**Definition:** Sickle cell disease is an inherited red blood cell disorder that can cause both acute and chronic complications. Sickle cell disease is used to refer to the many genotypes that cause the characteristic clinical syndrome.\(^1\)

**Pathophysiology:** Sickle cell anemia (otherwise known as HbSS, or homozygous β⁺ allele) is the most common form, with the second most prevalent type being HbSC, or HbS/β-thalassemia.\(^1\) The genetic mutation that causes sickle cell disease creates an HbS polymerization that can disrupt hemoglobin architecture and flexibility and oxidative cellular stress.\(^1\) The mutation can result in the processes of vaso-occlusion with ischemia and reperfusion injury and hemolytic anemia.\(^1\)

**Epidemiology:** It is estimated that sickle cell disease affects approximately 100,000 Americans in the United States, and occurs in 1 of every 365 Black or African American births, and 1 of every 16,300 Hispanic-American births. Approximately 1 in 13 African-American babies is born with sickle-cell trait. With the utilization of pneumococcal vaccines and hydroxyurea therapy, the mortality rate for sickle cell disease has been dramatically reduced.\(^2\)

**Etiology:** Vaso-occlusive crises (VOCs) are thought to be caused by microvascular obstruction and tissue ischemia (ischemia-reperfusion injury) and hemolytic anemia.\(^1\) Although VOCs commonly occur in the extremities, when they occur in other sites they may be confused with, or can be in the early stages of, other acute complications, and etiology of the pain must be determined in order to rule out potential causes other than uncomplicated VOC.\(^3\) Other acute complications that can manifest in acute vaso-occlusive pain include stroke, acute chest syndrome, renal infarction, myocardial infarction, priapism, splenic or hepatic sequestration.\(^3\)

**Inclusion Criteria**
- Patients with pain from sickle cell disease

**Exclusion Criteria**
- Patients who exhibit signs of stroke

**Differential Diagnosis**
- Vaso-occlusive Crisis
- Acute Chest Syndrome
- Osteomyelitis
- Avascular Necrosis
- Pulmonary Embolism
- Stroke
- Renal Infarction
- Myocardial Infarction
- Priapism
- Splenic Sequestration
- Hepatic Sequestration

**Diagnostic Evaluation**

**History:** Assess for
- Description of pain
- Duration of pain
- Presence of chronic pain
- Treatment provided prior to visit
- Vaccination status

**Physical Examination**
- Assessment for the possibility of other serious complications concurrently with the treatment of pain
- Assess for abnormal vital signs, particularly changes in respiratory rate (RR), use of accessory muscles, color
- Assess for pain associated with abdominal distension for hepatic or splenic sequestration or acute cholecystitis, jaundice, or hematuria,

**Laboratory Tests:**
- Obtain a complete blood count with reticulocyte count and note changes in baseline CBC or reticulocyte count or any laboratory abnormalities (such as increasing creatinine, liver function tests, coagulation abnormalities, etc.)
- If febrile, consider obtaining blood cultures and reference the Sickle Cell Fever Guideline.
- Consider obtaining type and screen if concerned for need for transfusion

**Diagnostic Imaging Studies:**
- Consider a chest radiograph if patient has respiratory symptoms at presentation to the hospital or during admission. Fever in the absence of these symptoms does not necessitate evaluation with a chest radiograph.
Evidence Supports

- The following criteria should be utilized when choosing a starting dosing strategy for patient controlled analgesia (PCA) for patients with sickle cell disease. Patients should receive frequent pain assessments and dosing should be adjusted as needed. [3-14] – Strong recommendation with low quality evidence
  - Dosing strategies for PCA should be based on the patient’s tolerance to opioids (i.e. Opioid naïve versus opioid tolerant).
    - Utilize the criteria below when determining opioid tolerance for the patient.
      - Last pain admission <3 months ago
      - Pain score >7
      - Patient on home opioids
  - Basal and on-demand dosing should be utilized in most patients. Use the basal dose selection to guide the on-demand dose. On-demand dose should be close to the basal dose.
  - When initiating a morphine PCA, use the dosing parameters below when choosing a starting point.
    - Loading dose: 0.1 mg/kg
    - Continuous Infusion: 0.01 – 0.03 mg/kg/hour
    - Interval Dose: 0.015 – 0.025 mg/kg Lockout Interval: 10 minutes
    - 4-hour limit: 0.25 – 0.35 mg/kg

Remarks: There is on-going research on the most effective dosing strategy for patient-controlled analgesia in patients with sickle cell. New research on this topic should impact the update of this recommendation. Utilize the patient’s historical documentation from past hospitalizations to choose the most appropriate dosing strategies.

