CCHCS Care Guide: End Stage Liver Disease (Cirrhosis)

SUMMARY

GOALS
- Diagnose Cirrhosis Early
- Diagnose Complications
- Delay Decompensation

DIAGNOSTIC CRITERIA

Cirrhosis is best predicted by these findings:
- Ascites (likelihood ratio for cirrhosis [LR] 7.2)
- Platelet count <160,000/mm³ (LR 6.3)
- Spider angiomata on physical exam (LR 4.3)
- Bonacini cirrhosis discriminant score greater than 7 (LR 9.4) (see page 2)

Cirrhosis (liver fibrosis stage 4) is diagnosed with one or more of the following:
- Imaging: hepatic ultrasound, CT, MRI
- Calculations: FIB4, Bonacini Cirrhosis Discriminant Score
- Procedure: liver biopsy, transient elastography (FibroScan™)
- Physical exam

Decompensated cirrhosis is defined by the presence of:
- Ascites
- Hepatic encephalopathy (HE)
- Hepatocellular carcinoma (HCC)
- Hepatorenal syndrome
- Hepatopulmonary syndrome
- Child-Pugh class C (see page 2)
- Spontaneous bacterial peritonitis (SBP)
- Variceal bleeding

EVALUATION

Complete clinical history and physical exam
- HX: Especially risk factors for hepatitis; symptoms of significant liver disease: hematochezia, melena, hematemesis, edema, weight gain
- PE: Particularly mental status changes, skin changes, hepatosplenomegaly, spider angiomata

Lab/Diagnostics
- CBC, CMP, PT/INR, hepatitis serologies, HIV testing
- EGD (baseline) to screen for esophageal varices
- Ultrasound to screen for HCC (AFP not recommended for HCC screening)

TREATMENT (see pages 3-5)

Vaccinations: influenza, HAV, pneumococcal vaccines
Review medication list: avoid hepatotoxins and chronic NSAIDs
Medications or other therapies based on specific patient findings (see below and pages 3-5)
- Ascites: optimize diuretics
- Esophageal varices: determine if nonselective beta-blocker indicated and EGD follow-up interval
- Hepatocellular carcinoma: obtain consultation
- Hepatic encephalopathy: optimize lactulose
- Hepatitis C: determine treatment eligibility
- Liver transplantation: consult with the CME or regional DME for potential transplant candidates
- Spontaneous bacterial peritonitis: antibiotic prophylaxis

MONITORING (see pages 3-5)

Follow-up visit
- Every 90 days if stable, more frequently if indicated
- Monitor: mental status, weight, VS, abdominal girth, skin changes

Labs
- CMP every 1-2 months for ascites patients on diuretics
- Consider CBC, CMP, PT/INR annually or more frequently as indicated

Ultrasound
- Every 6 months (HCC screening)

EGD
- EGD at baseline, then as recommended by GI, generally within 2-3 years (see page 3 for more details)

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Information contained in the Care Guide is not a substitute for a health care professional's clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to “Disclaimer Regarding Care Guides” for further clarification.

BONACINI CIRRHOSIS DISCRIMINANT SCORE (CDS)\(^1\)

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Based on platelets (PLT), ALT/AST ratio, INR
Possible score = between 0 and 11. Higher score increases the likelihood of cirrhosis
- Bonacini CDS < 3: cirrhosis unlikely
- Bonacini CDS > 7: cirrhosis likely (LR 9.4)*
*Likelihood ratio: LR >1 indicates that a test is associated with disease

FIBROSIS-4 (FIB-4) CALCULATOR\(^2\)

\[
FIB4 = \frac{\text{Age(y)} \times \text{AST(U/L)}}{\text{PLT}(10^9/L) \times \text{ALT(U/L)}^{1/2}}
\]

<table>
<thead>
<tr>
<th>FIB4</th>
<th>Interpretation</th>
</tr>
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<tbody>
<tr>
<td>&lt;1.45</td>
<td>unlikely to have significant fibrosis</td>
</tr>
<tr>
<td>1.45-3.25</td>
<td>not accurate at this range; other staging method required</td>
</tr>
<tr>
<td>&gt;3.25</td>
<td>likely to have advanced fibrosis/cirrhosis (Fibrosis stage 3–4)</td>
</tr>
</tbody>
</table>

