mouth twice daily for 10 days
2nd Line Treatment or Penicillin allergy alternative		
❑ Cephalexin	Dispense ❑ _____mg (20mg/kg) #20 doses No refills	***MAX 500mg per dose*** Sig: 20mg/kg/dose by mouth twice daily for 10 days
3rd Line Treatment		
❑ Azithromycin	Dispense ❑ _____mg (12mg/kg) #5 doses No refills	***MAX 500mg per dose*** Sig: 12mg/kg/dose by mouth daily for 5 days
Symptomatic treatments (over the counter)		
❑ Acetaminophen regular strength (325mg) → 325 mg q4-6hr prn (MAX 1,625 mg/day) OR ____mg q4-6h prn 10-15 mg/kg/dose MAX 75 mg/kg/day not to exceed 4,000 mg/day ❑ Ibuprofen → for pain _____ mg q6-8hr if <50kg 4-10 mg/kg/dose (MAX single dose 400mg MAX daily 40mg/kg/day) For fever: ____mg q6-8h (MAX daily dose is 40mg/kg/day up to 1,200mg. MAX single dose 400mg) ❑ Lozenges/drops containing menthol, dyclonine, benzocaine, or hexylresorcinol ❑ Throat spray containing phenol or benzocaine ❑ Hot/cold liquids or foods→ cold food provide hydration and numbing, hot foods feel good on sore throat. SOFT FOODS preferable to rough or hard foods ❑ Tea/honey → coats throat to provide relief of pain and irritation		

Patient:_____ DOB:_____

Prescribed by:_____

Signature:_____Date:_____

References:

1. Infectious Diseases Society of America. Influenza Guidelines. http://www.idsociety.org
2. LexiComp. Wolters Kluwer Clinical Drug Information. http://online.lexi.com

Pediatric Vital Signs Reference Chart

Heart Rate (beats/min)		
Age	**Awake**	**Asleep**
Neonate (<28 d)	100-205	90-160
Infant (1-12 mos)	100-190	
Toddler (1-2 y)	98-140	80-120
Preschool (3-5 y)	80-120	65-100
School-age (6-11 y)	75-118	58-90
Adolescent (12-15 y)	60-100	50-90

Respiratory Rate (breaths/min)	
Age	**Normal**
Infant (<1 y)	30-53
Toddler (1-2 y)	22-37
Preschool (3-5 y)	20-28
School-age (6-11 y)	18-25
Adolescent (12-15 y)	12-20

Reference: PALS Guidelines, 2015

Blood Pressure (mmHg)				
Age		**Systolic**	**Diastolic**	**Systolic Hypotension**
Birth (12 h)	<1 kg	39-59	16-36	<40-50
	3 kg	60-76	31-45	<50
Neonate (96 h)		67-84	35-53	<60
Infant (1-12 mos)		72-104	37-56	<70
Toddler (1-2 y)		86-106	42-63	<70 + (age in years × 2)
Preschool (3-5 y)		89-112	46-72	
School-age (6-9 y)		97-115	57-76	
Preadolescent (10-11 y)		102-120	61-80	<90
Adolescent (12-15 y)		110-131	64-83	

Reference: PALS Guidelines, 2015
For diagnosis of hypertension, refer to the 2017 AAP guidelines Table 4 & 5:
http://pediatrics.aappublications.org/content/early/2017/08/21/peds.2017-1904

Temperature (°C)	
Method	**Normal**
Rectal	36.6-38.0
Tympanic	35.8-38.0
Oral	35.5-37.5
Axillary	36.5-37.5

Ranges do not vary with age.
Screening: axillary, temporal, tympanic (↓ accuracy)
Definitive: rectal & oral (↑ reflection of core temp.)
Reference: CPS Position Statement on Temperature Measurement in Pediatrics (2015)

Oxygen Saturation (SpO_2)

SpO_2 is lower in the immediate newborn period. Beyond this period, a SpO_2 of **<90-92%** may suggest a **respiratory condition** or **cyanotic heart disease**.

Dr. Chris Novak & Dr. Peter Gill for www.pedscases.com
(Edited March 2020 by Richard He)