# CARE GUIDE: Cancer Chemotherapy-Related Anemia and Fatigue

<table>
<thead>
<tr>
<th>Patient/Family Education &amp; Counseling</th>
<th>General Strategies for Management of Fatigue</th>
<th>Non-pharmacologic</th>
<th>Pharmacologic</th>
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<tbody>
<tr>
<td>Information about known pattern of fatigue during and following treatment:</td>
<td>Energy conservation:</td>
<td>Activity enhancement</td>
<td>• Consider psychostimulants after ruling out other causes of fatigue</td>
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<tr>
<td>• Reassurance that treatment – related fatigue is not necessarily an indicator of disease progression</td>
<td>• Set priorities</td>
<td>• Maintain optimal level of activity</td>
<td>• Treat for anemia as indicated</td>
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<td>• Daily self-monitoring of fatigue levels to evaluate effectiveness of interventions and treatment</td>
<td>• Pace</td>
<td>• Consider initiation of exercise program</td>
<td>• Consider medication for sleep</td>
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<td>• Delegate</td>
<td>• Consider referral to physical therapy/physical medicine &amp; occupational therapy as appropriate</td>
<td>• Consider corticosteroids in EOL patients</td>
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<td>• Schedule activities at times of peak energy</td>
<td>• Caution:</td>
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<td></td>
<td>• Postpone non-essential activities</td>
<td>➢ Bone metastasis</td>
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<td>• Take naps that do not interrupt night-time sleep quality – limit to 20-30 minutes at a time</td>
<td>➢ Immunosuppression/neutropenia</td>
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<td></td>
<td>• Structured daily routine</td>
<td>➢ Thrombocytopenia</td>
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<td>• Attend to one activity at a time</td>
<td>➢ Fever</td>
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<td>• Labor saving devices</td>
<td>➢ Anemia</td>
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<td>Distraction (i.e., games, music, reading, socialization)</td>
<td>➢ Limitations due to metastases or other illness</td>
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<td>➢ Late effects of treatment (cardiomyopathy) for long-term treatment</td>
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<td>Physically-based therapies</td>
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<td>• Massage therapy</td>
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<td>Psychosocial interventions:</td>
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<td>• Cognitive behavioral therapy (CBT)/Behavioral therapy (BT)</td>
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<td>• Psycho-educational therapies/Educational therapies</td>
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<td>• Supportive expressive therapies</td>
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<td>Nutrition consultation</td>
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<td>CBT for sleep</td>
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<td>• Sleep restriction</td>
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<td>• Sleep hygiene</td>
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<td>• Stimulus control</td>
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### Erythropoietic Therapy, Dosing & Titration

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<th>Initial Dosing</th>
<th>Titration for No Response</th>
<th>Titration for Response</th>
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<tbody>
<tr>
<td><strong>Package Insert Dosing Schedule</strong>&lt;br&gt;Epoetin alfa 150 units/kg 3 times weekly by subcutaneous (SQ) injection&lt;br&gt;or&lt;br&gt;Epoetin alfa 40,000 units q wk by SQ injection&lt;br&gt;or&lt;br&gt;Darbepoetin (Aranesp) 2.25 mcg/kg q wk by SQ injection&lt;br&gt;or&lt;br&gt;Darbepoetin alfa 500 mcg q 3 wks by SQ injection</td>
<td>→ Increase dose of epoetin alfa to 300 units/kg 3 times weekly by SQ injection&lt;br&gt;→ Increase dose of epoetin alfa to 60,000 units q wk by SQ injection&lt;br&gt;→ Increase darbepoetin to up to 4.5 mcg/kg q every wk by SQ injection</td>
<td>• Dose should be adjusted for each individual to maintain the lowest hemoglobin (Hb) level sufficient to avoid blood transfusion.</td>
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<td><strong>Alternative Regimes</strong>&lt;br&gt;Darbepoetin alfa 100 mcg fixed dose q wk by SQ injection&lt;br&gt;or&lt;br&gt;Darbepoetin alfa 200 mcg fixed dose q 2 wks by subcutaneous injection&lt;br&gt;or&lt;br&gt;Darbepoetin alfa 300 mcg fixed dose q 3 wks by SQ injection&lt;br&gt;or&lt;br&gt;Epoetin alfa 120,000 units q 2 wks by SQ injection&lt;br&gt;or&lt;br&gt;Epoetin alfa 120,000 units q 3 wks by SQ injection</td>
<td>→ Increase darbepoetin to 150-200 mcg fixed dose q wk by SQ injection&lt;br&gt;→ Increase darbepoetin to up to 300 mcg fixed dose q 2 wks by SQ injection&lt;br&gt;→ Increase darbepoetin alfa up to 500 mcg fixed dose q 3 wks by SQ injection</td>
<td>• If Hb reaches a level needed to avoid transfusion or increases by more than 1 g/dL in a 2 week period, dose should be reduced by 25% for epoetin alfa and by 40% for darbepoetin alfa</td>
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## Screening for Cancer – Related Fatigue