Based on age, AST, ALT, platelets
Online calculator: [http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4](http://www.hepatitisc.uw.edu/page/clinical-calculators/fib-4)

CHILD PUGH CLASSIFICATION OF SEVERITY OF CIRRHOSIS

<table>
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<tr>
<th>CHILD-PUGH POINTS</th>
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<tbody>
<tr>
<td>1</td>
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<tr>
<td>Encephalopathy</td>
</tr>
<tr>
<td>Ascites</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
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<tr>
<td>Albumin (g/dl)</td>
</tr>
<tr>
<td>PT (seconds prolonged)</td>
</tr>
<tr>
<td>INR</td>
</tr>
</tbody>
</table>

Child-Pugh is a tool used to help assess prognosis in patients with liver disease. Variations in the timing and subjectivity inherent in the scoring (e.g., in grading ascites or encephalopathy) are its major limitations.


ESLD COMPLICATIONS—DIAGNOSIS / MANAGEMENT

ASCITES

**DIAGNOSIS**
- Diagnose with appropriate imaging study or physical exam
- Differential diagnosis: ascites may be caused by conditions other than liver disease; about 15% are due to heart failure, nephrotic syndrome, cancer, tuberculosis, or other conditions
- Paracentesis for diagnosis may be indicated (especially with clinically apparent new onset ascites if etiology is unclear)

**TREATMENT / PROPHYLAXIS**
- Evaluation of ascitic fluid:
  - Routine tests on ascitic fluid
    - Cell count and differential
    - Albumin level
    - Total protein level
    - Culture in blood culture bottles
  - Optional tests
    - Glucose level
    - LDH level
    - Gram stain
    - Amylase level
  - Unusual tests
    - Tuberculosis smear and culture
    - Cytology
    - Triglyceride level
    - Bilirubin level
- Serum to Ascitic Albumin Fluid Gradient (SAAG) > 1.1 indicates portal hypertension with 97% accuracy; SAAG < 1.1 suggests ascites from other causes
- Patient may require large volume paracentesis
- Diuretics: Start at low dose and titrate up. Optimal ratio spironolactone to furosemide is 100 mg to 40 mg;
  - Spironolactone: 100 mg/day or 50 mg/day for patients ≤ 50 kg
  - Furosemide: 40 mg/day or 20 mg/day for patients ≤ 50 kg
  - Increase doses of both agents every 3-5 days if tolerated, up to 400 mg spironolactone with 160 mg furosemide
- Alternative agents: amiloride starting at 5-10 mg/day can be used as substitute for spironolactone if side effects (e.g., gynecomastia) noted
- Dietary sodium restriction: 2 gm/day (consider dietary consult or handout)
- Avoid: alcohol, ACE inhibitors, ARBs, NSAIDs
- Refractory ascites: discontinue beta blockers; serial paracentesis; TIPS (may precipitate encephalopathy)

**MONITORING**
- Monitor patient weight and abdominal girth.
- Obtain CMP every one to two months or as indicated for patients on diuretics.

ESOPHAGEAL VARICES

**DIAGNOSIS**
- Baseline EGD to screen for varices indicated when cirrhosis is first diagnosed
- EGD to diagnose when varices suspected

**TREATMENT / PROPHYLAXIS**
- No varices seen on EGD: beta blockers are not recommended for "pre-primary prophylaxis"
- **Primary prophylaxis:**
  - Small varices that haven't bled: if Child Pugh class A and no red wales on EGD - can use surveillance EGD in place of beta blockers; if Child Pugh B or red wales on EGD - consider nonselective beta blockers (propranolol, nadolol). With beta-blockers: Do not lower systolic BP<90 or heart rate < 55.
  - Medium/large varices that haven't bled: non selective beta blockers or esophageal variceal ligation (EVL). If bleeding risk is not high, beta blockers preferred over EVL. With large varices, EVL preferred.
  - These agents are not recommended for primary prophylaxis: nitrates, combination beta blockers and EVL, shunt therapy, or sclerotherapy.
- **Secondary prophylaxis:**
  - Patients who survive an EV bleed should receive both beta blockers and EVL. Repeat EGD every 1-2 weeks until varices obliterated, then every 1-3 months, then every 6-12 months for surveillance.
  - Consider TIPS if bleeding recurs despite combination beta blockers and EVL.
  - Sclerotherapy is not recommended for secondary prophylaxis.
  - Consider TIPS in Child class A/B patients with recurrent bleeding despite beta blockers and EVL.