- For children with acute pain from sickle cell disease where opioid use is exhaustive and there is not an option of intravenous ketamine, consider a trial of oral ketamine. (15-18) – Weak recommendation with very low quality evidence

Evidence Lacking/Inconclusive

- Use of a risk score to predict 30-day emergency department revisit. (14,19-27) – Unable to make a recommendation
- Using functional pain scales as compared to traditional pain scales to assess acute pain in children with sickle cell disease. (28,29) – Unable to make a recommendation

Remarks: Traditional pain scales can be used to benchmark pain for a particular patient. A baseline pain score should be assessed and patient and provider should discuss a goal pain score for discharge. Functional goals (e.g. ability to return to school, physical activity) and pain intensity should be used to guide therapies.

Recommendations Adopted/Adapted from National Guidelines

- Administer a short course (5 days) of ketorolac in patients with pain related to sickle cell disease in the absence of contraindications. (4)

Remarks – Patients respond better to pain control intervention with a multi-modal response. Due to the pathophysiology of vaso-occlusive crisis in sickle cell disease, the addition of ketorolac for a five-day therapy followed by ibuprofen therapy after the five-days in addition to pharmacologic and non-pharmacologic strategies may improve the patient’s pain control.

- Patients with acute pain from SCD should have rapid (within 1 hour of emergency department arrival) assessment and administration of analgesia with frequent reassessments (every 20 minutes) to optimize pain control. (4)

Remarks - Non-IV routes of administration (e.g. intranasal) can facilitate rapid analgesic treatment.

- In patients with acute pain from SCD, use adjunctive non-pharmacologic approaches in addition to standard pharmacological management to treat pain. (4)

- In patients presenting with acute pain related to SCD, a subanesthetic ketamine infusion may be considered as adjunctive treatment for pain that is refractory or not effectively treated by opioids alone. (4)

Remarks - Subanesthetic ketamine infusions for analgesia may be used for sickle cell patients outside of this recommendation based upon the approval of the Pain and Hematology services. The determination of whether pain is refractory will be based upon consultation with Pain and Hematology services.

- For age appropriate children with SCD who have chronic (as opposed to episodic) pain from the SCD-related identifiable cause of avascular necrosis of bone, consider the use of duloxetine (and other serotonin and norepinephrine reuptake inhibitor [SNRI] medications, because there is evidence of a class effect) as an option for management, in the context of a comprehensive disease and pain management plan. (4)

Remarks – This recommendation was developed by the ASH guideline using indirect evidence in the adult population. There is a lack of data in the pediatric population for the use of SNRIs for the treatment of SCD chronic pain caused by avascular necrosis of bone. Evaluate the use of duloxetine in pediatric patients on a case-by-case basis with an understanding on the safety profile of this medication.

- For age appropriate children with SCD who have chronic (as opposed to episodic) pain from the SCD-related identifiable cause of avascular necrosis of bone, consider the use of NSAIDs as an option for management, in the context of a comprehensive disease and pain management plan. (4)

- For age appropriate children who have SCD-related chronic pain with no identifiable cause beyond SCD, consider the use of SNRIs (e.g., duloxetine) as options for pain management. Psychotherapy should be incorporated into the care plan for a patient on an SNRI. (4)

Remarks: This recommendation is based largely on indirect evidence from adult patients without SCD affected with fibromyalgia. Fibromyalgia was selected by panel consensus as the entity most closely aligned with chronic pain in SCD (with no identifiable cause beyond SCD). Antidepressants may increase the risk of suicidal ideation and behavior in children and adolescents with major depression disorder and other psychiatric disorders.