<table>
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<tr>
<th>Severity</th>
<th>Education plus vital signs at regular intervals</th>
<th>Education plus general strategies to manage fatigue</th>
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<td>None to Mild (0-3)</td>
<td>None to Mild (0-3) → Education plus vital signs at regular intervals</td>
<td>Education plus general strategies to manage fatigue</td>
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<tr>
<td>Moderate (4 – 6) or Severe (7 – 10)</td>
<td>Moderate (4 – 6) or Severe (7 – 10) → Education plus general strategies to manage fatigue</td>
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### Primary Evaluation for Fatigue Score (4 – 10)

**Focused History**
- Disease status and treatment
  - Rule out recurrence or progression
  - Current medication and/or medication changes (include over-the-counters (OTCs) and supplements)
- Review of systems
- In – depth fatigue assessment
  - Onset, pattern, duration
  - Change over time
  - Associated or alleviating factors
  - Interference with function
Assessment of Treatable Contributing Factors:

Pain
Emotional distress (depression, anxiety)
Sleep disturbance (obstructive sleep apnea, restless leg syndrome, narcolepsy, insomnia)
Anemia
Nutrition Assessment:
  • Weight/calorie intake changes
  • Fluid electrolyte imbalance: sodium, potassium, calcium, magnesium
Activity Level:
  • Decreased activity
  • Decreased physical fitness
Medication side effects profile
Alcohol/substance abuse
Comorbidities:
  • Infection
  • Cardiac dysfunction
  • Renal dysfunction
  • Hepatic dysfunction
  • Neurological dysfunction
  • Endocrine dysfunction – hypothyroidism and other disorders
  • Pulmonary dysfunction
Screening Evaluation

Non-cancer or non-treatment related anemia specific cause:
- Bleeding
- Hemolysis
- Nutritional deficiency
- Hereditary
- Renal dysfunction

Hemoglobin (Hb) ≤11 g/dL or ≥ 2g/dL below baseline
- CBC with indices
- Review of peripheral smear, as clinically indicated
- Other studies as indicated to identify cause

Cancer or treatment related anemia

Risk Assessment
- Disease specific anemia
- Acuity
- Duration
- Severity
  - Mild (Hb 10 g/dL - lower limit of normal)
  - 2. Moderate (Hb 8 - <10 g/dL)
  - 3. Severe (Hb 6.5 - <8 g/dL)
  - 4. Life-threatening (life-threatening)
  - 5. Death (death)

- Symptoms – physiological
  - Cardiac symptoms
  - Fatigue

- Comorbidities
  - Cardiac history/decompensation
  - Chronic pulmonary disease
  - Cerebral vascular disease

Treat as indicated

Immediate Correction Required

Immediate Correction Not Required

Transfuse as indicated based on institutional guidelines

Complete symptom assessment:
Symptoms functional:
- Quantitative scales
- Activity level
- Performance status
- Patient reported fatigue
**Symptomatic**

- Evaluate:
  - Symptoms (such as tachycardia, tachypnea, chest pain, dyspnea on exertion, lightheadedness, syncope, severe fatigue preventing work and usual activities) and institutional guidelines

- **Hb 10-11 g/dL:** Consider erythropoietic (ESA) therapy
- **Hb < 10 g/dL:** Strongly consider ESA therapy

**Asymptomatic**

- Periodic re-evaluation for symptoms
- Transfuse as indicated based upon symptoms and institutional guidelines

**Iron Studies:**
Iron panel (serum iron, total iron, binding capacity, serum ferritin)

**Iron Deficiency Anemia**

- Evaluate:
  - Comorbidities
  - Cardiac including congestive heart failure and coronary heart disease
  - Chronic pulmonary disease
  - Cerebral vascular disease
  - High Risk
  - Progressive decline in hemoglobin with recent intensive chemotherapy or radiation