**MONITORING**
- Cirrhosis without varices on EGD → repeat EGD within 3 years
- Small varices and no beta blocker used → repeat EGD within 2 years
- Small/medium/large and beta blockers maximized (see page 9): consider EGD within 2-3 years
- Medium/large and EVL used: → repeat EGD every 1-2 weeks until varices obliterated, then every 1-3 months, then every 6-12 months
- Decompensated cirrhosis: → repeat EGD at time of diagnosis and annually or more often as indicated

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1Runyon, BA et al. Management of adult patients with ascites due to cirrhosis: Update 2012. Hepatology. 2013 Apr;57(4);
2From UpToDate: Runyon, BA. et al. Evaluation of the adult with ascites. April 2015;
## HEPATIC ENCEPHALOPATHY (HE)\(^1\)

### DIAGNOSIS
- Presentation may vary from mild subclinical changes in mentation to overt psychiatric symptoms to deep coma. Presenting symptoms can include confusion, decreased attention, mental slowing, asterixis, irritability, sleep disorder, lethargy or unresponsiveness.

### TREATMENT / PROPHYLAXIS
- Correct precipitating cause(s):
  - Precipitating factors: GI bleed, infection (including SBP), blood transfusion, HCC, excess protein intake, constipation, dehydration, drugs, poor adherence to medications, and portohepatic shunts
- **Treatment overt HE**
  - Lactulose: give lactulose when patient is able to take medications orally for treatment and prophylaxis. Recommended starting dose: 30 ml po BID -TID. Consider NA or DOT administration for recurrent symptoms in selected cases, e.g., nonadherence. Titrate dose to no more than three to four BMs/day
  - Rifaximin-(NF) only after optimized lactulose treatment. Recommended dose: rifaximin 550 mg two times daily
  - Patients with significant mental status changes should be referred to a higher level of care.
  - Consider lactulose enemas when patient is comatose (inpatient setting only).
- **Prophylaxis:**
  - After 1st episode: lactulose
  - After 2nd episode: add rifaximin (NF) to lactulose\(^3\)

### MONITORING
- Medication adherence, bowel movement frequency, mental status, functional status

## HEPATOCELLULAR CARCINOMA (HCC)\(^2\)

### DIAGNOSIS
- Screen for HCC with ultrasound every 6 months.
- Evaluate mass on ultrasound with contrast enhanced imaging study imaging (dynamic triphasic or quadriphasic CT or MRI with gadolinium).
- Hepatic mass identified on contrast enhanced imaging (see liver mass evaluation page 5).
- Biopsy, as indicated.
- Consultation recommended with a specialist knowledgeable in the diagnosis and management of HCC.

### TREATMENT / PROPHYLAXIS
- Classification and diagnosis complements the Barcelona Clinic Liver Cancer (BCLC) staging and treatment criteria:
  - Very early to early stage disease— may be cured with ablation, resection, or liver transplant
  - Intermediate Stage- usually treated with chemoembolization
  - Advanced Stage-sorafenib (trade name NexAVAR\(^\circ\))
  - Terminal Stage-Child Pugh C with liver biopsy evidence of stage 3-4 disease - initiate supportive care

### MONITORING
- Monitor change in tumor size with imaging, new symptoms.

## HEPATOPULMONARY SYNDROME (HPS)\(^3\)

### DIAGNOSIS
- Symptoms:
  - Platypnea: dyspnea that worsens when sitting up from supine
  - Orthodeoxia: arterial deoxyhemoglobin saturation decrease >5% when sitting up from supine
- Diagnosis:
  - Contrast-enhanced echocardiography
  - Pulmonary angiography
  - Nuclear scanning to view intravascular pulmonary dilatations

### TREATMENT / PROPHYLAXIS
- There are no effective treatments for HPS
- Long term oxygen therapy for hypoxemia
- Transplant may be a treatment option; if recommended, consult with CME or DME.

