CARE GUIDE: Cancer Chemotherapy-Related Anemia and Fatigue

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

Erythropoietic Therapy, Dosing & Titration

<table>
<tr><th>Initial Dosing</th><th>Titration for No Response</th><th>Titration for Response</th></tr>
<tr><td>Package Insert Dosing Schedule
Epoetin alfa 150 units/kg 3 times weekly by subcutaneous (SQ) injection
or
Epoetin alfa 40,000 units q wk by SQ injection
or
Darbepoetin (Aranesp) 2.25 mcg/kg q wk by SQ injection
or
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

→ Increase dose of epoetin alfa to 60,000 units q wk by SQ injection

→ Increase darbepoetin to up to 4.5 mcg/kg q every wk by SQ injection</td><td rowspan="2">• Dose should be adjusted for each individual to maintain the lowest hemoglobin (Hb) level sufficient to avoid blood transfusion.

• 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></tr>
<tr><td>Alternative Regimes
Darbepoetin alfa 100 mcg fixed dose q wk by SQ injection
or
Darbepoetin alfa 200 mcg fixed dose q 2 wks by subcutaneous injection
or
Darbepoetin alfa 300 mcg fixed dose q 3 wks by SQ injection
or
Epoetin alfa 120,000 units q 2 wks by SQ injection
or
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

→ Increase darbepoetin to up to 300 mcg fixed dose q 2 wks by SQ injection

→ Increase darbepoetin alfa up to 500 mcg fixed dose q 3 wks by SQ injection</td></tr>
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Screening for Cancer – Related Fatigue		
Screen every patient for fatigue as a vital sign at regular intervals (age >12 y): • Severity: 0 -10 scale • 0 – No fatigue: 10 – Worst fatigue you can imagine or None, mild, moderate, severe • "Since your last visit, how would you rate your worst fatigue on a scale of 0 – 10?"	None to Mild (0-3) → Education plus vital signs at regular intervals Moderate (4 – 6) or Severe (7 – 10)	→ Education plus general strategies to manage fatigue → Education plus general strategies to manage fatigue

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/caloric intake changes
- Fluid electrolyte imbalance: sodium, potassium, calcium, magnesium

Activity Level:

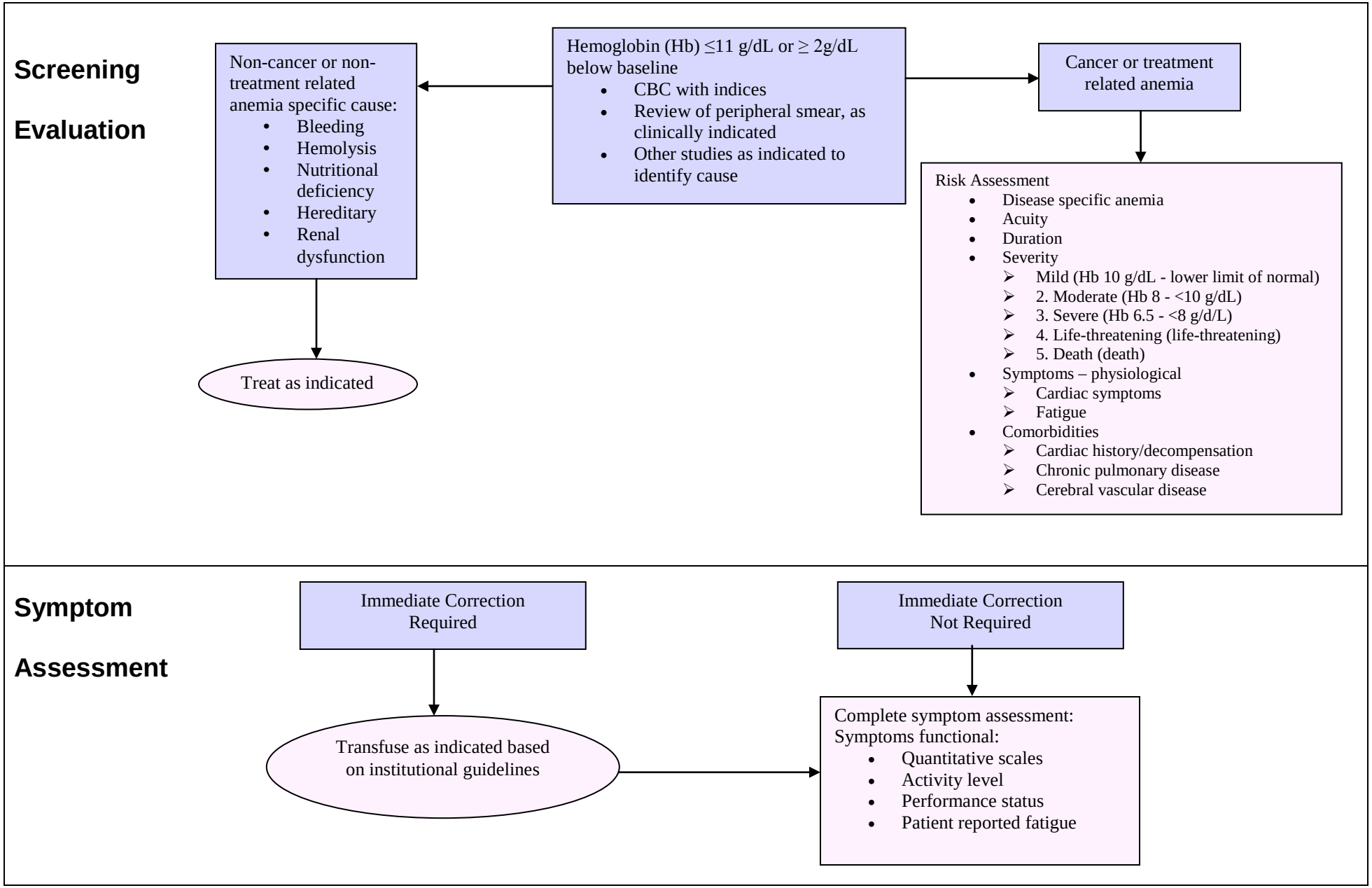
- Decreased activity
- Decreased physical fitness