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August 2023

Critical Points of Evidence*

Evidence Lacking/Inconclusive

- Use of a risk score to predict 30-day emergency department revisit. (14,19-27) – Unable to make a recommendation
- Using functional pain scales as compared to traditional pain scales to assess acute pain in children with sickle cell disease. (28,29) – Unable to make a recommendation

Remarks: Traditional pain scales can be used to benchmark pain for a particular patient. A baseline pain score should be assessed and patient and provider should discuss a goal pain score for discharge. Functional goals (e.g. ability to return to school, physical activity) and pain intensity should be used to guide therapies.

*NOTE: The references cited represent the entire body of evidence reviewed to make each recommendation.
• For age appropriate children who have SCD-related chronic pain with no identifiable cause beyond SCD, consider the use of tricyclic antidepressants (TCAs; e.g., amitriptyline) as an option for pain management. [4]

Remarks: This recommendation is based largely on indirect evidence from adult patients without SCD affected with fibromyalgia. Fibromyalgia was selected by panel consensus as the entity most closely aligned with chronic pain in SCD with no identifiable cause. Antidepressants may increase the risk of suicidal ideation and behavior in children and adolescents with major depression disorder and other psychiatric disorders. The increased adverse effect profile for this drug includes, but is not limited to, prolonged QT, orthostasis, cognitive impairment, dry mouth, and anticholinergic effects. Patients should be monitored for adverse effects. An EKG should be obtained prior to starting treatment. These adverse effects should be considered and discussed with patients.

• For age appropriate children who have SCD-related chronic pain, consider the use of gabapentin and pregabalin as options for pain management. [4]

Remarks: This recommendation is based largely on indirect evidence from adult patients without SCD affected with fibromyalgia. Fibromyalgia was selected by panel consensus as the entity most closely aligned with chronic pain in SCD with no identifiable cause.

• For adults and children with SCD who have chronic pain related to SCD, consider the use of cognitive and behavioral pain management strategies in the context of a comprehensive disease and pain management plan. [4]

Remarks: The cognitive or behavioral pain management strategy with the broadest evidence base is cognitive behavioral therapy (CBT). Other strategies considered by the panel with lower certainty in evidence include acceptance and commitment therapy (ACT), mindfulness-based treatments, coping skills training, and operant therapy.

Management of Acute Pain

Treatment should be based on patient report of pain intensity and functional goals.

Outpatient / Emergency Center

Mild Pain (Pain Score 1 – 3)
- Utilize oral and/or intranasal opioids for treatment.
- Administer ibuprofen if not done in the last six hours.
- Provide oral hydration
- Utilize non-pharmacological pain treatment

Moderate-to-Severe Pain (Pain Score 4 – 10)
- Utilize intravenous and intranasal opioids for treatment.
- Administer normal saline bolus and provide intravenous hydration at 1 x maintenance.
- If pain persists, dose may be repeated every 20 minutes up to 3 times.
- Administer a 5-day course of ketorolac.
- Utilize non-pharmacological pain treatment
- Continue frequent pain assessments.
- Utilize PCA if pain not well controlled.

Inpatient

Utilize Pain Management Plan if available to guide treatment

Mild Pain (Pain Score 1 – 3)
- Administer ibuprofen or a 5-day course of ketorolac.
- If pain persisted, consider oral morphine or narcotic equivalent.
- If pain remains uncontrolled, initiate PCA if not already done and treat as moderate-to-severe pain.

Moderate-to-Severe Pain (Pain Score 4 – 10)
- Initiate PCA if not already done. Dose PCA based upon patient’s tolerance to opioids.
- If pain persists, increase PCA dosing in a stepwise approach.
- If continued pain, consider opioid rotation or non-opioid adjuncts.
- Consult the Hematology and/or Pain Service if pain remains uncontrolled.

Management of Chronic Pain

Chronic Pain Definition
• Patient reports of ongoing pain present on most days over the past 4 - 6 months in either a single location or multiple locations.
  - Chronic SCD pain without contributory disease complications: Chronic pain is more likely due to central or peripheral nervous system sensitization and has a non-identifiable cause.
  - Chronic SCD pain with contributory disease complications: Chronic pain is end-organ related and has an identifiable cause (e.g., avascular necrosis, leg ulcers).