### MONITORING
- Breathing symptoms as described
- Pulse oximetry as indicated

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\(^3\)Lange, PA. Hepatopulmonary syndrome: Natural history, treatment, and outcomes. UpToDate: March 2015. Lange, PA. UpToDate: Hepatopulmonary syndrome: Prevalence, causes, clinical manifestations and diagnosis March 2015.
**ESLD COMPLICATIONS—DIAGNOSIS / MANAGEMENT**

### HEPATORENAL SYNDROME (HRS)\(^1\)

**DIAGNOSIS**
- Progressive rise in serum creatinine
- Urine sediment often normal with no or minimal proteinuria (less than 500 mg per day)
- Very low rate of sodium excretion (i.e., urine sodium concentration less than 10 mEq/l)
- Oliguria

**TREATMENT / PROPHYLAXIS**
There are two forms of Hepatorenal Syndrome (HRS) based on the speed of onset of renal failure:
- **Type I HRS** is more serious and generally develops in less than two weeks with serum creatinine increasing two fold to >2.5 mg/dl and Clcr falling to below 20 ml/min.
- **Type II HRS** is less severe renal insufficiency associated with diuretic resistant ascites. Serum creatinine level increases over days to weeks.

Hepatorenal syndrome is usually treated in a hospital setting as it has high mortality rate and requires specialty care.

**MONITORING**
- Serum creatinine, urine output

### LIVER MASS EVALUATION \(^2\)

**DIAGNOSIS**
- **Lesions < 1 cm**
  - Repeat ultrasound every three months for 24 months
  - If lesion remains < 1 cm, resume every six month US screening
  - Not feasible to definitively diagnose liver lesions < 1cm
- **Lesions > 1 cm or multiple masses and at least 1 is > 1cm**
  - Perform contrast enhanced imaging study such as dynamic triphasic or quadriphasic CT or MRI with gadolinium
  - Look for arterial hypervascularization and venous or delayed washout as diagnostic of HCC (see HCC page 4)
  - If CT/MRI is not typical for HCC, a biopsy is needed to diagnose HCC
  - Multiple masses, all < 1 cm
  - Refer to a specialist knowledgeable in the diagnosis of HCC

**TREATMENT / PROPHYLAXIS**
- Treatment of HCC: See page 4

**MONITORING**
- Imaging

### SPONTANEOUS BACTERIAL PERITONITIS (SBP)\(^3\)

**DIAGNOSIS**
- SBP may present without obvious symptoms or may present with fever, abdominal pain, altered mental status. Any or all symptoms may be subtle or absent
- Diagnosis: ascitic fluid with \(\geq 250\) PMNs/ml and/or positive culture
  - (Most often E. coli, or klebsiella; can be streptococcus or rarely staphylococcus)

**TREATMENT / PROPHYLAXIS**
- **Treatment**
  - Stop beta blocker prophylaxis indefinitely
  - Empiric IV antibiotic while awaiting culture results if patient has temp >100, ascitic PMN \(\geq 250\) cells/ml, abdominal pain, altered mental status
  - Usually in hospital with IV cefotaxime. Use quinolone for patients with allergy to \(\beta\)-lactamase antibiotics, unless quinolone used for prophylaxis. Avoid aminoglycosides (due to nephrotoxicity)
  - Treatment duration usually 5 days, unless unusual organism or presentation
- **Prophylaxis**
  - All patients with history of prior SBP, significant ascites, or impaired renal function should be treated indefinitely with:
    - Ciprofloxacin 500 mg daily or sulfamethoxazole/trimethoprim DS one tablet daily. (Weekly dosing is not recommended.)
    - Patients with cirrhosis who are hospitalized with GI bleed should receive antibiotic prophylaxis: either IV cefotaxime or sulfamethoxazole/trimethoprim DS for seven days
- Prophylaxis also recommended during GI bleed