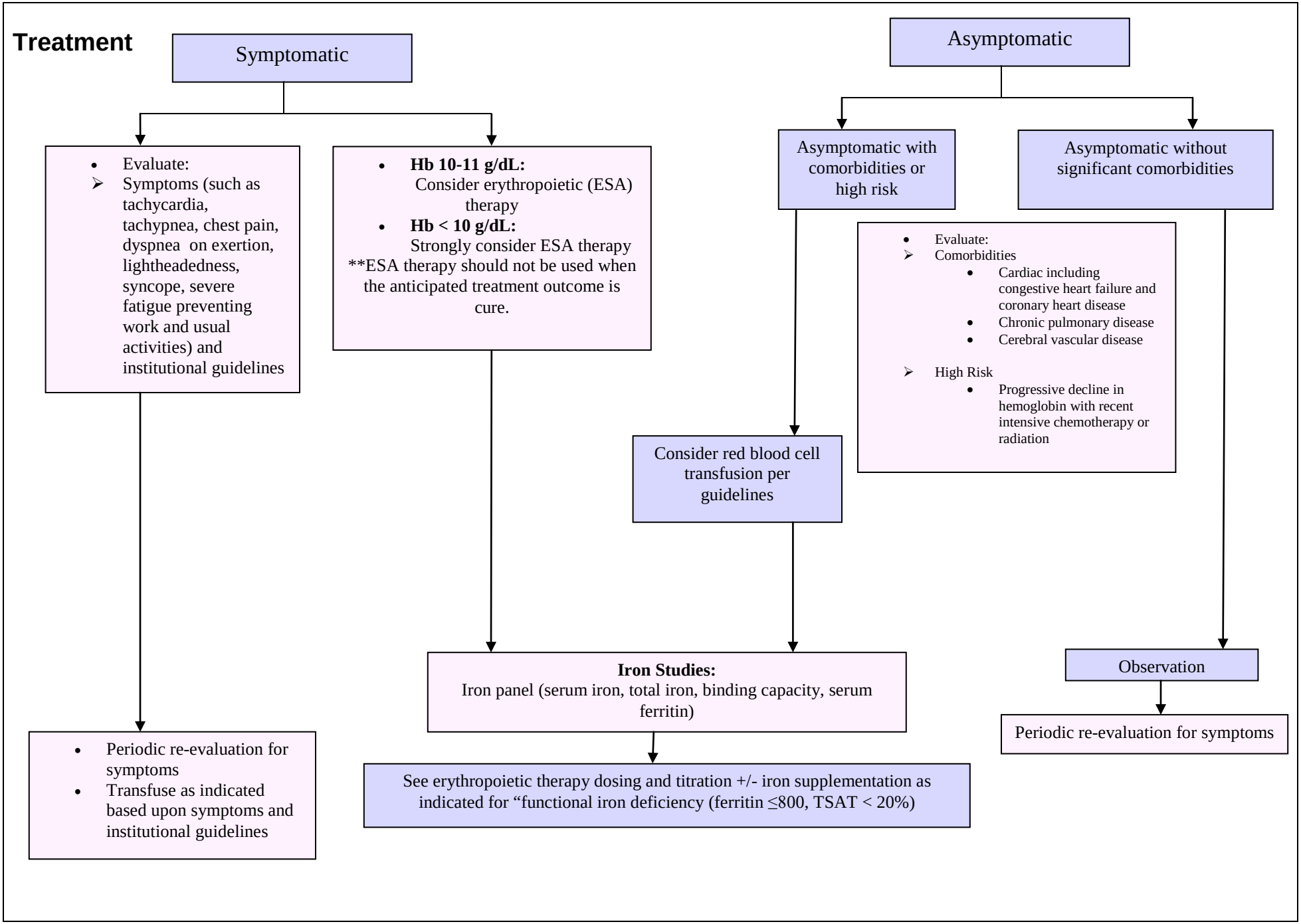
Medication side effects profile

Alcohol/substance abuse

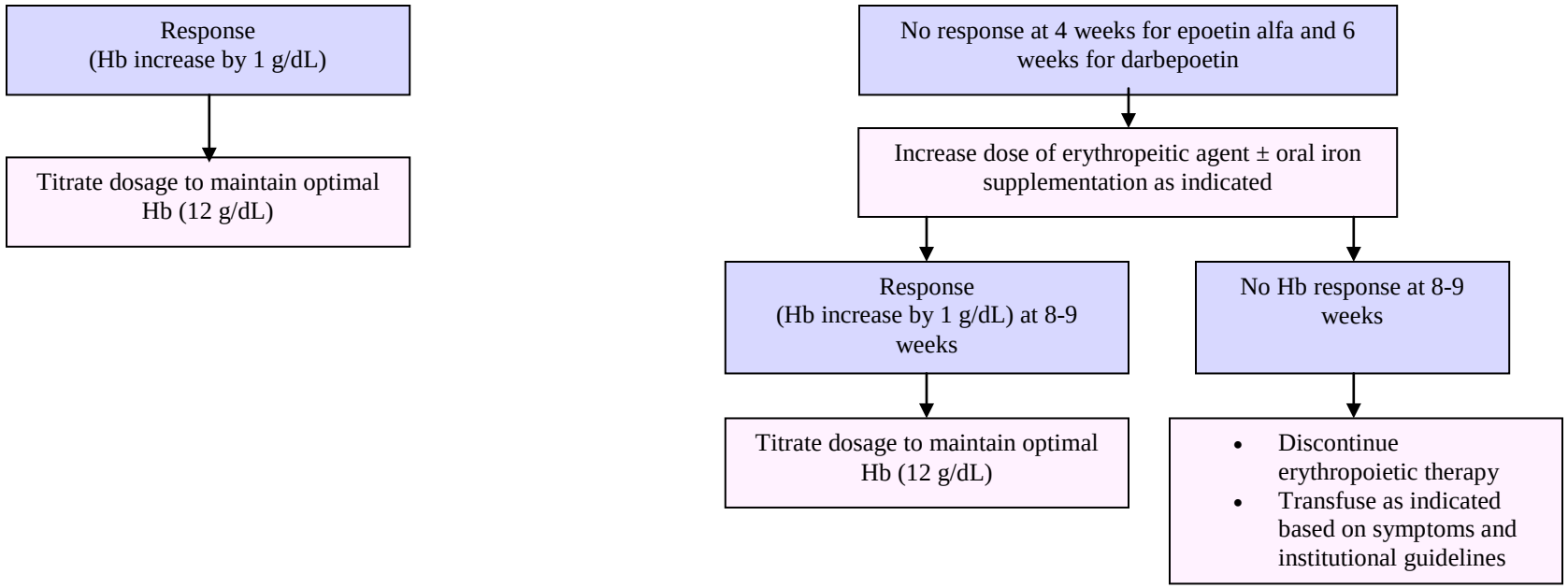
Comorbidities:

- Infection
- Cardiac dysfunction
- Renal dysfunction
- Hepatic dysfunction
- Neurological dysfunction
- Endocrine dysfunction – hypothyroidism and other disorders
- Pulmonary dysfunction