Chronic Pain Treatment
• Assess for acute on chronic pain
• Consider management with chronic pain medications (see Table 1)
• Ensure patient’s maintenance medications have been resumed.
• Consider Pain Service consult upon admission

Consults/Referrals:
• Consider Pain Service consult for: complicated pain history and/or consideration for Subanesthetic ketamine infusion
• Consider Child Life request to see for coping concerns and/or procedural preparations
• Consider Psychology consult
• Consider Psychiatry consult for questions regarding chronic pain medication

Discharge Criteria:
• Taking adequate oral fluids and able to take PO medications, if applicable
• Adequate pain relief with oral analgesics, if applicable
• Home care agencies notified as needed

Caregiver understands:
• Discharge care, including opioid wean, if applicable
• When Hematology Clinic follow-up scheduled
• Medications and how to obtain them

Table 1

Condition-Specific Elements of Clinical Management
Measures

Process
- Order set utilization in the EC and inpatient units
- Time to PCA initiation
- Number of consults to the Pain Service

Outcome
- ED and IP LOS
- Time on opioid
- Total PCA morphine dose
- Number of patients with unscheduled return visit to the ED/triage and/or admission for the same diagnosis within 14 days of discharge

Table 1. Chronic Pain Medications for Sickle Cell

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Drug Name</th>
<th>Dose</th>
<th>Adverse Effects</th>
<th>Monitoring</th>
<th>Caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID</td>
<td>Ketorolac</td>
<td>≥2 yrs or &lt;50 kg: IV: 0.5 mg/kg/dose Q6H (max 15 mg/dose; max 20 doses)</td>
<td>-Abdominal pain</td>
<td>Baseline CBC and renal function with period monitoring</td>
<td>-Caution in renal impairment -Avoid in CrCl&lt;30 mL/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≥17 yrs and ≥250 kg: IV: 30 mg Q6H (max 20 doses)</td>
<td>-Increase risk for bleeding -nephrotoxicity</td>
<td>-Baseline LFT</td>
<td></td>
</tr>
<tr>
<td>Tricyclic</td>
<td>Amitriptyline</td>
<td>≥2 yrs: PO: 0.1 mg/kg once daily at bedtime (max initial dose 10 mg)</td>
<td>-Constipation, dry mouth, dizziness, headache and somnolence</td>
<td>-Baseline LFT</td>
<td>-U. S. Boxed Warning – Suicidality and Antidepressant Drugs -Avoid in those with QTc prolongation -Caution when using with CYP3A4 inhibitor</td>
</tr>
<tr>
<td>antidepressant;</td>
<td></td>
<td>(max initial dose 10 mg) Titrate in weekly intervals to max of 150 mg/day once daily at bedtime or in 2 divided doses)</td>
<td>-QTc prolongation</td>
<td>-Baseline EKG if history of cardiac problems or QTc prolongation</td>
<td></td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td></td>
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<tr>
<td>SNRI</td>
<td>Duloxetine</td>
<td>≥7 yrs: PO: 30 mg once daily may increase after 1 week based on tolerability/response (max 60 mg/day)</td>
<td>-headache, drowsiness, nausea, abdominal pain, dry mouth, diarrhea</td>
<td>-Baseline LFT and renal function</td>
<td>-May impair platelet aggregation</td>
</tr>
<tr>
<td>antidepressant;</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>Gabapentin</td>
<td>PO: 5 mg/kg/dose once daily at bedtime to be titrated to 5 mg/kg/dose TID (max initial 300 mg/dose)</td>
<td>-dizziness, ataxia, fatigue, hyperkinesia, tremor, weight gain</td>
<td>-Baseline renal function</td>
<td>-Requires renal dose adjustment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further titrate dose to effect (max 35 mg/kg/day divided TID or 3600 mg/day)</td>
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<tr>
<td>Antiseizure;</td>
<td>Pregabalin (Controlled</td>
<td>PO: 1-2 mg/kg/dose BID (max initial dose 25 mg) x 1 week. Titrate to response/tolerability (max 450 mg/day in 2 to 3 divided doses)</td>
<td>-dizziness, ataxia, fatigue, hyperkinesia, tremor, weight gain</td>
<td>-Baseline renal function</td>
<td>-Requires renal dose adjustment</td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>substance)</td>
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</table>
TCH Evidence-Based Outcomes Center
Emergency Department/Outpatient Hematology Center
Pain Management Algorithm for Patients With Sickle Cell Disease in Vaso-Occlusive Crisis

Begin

Child with sickle cell disease presents with persistent pain¹

[Notify Hematology on call after initial assessment as needed]

Does the patient have a pain management plan?