**MONITORING**
- Fever, abdominal pain, change in mental status

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\(^{1}\) Runyon, BA. Hepatorenal syndrome. UpToDate: March 2015.  
\(^{3}\) Runyon, BA. Management of adult patients with ascites due to cirrhosis: Update 2012. Hepatology, 2013 Apr;57(4)
<table>
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<tr>
<th>INDICATION: ASCITES</th>
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</table>
| **furosemide** (Lasix®) | Tablet: 20 mg, 40 mg | $ | **Recommended starting dose:** 40 mg by mouth daily (with 100 mg spironolactone)  
**Recommended starting dose for patients ≤ 50 kg:** 20 mg/day  
**Increase every 3-5 days as needed up to 160 mg furosemide with 400 mg spironolactone** | **Electrolyte imbalances:** hypokalemia, possibly severe, hypomagnesemia, hypocalcemia, hyperglycemia, hyperuricemia, metabolic alkalosis  
**Hypovolemia; dehydration**  
**Ototoxicity, tinnitus**  
**Thrombocytopenia/thrombosis, anemia (hemolytic/aplastic), leukopenia, agranulocytosis, eosinophilia**  
**Rash including erythema multiforme, drug reaction with eosinophilia and systemic symptoms (DRESS); Stevens Johnson Syndrome (SJS), toxic epidermal necrolysis (TENS), pruritus, photosensitivity**  
**SLE exacerbation**  
**Urinary frequency**  
**Dizziness, weakness, hypotension, anorexia**  
**Nausea, vomiting, diarrhea, abdominal cramps** |
| **spironolactone** (Aldactone®) | Tablet: 25 mg, 50 mg, 100 mg | $ | **Recommended starting dose:** 100 mg by mouth daily with food with 40 mg furosemide  
**Recommended starting dose for smaller patient ≤ 50 kg:** 50 mg/day  
**Increase every 3-5 days as needed up to 400 mg spironolactone with 160 mg furosemide** | **Hyperkalemia,** possibly severe  
**Renal failure**  
**Rash including: DRESS, SJS, TENS, vasculitis**  
**Agranulocytosis, leucopenia, thrombocytopenia**  
**Gynecomastia**  
**Nausea, vomiting, abdominal cramping, diarrhea**  
**Headache, dizziness, lethargy**  
**Pruritus, hyperuricemia** |
| **amiloride** (Midamor®) | Tablet: 5 mg | $$ | **Recommended starting dose:** 5-10 mg/day  
**Max dose:** 40 mg | **Hyperkalemia**  
**Aplastic anemia, neutropenia, hyperuricemia**  
**Headache, weakness, nausea, vomiting, diarrhea, dizziness** |

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<thead>
<tr>
<th>INDICATION: HEPATIC ENCEPHALOPATHY (HE)</th>
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| **lactulose** (Constulose®, Enulose®) | Soln: 10 g/15ml | $$ | **Recommended dose:** 30-45 ml by mouth, two to three times daily  
**Titrate dose to no more than three to four bowel movements per day** | **Abdominal discomfort, cramping, flatulence, nausea, vomiting**  
**With excessive dosing: electrolyte imbalance, diarrhea, metabolic acidosis** |
| **rifaximin** (Xifaxan®) | Tablet: 550 mg | $$$$$ | **Recommended dose:** 550 mg by mouth, twice daily  
**Indicated for breakthrough HE despite optimized lactulose dosing** | **Bacterial or fungal superinfection may occur with prolonged use, including C difficile-associated diarrhea**  
**Headache, fatigue, angioedema, pruritus, rash**  
**Avoid use in patients with diarrhea and fever or blood in stool** |

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<thead>
<tr>
<th>INDICATION: HEPATOCELLULAR CARCINOMA (HCC)</th>
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| **sorafenib** (Nexavar®) | Tablet: 200 mg | $$$$$ | **Recommended dose:** 400 mg (200 mg x 2) by mouth, twice daily without food (at least 1 hour before or 2 hours after a meal) | **Hand-foot syndrome, severe**  
**Hypersensitivity reaction, SJS, TENS, erythema multiforme**  
**GI perforation, pancreatitis, renal failure**  
**MI, CHF, hypertensive crisis, QT prolongation, HTN**  
**Rhabdomyolysis**  
**Interstitial lung disease**  
**Skin carcinoma**  
**Hypokalemia, hypoalbuminemia, AST/ALT elevations, hypocalcemia, hypophosphatemia, anemia, lymphopenia, thrombocytopenia, prolonged INR**  
**Headache, fatigue**  
**Diarrhea, constipation, abdominal pain, nausea, vomiting**  
**Anorexia, stomatitis, weight loss, sensory neuropathy**  
**Alopecia, desquamating rash** |