**Consider red blood cell transfusion per guidelines**

**Asymptomatic with comorbidities or high risk**

**Asymptomatic without significant comorbidities**

- Periodic re-evaluation for symptoms

See erythropoietic therapy dosing and titration +/- iron supplementation as indicated for “functional iron deficiency (ferritin ≤800, TSAT < 20%)”
Initial Response Assessment

Response (Hb increase by 1 g/dL)

- Titrate dosage to maintain optimal Hb (12 g/dL)

No response at 4 weeks for epoetin alfa and 6 weeks for darbepoetin

- Increase dose of erythropoietic agent ± oral iron supplementation as indicated

Follow-up Therapy

- Re-evaluate symptoms at each visit
- If hemoglobin level decreases, check iron stores and evaluate for development of other anemia specific causes

Hb 12 g/dL or Hb > 2 g/dL from baseline

- No improvement in symptoms
  - Consider erythropoietic therapy to maintain optimal Hb

- Improvement in symptoms
  - Titrate dosage to maintain optimal Hb (12 g/dL)

- Discontinue erythropoietic therapy
- Transfuse as indicated based on symptoms and institutional guidelines
Recommendations for the 3 Key Points: Fatigue

1. Cancer-related fatigue is a distressing persistent, subjective sense of tiredness or exhaustion related to cancer or cancer treatment that interferes with usual functioning and is more severe, more distressing and less likely to respond to rest, compared to fatigue in healthy people.

2. Fatigue is a nearly universal symptom in patients receiving chemotherapy or radiation therapy and affects 70-100% of cancer patients. It is perceived by them to be the most distressing symptom associated with cancer and its treatment. Patients should be screened for fatigue at the initial visit, at appropriate intervals and as indicated.

3. Assess for common causes of fatigue such as the current disease and treatment status. Also, assess for the treatable factors known to contribute to fatigue: pain, emotional distress, sleep disturbance, anemia, alterations in nutrition, activity level, medication side effects, alcohol/substance abuse and co-morbidities.

3 Key Points: Anemia

1. Screen all patients at risk for disease or treatment-related anemia by hemoglobin testing. Identify non-cancer related causes of anemia. Classify severity of anemia* where:
   - 1. Mild = 10 – lower limit of normal (LLN)
   - 2. Moderate = 8 – <10 g/dl
   - 3. Severe = 6.5 - < 8 g/dl
   - 4. Life-threatening = life-threatening
   - 5. Death = death

2. Following the identification of anemia (defined for the purpose of intervention as Hb ≤ 11 g/dl) and the evaluation for specific causes, the next step is to determine whether immediate correction is required.

3. Consider EPO therapy for patients with cancer treatment-related symptomatic anemia or risk factors for development of symptomatic anemia. Add iron therapy for “functional iron deficiency” when ferritin <800 or transferrin saturation <20%. Titrate dose of EPO to maintain Hb ≥ 12 g/dl.

* Adapted from the Common Terminology Criteria for Adverse Events. http://evs.nci.nih.gov/ftp1/CTCAE/about.html
Indications for Blood Cell Transfusion in Cancer Patients

GOAL: Prevent or treat deficit of oxygen-carrying capacity

Asymptomatic
- Hemodynamically stable chronic anemia without acute coronary syndrome:
  ➢ Transfusion goal to maintain hemoglobin 7 – 9 g/dL

Symptomatic
- Acute hemorrhage with evidence of hemodynamic instability or inadequate oxygen delivery:
  ➢ Transfuse to correct hemodynamic instability and maintain adequate oxygen delivery
- Symptomatic (including tachycardia, tachypnea, postural hypotension) anemia (hemoglobin less than 10 g/dL):
  ➢ Transfusion goal to maintain hemoglobin 8 – 10 g/dL as needed for prevention of symptoms
- Anemia in setting of acute coronary syndromes or acute myocardial infarction:
  ➢ Transfusion goal to maintain hemoglobin ≥ 10 g/dL

References
1. NCCN Clinical Guidelines in Oncology. Cancer – Related Fatigue V.1.2010
6. NCCN Clinical Guidelines in Oncology, Cancer – and Treatment – Related Anemia V.2.2011