- Yes:
  - Manage patient as per pain management plan
  - OFF Algorithm

- No:
  - Enlist another provider to assist with pain management

Moderate/Severe pain

(score 4-10)

NS bolus followed by 1 x maintenance

- Administer intranasal Fentanyl 1.5 mcg/kg (MAX: 100 mcg/dose)
- Morphine 0.1 – 0.2 mg/kg/dose (MAX: starting dose: 6 mg/HV: If pain persists, morphine may be repeated every 20 minutes up to 3 doses.
- Ketorolac: 1 mg/kg for first dose, then 0.5 mg/kg every 6 h not to exceed 20 doses (MAX: 30 mg/dose) (NOTE: avoid use of ketorolac in pts w/ renal dysfunction, ARF, ESRD, or Scv > 2 x baseline, or active bleeding)
- Assess pain 20 - 30 min after administration of ketorolac

Pain well controlled?

- Yes:
  - Pain remains well controlled?
    - Yes:
      - Give dose of oral morphine (0.2–0.5 mg/kg) or opioid equivalent and observe for at least 30 min in ED
    - No:
      - Pain remains well controlled?
        - Yes:
          - Discharge on oral morphine (0.2–0.5 mg/kg/dose Q6 h) or opioid equivalent (alternate w/ ibuprofen)
          - Emphasize fluid intake
          - Give SCDI discharge instruction sheet
          - Instruct patient to contact Hematology clinic in 3-5 days
        - No:
          - Pain remains well controlled?
            - Yes:
              - Discharge on oral morphine (0.2–0.5 mg/kg/dose Q6 h) or opioid equivalent (alternate w/ ibuprofen)
              - Emphasize fluid intake
              - Give SCDI discharge instruction sheet
              - Instruct patient to contact Hematology clinic in 3-5 days
            - No:
              - Initiate morphine PCA²:
                - Loading dose: 0.1 mg/kg
                - Continuous Infusion: 0.005 – 0.006 mg/kg/hr
                - Interval Dose: 0.015 – 0.025 mg/kg
                - Lockout Interval: 10 minutes
                - 4-hour Limit: 0.35 – 0.55 mg/kg
                - IV fluids 1 x maintenance if not already done
                - Initiate bowel regimen
              - Notify PCP

Pain not well controlled?

- Yes:
  - Pain remains not well controlled?
    - Yes:
      - Initiate bowel regimen
      - Notify PCP
    - No:
      - Evaluate patient for pain:
        - Mild pain (score 1-3)
          - Oral fluids
            - Apply warm packs to painful areas
            - Give oral morphine (0.2–0.5 mg/kg; MAX: 30 mg Q4 hours) or opioid equivalent
            - Administer intranasal Fentanyl 1.5 mcg/kg (MAX: 100 mcg/dose) if in emergency center
            - Give ibuprofen oral 10 mg/kg/dose Q6 hours (MAX 600 mg/dose) (if none within last 6 hours)
        - Moderate or severe pain (score > 3)
          - Narcotic given at home within last 12 h?
            - Yes:
              - Pain well controlled?
                - Yes:
                  - Observe for at least 30 min - 1 h in ED based upon amount of opioid administered
                - No:
                  - Pain remains well controlled?
                    - Yes:
                      - Discharge on oral morphine (0.2–0.5 mg/kg) or opioid equivalent and observe for at least 30 min in ED
                    - No:
                      - Initiate morphine PCA²:
                        - Loading dose: 0.1 mg/kg
                        - Continuous Infusion: 0.005 – 0.006 mg/kg/hr
                        - Interval Dose: 0.015 – 0.025 mg/kg
                        - Lockout Interval: 10 minutes
                        - 4-hour Limit: 0.35 – 0.55 mg/kg
                        - IV fluids 1 x maintenance if not already done
                        - Initiate bowel regimen
                        - Notify PCP
              - Notify Hematology on call after initial assessment as needed
            - No:
              - Pain not well controlled?
                - Yes:
                  - Observe for at least 30 min - 1 h in ED based upon amount of opioid administered
                - No:
                  - Pain remains well controlled?
                    - Yes:
                      - Discharge on oral morphine (0.2–0.5 mg/kg) or opioid equivalent and observe for at least 30 min in ED
                    - No:
                      - Notify Hematology on call after initial assessment as needed