*See prescribing information for complete description of adverse effects and drug interactions. Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.
**SUMMARY**

**DECISION SUPPORT**

**PATIENT EDUCATION/SELF MANAGEMENT**

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## CCHCS Care Guide: End Stage Liver Disease (Cirrhosis)

### MEDICATIONS (CONTINUED)

<table>
<thead>
<tr>
<th>INDICATION: PAIN MANAGEMENT: NONOPIOID</th>
<th>INDICATION: PAIN MANAGEMENT: OPIOIDS (AVOID OR USE SPARINGLY IN CIRRHOSIS)</th>
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</thead>
<tbody>
<tr>
<td><strong>acetaminophen</strong> (Tylenol®)</td>
<td><strong>morphine sulfate</strong> Morphine (MSIR®, MS Contin®)</td>
</tr>
<tr>
<td>Tablets: 325 mg</td>
<td><strong>DOT/NA only</strong> Crush and float Cannot crush SR formulation</td>
</tr>
<tr>
<td>Suspension: 160 mg/ml</td>
<td><strong>Contraindications/Precautions</strong></td>
</tr>
<tr>
<td><strong>Hepatic impairment:</strong> Do not exceed 2 grams per day in cirrhosis</td>
<td><strong>Side effects common in long acting opiates:</strong></td>
</tr>
<tr>
<td><strong>Recommended dose in cirrhosis:</strong> 650 mg every 8 hours (not more than 2 grams daily)</td>
<td><strong>Potentiation of drug effect</strong> (including mental obtundation) may be observed in cirrhosis</td>
</tr>
<tr>
<td><strong>Renal impairment:</strong> Clcr 10-50 ml/min: Administer every 6 hours Clcr &lt;10 ml/min: Administer every 8 hours</td>
<td><strong>Respiratory depression, apnea, respiratory arrest</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Hypotension, severe; shock, bradycardia</strong></td>
</tr>
<tr>
<td><strong>No significant anti-inflammatory effect or GI toxicity</strong></td>
<td><strong>Intracranial pressure (ICP) increase</strong></td>
</tr>
<tr>
<td><strong>May be hepatotoxic in acute or chronic overdosage</strong></td>
<td><strong>Seizures</strong></td>
</tr>
<tr>
<td><strong>Interacts with warfarin to prolong INR</strong></td>
<td><strong>Dependency, abuse</strong></td>
</tr>
<tr>
<td><strong>NSAIDs</strong></td>
<td><strong>Withdrawal symptoms with abrupt discontinuation</strong></td>
</tr>
<tr>
<td>♦ NSAIDs (including aspirin and COX-2 inhibitors) should generally be avoided in cirrhosis</td>
<td><strong>Opioid induced androgen deficiency</strong></td>
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<td>♦ Associated with increased risk of variceal hemorrhage, impaired renal function, hepatorenal syndrome, and the development of diuretic resistant ascites</td>
<td><strong>Sedation</strong></td>
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<td><strong>Pruritus, flushing</strong></td>
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<td><strong>Urinary retention</strong></td>
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**MEDICATION**

**DOSING**

**ADVERSE EFFECTS*/ INTERACTIONS/ COMMENTS**

*See prescribing information for complete description of adverse effects and drug interactions. Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.