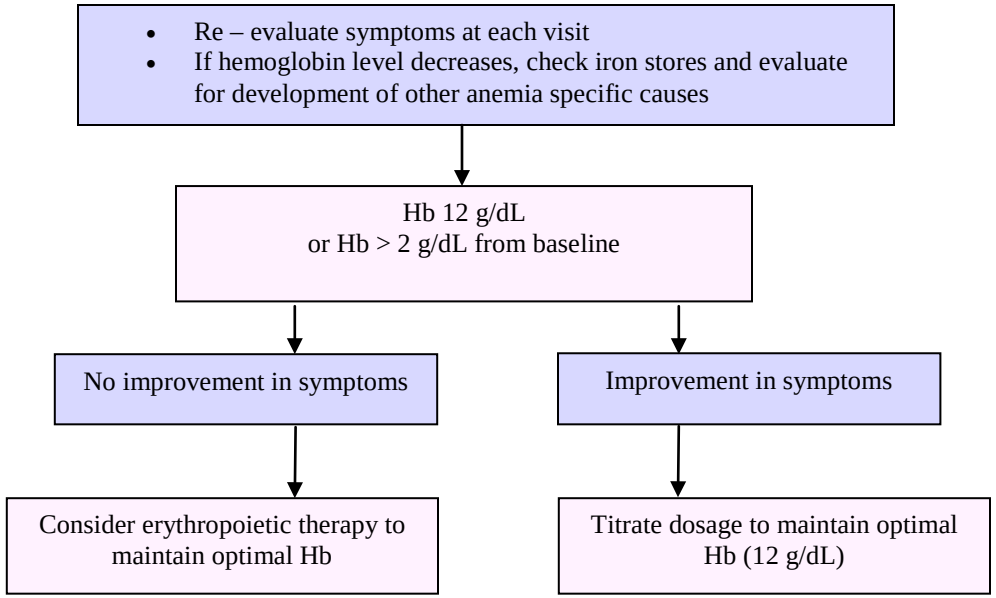

Screening
Evaluation
Hemoglobin (Hb) ≤11 g/dL or ≥ 2g/dL below baseline
CBC with indices
Review of peripheral smear, as clinically indicated
Other studies as indicated to identify cause
Non-cancer or non-treatment related anemia specific cause:
Bleeding
Hemolysis
Nutritional deficiency
Hereditary
Renal dysfunction
Treat as indicated
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/d/L)
4. Life-threatening (life-threatening)
5. Death (death)
Symptoms – physiological
Cardiac symptoms
Fatigue
Comorbidities
Cardiac history/decompensation
Chronic pulmonary disease
Cerebral vascular disease
Symptom
Assessment
Immediate Correction Required
Transfuse as indicated based on institutional guidelines
Immediate Correction Not Required
Complete symptom assessment:
Symptoms functional:
Quantitative scales
Activity level
Performance status
Patient reported fatigue


Treatment
Symptomatic
Asymptomatic
Asymptomatic with comorbidities or high risk
Asymptomatic without significant comorbidities
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
**ESA therapy should not be used when the anticipated treatment outcome is cure.
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
Iron Studies:
Iron panel (serum iron, total iron, binding capacity, serum ferritin)
See erythropoietic therapy dosing and titration +/- iron supplementation as indicated for "functional iron deficiency (ferritin ≤800, TSAT < 20%)
Observation
Periodic re-evaluation for symptoms
Periodic re-evaluation for symptoms
Transfuse as indicated based upon symptoms and institutional guidelines

Initial Response Assessment



Follow – up Therapy



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 $\leq$ 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 $\geq$ 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
2. Littlewood TJ et al. Effects of epoetin alfa on hematologic parameters and QOL in cancer patients receiving non-platinum chemotherapy: results of a randomized double blind, placebo-controlled trial. JCO 19:2865-2874, 2001
3. Patton J et al. Effectiveness of darbepoetin alfa versus epoetin alfa in patients with chemotherapy-induced anemia treated in clinical practice. Oncologist 9: 451-458, 2004
4. Rizzo JD et al. Use of epoetin in patients with cancer: evidence based clinical practice guidelines of ASCO and ASH. JCO 19: 4083-4107, 2002.
5. Wagner LI and Cella D. Fatigue and cancer: causes, prevalence, and treatment approaches. Br J Cancer 91: 822-828, 2004.
6. NCCN Clinical Guidelines in Oncology, Cancer – and Treatment – Related Anemia V.2.2011