¹NOTE: If pt asleep after administering pain meds, wake patient up to reassess pain as directed. (e.g., q 20 min x 3)
²NOTE: If patient is unable to tolerate morphine, use Hydromorphone IV/PCA at standard 1:7 conversion

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August 2023
References


Clinical Standards Preparation
This clinical standard was prepared by the Evidence-Based Outcomes Center (EBOC) team in collaboration with content experts at Texas Children’s Hospital. Development of this clinical standard supports the TCH Quality and Patient Safety Program initiative to promote clinical standards and outcomes that build a culture of quality and safety within the organization.

Sickle Cell Disease Management of Acute and Chronic Pain

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EBOC Team

No relevant financial or intellectual conflicts to report.

Development Process
This clinical standard was developed using the process outlined in the EBOC Manual. The literature appraisal documents the following steps:
1. Review Preparation
   - PICO questions established
   - Evidence search confirmed with content experts
2. Review of Existing External Guidelines
3. Literature Review of Relevant Evidence
   - Searched: PubMed, Cochrane
4. Critically Analyze the Evidence
   - One meta-analyses, three randomized controlled trials, and twenty nonrandomized studies
5. Summarize the Evidence
   - Materials used in the development of the clinical standard, literature appraisal, and order sets are maintained in a sickle cell disease management of acute and chronic pain evidence-based review manual within EBOC.

Evaluating the Quality of the Evidence
Published clinical guidelines were evaluated for this review using the AGREE II criteria. The summary of these guidelines are included in the literature appraisal. AGREE II criteria evaluate Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity and Presentation, Applicability, and Editorial Independence using a 4-point Likert scale. The higher the score, the more comprehensive the guideline.

This clinical standard specifically summarizes the evidence in support of or against specific interventions and identifies where evidence is lacking/inconclusive. The following categories describe how research findings provide support for treatment interventions.

“Evidence Supports” provides evidence to support an intervention
“Evidence Against” provides evidence against an intervention.
“Evidence Lacking/Inconclusive” indicates there is insufficient evidence to support or refute an intervention and no conclusion can be drawn from the evidence.

The GRADE criteria were utilized to evaluate the body of evidence used to make practice recommendations. The table below defines how the quality of the evidence is rated and how a strong versus weak recommendation is established. The literature appraisal reflects the critical points of evidence.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Quality</th>
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<td>STRONG</td>
<td>Desirable effects clearly outweigh undesirable effects or vice versa</td>
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<td>WEAK</td>
<td>Desirable effects closely balanced with undesirable effects</td>
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<tr>
<td>Low</td>
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<td>Very Low</td>
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Recommendations
Practice recommendations were directed by the existing evidence and consensus amongst the content experts. Patient and family preferences were included when possible. The Content Expert Team and EBOC team remain aware of the controversies in the management sickle cell disease. When evidence is lacking, options in care are provided in the clinical standard and the accompanying order sets (if applicable).

Approval Process
Clinical standards are reviewed and approved by hospital committees as deemed appropriate for its intended use. Clinical standards are reviewed as necessary within EBOC at Texas Children’s Hospital. Content Expert Teams are involved with every review and update.

Disclaimer
Practice recommendations are based upon the evidence available at the time the guideline was developed. Clinical standards (guidelines, summaries, or pathways) do not set out the standard of care, and are not intended to be used to dictate a course of care. Each physician/practitioner must use his or her independent judgment in the management of any specific patient and is responsible, in consultation with the patient and/or the patient family, to make the ultimate judgment regarding care.

Version History

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<th>Action</th>
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<td>June 2011</td>
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<tr>
<td>July 2017</td>
<td>Full update</td>
</tr>
<tr>
<td>Sept 2021</td>
<td>Revise Signs and Symptoms of Shock Table</td>
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<tr>
<td>August 2023</td>
<td>Update; Focus on assessment and treatment of acute and chronic pain</td>
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