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**Medication** | **Dosing** | **Adverse Effects*/ Interactions/ Comments**
---|---|---
***Methadone***<sup>1</sup>  
Tablet: 5 mg, 10 mg  
Soln: 10 mg/ml  
DOT/NA only  
crush & float  
$  
| Hepatic impairment: Lower initial doses and slower dose titration recommended  
Cirrhosis: avoid or use sparingly  
Initial dose in cirrhosis: 2.5 mg at bedtime  
Titration:  
2.5 mg twice daily for 7 days  
5 mg twice daily for 7 days  
7.5 mg twice daily for 7 days  
10 mg twice daily for 7 days  
10 mg three times daily for 7 days  
20 mg twice daily  
Max effect: 2-4 weeks  
| **Methadone use associated with more frequent deaths than other opioids**  
Side effects common in long acting opiates:  
- Potentiation of drug effects (including mental obtundation) may be observed in cirrhosis  
- Respiratory depression, apnea, respiratory arrest  
- Hypotension, severe; shock, bradycardia  
- Intracranial pressure (ICP) increase  
- Seizures  
- Paralytic ileus  
- Dependency, abuse  
- Withdrawal symptoms with abrupt discontinuation  
- Opioid induced androgen deficiency  
- Sedation  
- Nausea, vomiting, constipation, diaphoresis, dizziness  
| **Should not be used for PRN supplemental opioid therapy**  
Renal impairment: Lower initial dose, longer dosing intervals, slower dose titration recommended  
**Black Box Warning (BBW)**  
Life-threatening respiratory depression: Monitor for respiratory depression especially during initiation or following dose increase.  
Life-threatening QT prolongation: Closely monitor patients for changes in cardiac rhythm during initiation and titration.  
**Contraindications/Precautions**  
- QT prolongation: obtain EKG at baseline, 1 month & annually  
  - Increase EKG monitoring frequency if patient receiving >100 mg/day or if unexplained syncope or seizure occurs while on methadone  
  - If QTc is >450 ms but <500 ms; consider risk vs. benefit- monitor EKG more frequently  
  - If QTc is >500 ms consider alternative therapy, dose reduction, or elimination of contributing factors (e.g., other medications)  
- BPH, urethral stricture  
- Significant pulmonary disorder  
- Severe hepatic or renal insufficiency  
- Elderly  
- Pregnancy  
- Avoidance recommended in patients with severe liver disease (especially patients with portal hypertension and encephalopathy)  

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*See prescribing information for complete description of adverse effects and drug interactions. Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.

**Notes:**

- **Bold = Formulary**
- **See information for more details:**
  - CCHCS Care Guide: End Stage Liver Disease (Cirrhosis)

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## Indication: Portal Hypertension (Esophageal Varices)

### Nadolol (Corgard®)
- **Dosing:**
  - Tablet: 20 mg, 40 mg, 80 mg
  - Recommended starting dose: 40 mg daily
  - Titrate to reduce resting heart rate by 25%, but not below 55 beats/min, and to reduce systolic BP, but not below 90 mmHg

### Propranolol (Inderal®)
- **Dosing:**
  - Tablet: 10 mg, 20 mg, 40 mg, 60 mg
  - Recommended starting dose: 20 mg twice daily
  - Titrate to reduce resting heart rate by 25%, but not below 55 beats/min, and to reduce systolic BP, but not below 90 mmHg

### Adverse Effects*/Interactions/Comments
- **Side effects common to non-selective beta blockers:**
  - Cardiac: CHF, heart block, bradycardia, hypotension, impaired myocardial contractility, angina exacerbation or MI with abrupt d/c
  - Pulmonary: bronchospasm
  - Other: fatigue, dizziness, Raynaud’s phenomenon, pruritus, diarrhea, constipation, nausea
  - Hypersensitivity reaction
  - Rash including SJS, TENS (propranolol)

*See prescribing information for complete description of adverse effects and drug interactions. Hypersensitivity to the medication, medication class or a component of the formulation is a contraindication to use of the drug.
WHAT IS CIRRHOSIS? (SIR-O-SIS)

- Cirrhosis is when a healthy liver becomes damaged by scars and lumps.
- Cirrhosis is usually caused by viral infections (like hepatitis B and C), alcoholism, or fatty liver disease.
- You can live several years with cirrhosis if you get medical care.

HOW DO YOU KNOW IF YOU HAVE CIRRHOSIS?

You may not know if you have cirrhosis because you may not have any symptoms.

Your doctor will determine if you have cirrhosis by examining you and performing tests if needed.

You could have cirrhosis if you have:

- Swollen legs or belly
- Yellow colored skin
- Frequent nosebleeds
- Red palms
- A tendency to bruise easily
- Unexplained weight loss or weight gain
- Belly pain
- Frequent infections
- Trouble thinking clearly or confusion

END STAGE LIVER DISEASE – CIRRHOSIS: WHAT YOU SHOULD DO

- Eat from the CDCR “heart healthy” diet.
- Stay away from high salt, high fat food from the canteen and/or packages.
- Get regular exercise unless your health care provider tells you not to.
- Get vaccinated for Hepatitis A and B and pneumonia.
- Get a yearly flu shot.
- Do not drink any alcohol, including pruno, while you are in prison or after release.
- Discuss all medications with your health care provider.
- Take your medication as directed by your health care provider.
- Do not take more than 2 grams of acetaminophen daily.
- Stay away from NSAIDs like Advil®, Motrin®, or Aleve® unless recommended by your health care provider.
- Avoid protein and amino acid supplements.
- Avoid iron supplements.
- Do not take more than the recommended dose of Vitamins A, D, E, or K.

TELL YOUR HEALTH CARE PROVIDER IF YOU HAVE ANY OF THESE SYMPTOMS

- Vomiting blood or what looks like “coffee grounds”
- Feeling sleepy for long periods of time
- Trouble thinking or increasing confusion
- Black tarry stools
- Don’t pee as much as you used to
- Fever
- Problems breathing
### ENFERMEDAD HEPÁTICA EN ETAPA TERMINAL – CIRROSIS: LO QUE USTED DEBE SABER

#### ¿QUÉ ES LA CIRROSIS?
- La cirrosis es cuando se daña un hígado sano a causa de cicatrices y nódulos.
- Es causada principalmente por infecciones virales (como hepatitis B y C), alcoholismo o la enfermedad del hígado graso.
- Usted puede vivir varios años con cirrosis si recibe atención médica.

#### ¿CÓMO SABER SI TIENE CIRROSIS?

Puede que no sepa que tiene cirrosis porque no presenta ningún síntoma.

Su médico determinará si usted tiene cirrosis al examinarlo y practicarle algunos exámenes, de ser necesario.

Usted podría tener cirrosis si presenta:
- Hinchazón en las piernas o el vientre
- Piel amarillenta
- Hemorragias nasales frecuentes
- Palmas de las manos rojas
- Tendencia a sufrir de hematomas
- Pérdida o aumento de peso sin razón aparente
- Dolor abdominal
- Infecciones recurrentes
- Dificultad para pensar con claridad o confusión

### ENFERMEDAD HEPÁTICA EN ETAPA TERMINAL – CIRROSIS: LO QUE DEBE HACER

- Base su alimentación en la dieta "corazón sano" del CDCR.
- Evite los alimentos altos en sal y en grasas y/o las comidas empaquetadas.
- Practique ejercicio de manera regular a menos que su proveedor de cuidados de la salud le indique algo distinto.
- Vacúnese contra la Hepatitis A y B y contra la neumonía.
- Vacúnese anualmente contra la gripe.
- No ingiera nada de alcohol, incluyendo pruno, mientras esté en prisión ni cuando sea puesto en libertad.
- Consulte cualquier medicación con su proveedor de cuidados de la salud.
- Tome sus medicamentos como se los recetó su proveedor de cuidados de la salud.
- No tome más de 2 gramos de acetaminofén al día.
- Evite los medicamentos antiinflamatorios no esteroideos (Nonsteroidal anti-inflammatory drugs, NSAID) como el Advil®, Motrin® o Aleve® a menos que se lo recomiende su proveedor de cuidados de la salud.
- Evite los suplementos de proteínas y aminoácidos.
- Evite los suplementos de hierro.
- No tome más de la dosis recomendada de vitaminas A, D, E, o K.

### AVISE A SU PROVEEDOR DE CUIDADOS DE LA SALUD SI PRESENTA ALGUNO DE ESTOS SÍNTOMAS

- Vomita sangre o lo que parece ser deshechos de café
- Se siente somnoliento durante largos períodos de tiempo
- Dificultad para pensar o confusión creciente
- Deposiciones negro alquitranado
- No orina tan seguido como solía hacerlo
- Fiebre
- Dificultad para respirar