### Symptom Management Guidelines:
#### CANCER – RELATED FATIGUE AND ANEMIA

<table>
<thead>
<tr>
<th>Definition</th>
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<tbody>
<tr>
<td>Cancer – Related Fatigue (CRF): A subjective feeling of physical, emotional and/or cognitive tiredness; is often not relieved by rest.</td>
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<table>
<thead>
<tr>
<th>Contributing Factors</th>
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<tbody>
<tr>
<td><strong>Cancer Related &amp; Cancer Treatment Related</strong></td>
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<tr>
<td><em>Extent of disease may affect level of fatigue</em></td>
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<tr>
<td>• Chemotherapy (especially high dose chemotherapy followed by a blood or marrow transplant)</td>
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<tr>
<td>• Radiation therapy</td>
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<tr>
<td>• Surgery</td>
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<tr>
<td>• Biotherapy (especially high dose interferon)</td>
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<tr>
<td>• Inflammatory cytokines</td>
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<tr>
<td>• Immunotherapy – Checkpoint inhibitors</td>
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<table>
<thead>
<tr>
<th><strong>Relevant Medical History</strong></th>
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<tbody>
<tr>
<td>• Fever and/or infection</td>
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<tr>
<td>• Anemia</td>
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<tr>
<td>• Hypothyroidism</td>
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<tr>
<td>• Diabetes mellitus</td>
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<tr>
<td>• Electrolyte disturbances (Sodium, Potassium, Calcium, Magnesium)</td>
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<tr>
<td>• Cardiopulmonary, hepatic or renal dysfunction</td>
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<table>
<thead>
<tr>
<th><strong>Medications</strong></th>
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<tbody>
<tr>
<td>• Opioids</td>
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<tr>
<td>• Antidepressants</td>
</tr>
<tr>
<td>• Antihistamines</td>
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<tr>
<td>• Beta blockers</td>
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<tr>
<td>• Phenytoin and other anticonvulsants</td>
</tr>
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<td>• Benzodiazepines</td>
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<table>
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<tr>
<th><strong>Other</strong></th>
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</thead>
<tbody>
<tr>
<td>• Advanced age</td>
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<tr>
<td>• Life stressors, depression &amp; anxiety</td>
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<tr>
<td>• Sleep/wake disturbance</td>
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<tr>
<td>• Pain</td>
</tr>
<tr>
<td>• Decreased activity, bed rest, deconditioning</td>
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<tr>
<td>• Nutritional deficits, malnutrition and dehydration</td>
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<tr>
<td>• Alcohol/substance abuse</td>
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<table>
<thead>
<tr>
<th><strong>Consequences</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Chemotherapy dose delays, reductions, discontinuation of treatment</td>
</tr>
<tr>
<td>• Quality of life – distress, compromised role function and cognition, decreased functional status, exacerbation of other symptoms</td>
</tr>
</tbody>
</table>

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# Focused Health Assessment

## General Assessment

### Contact and General Information
- Physician name - oncologist, family physician
- Pharmacy
- Home health care
- Other healthcare providers
- Allergies

### Consider Contributing Factors
- Cancer diagnosis
- Cancer treatment(s) – note type and date of last treatment(s), concurrent treatments
- Medical history
- Medication profile
- Recent lab or diagnostic reports (e.g. CBC, electrolyte)
- Nutritional deficits or dehydration
- Decreased activity, bed rest and deconditioning
- Depression and anxiety
- Pain
- Anemia
- Fever and/or infection
- Sleep / wake disturbance

## Symptom Assessment

### Normal
- What is your normal energy/activity level/exercise?

### Onset
- When did the fatigue begin? Is it related to a change in cancer treatment?

### Provoking / Palliating
- What brings on the fatigue?
- Is there anything that makes the fatigue better? Worse?
- When do you feel the most tired?

### Quality
- What does it feel like?
- Explore whether symptoms reflect drowsiness versus physical fatigue or mental versus physical fatigue

### Region / Radiation - N/A

### Severity / Other Symptoms
- Since your last visit, how would you rate your fatigue between 0-10? What is it now? At worst? At best? On average?
- Do you have any other accompanying symptoms such as shortness of breath at rest or with activity, rapid heart rate, chest pain or leg heaviness?

### Treatment
- What medications or treatments are you using or have you used in the past? How effective are they? Any side effects?
- Have you had a blood transfusion? When?
- When was your last cancer treatment?

### Understanding / Impact on You
- Is fatigue affecting your mood? Anxiety, sadness, feeling stressed?
- How much are you able to do in a day?
- How is your fatigue impacting your activities of daily living (ADL)?
- How many hours do you sleep at night? In the day?

### Value
- What do you believe is causing this symptom? Is this impacting you and/or your family?
- What is your comfort goal or acceptable level for this symptom? (0-10)

### Vital Signs
- Frequency – as clinically indicated

### Observe for:
- Pallor
- Blood loss
- Labored breathing
- Poor capillary refill
- Poor posture
- Cachexia
- Altered mobility, gait
- Peripheral edema
- Cognitive impairment
- Chest pain

### Weight
- Take current weight and compare to pre – treatment or last recorded weight

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**FATIGUE GRADING SCALE**

*NCI Common Terminology Criteria for Adverse Events (Version 4.03)*

<table>
<thead>
<tr>
<th>GRADE 1 (Mild)</th>
<th>GRADE 2 (Moderate)</th>
<th>GRADE 3 (Severe)</th>
<th>GRADE 4</th>
<th>GRADE 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue relieved by rest</td>
<td>Fatigue not relieved by rest; limiting instrumental ADL (e.g. preparing meals, shopping, managing money)</td>
<td>Fatigue not relieved by rest, limiting self-care ADL (e.g. bathing, dressing, feeding self, using the toilet, taking medications)</td>
<td>—</td>
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</tbody>
</table>

*A semi-colon indicates ‘or’ within the description of the grade and a single dash (-) indicates a grade is not available

*Step-Up Approach to Symptom Management: Interventions Should Be Based On Current Grade Level and Include Lower Level Grade Interventions As Appropriate

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**GRADE 1**

**NON – URGENT Support, teaching, & follow-up as clinically indicated**

**Patient Care and Assessment**
- Collaborate with physician to rule out other causes or concomitant causes of fatigue (e.g. Anemia) and to determine need for further investigation
  
  *Appendix A: Cancer and Treatment-related Anemia below*

**Patient Education**
- Reinforce that Cancer Related Fatigue is:
  - Normal, often treatable, and needs to be reported
  - Different than ‘normal’ fatigue and may not be relieved by rest
  - Not necessarily a sign of cancer progression or that treatment is not working

**Exercise**
- If recommending exercise, assess for facilitating/inhibiting factors, co-morbidities such as bone metastases, thrombocytopenia, anemia, fever, or active infection
- Set goals that are specific, achievable and realistic based on current health status
- Exercise during and after cancer treatment can result in more physical energy, improved appetite and increased ability to perform ADLs
- Start with light activity for short periods of time and encourage patient to gradually increase activity level to include 20 minutes (+) of endurance activities (e.g. walking, jogging, swimming) and muscle and bone strengthening activities 2x/week (e.g. light weights)

**Energy Conservation**
- Pacing
  - Balance activities with rest
  - Slow and steady pace uses less energy
- Planning
  - Organize your time, methods, and space
  - Encourage activities which are most enjoyed on days when feeling best
  - Develop a routine for rest and activity
- Priority setting
  - Eliminate unnecessary tasks, delegate responsibilities and ask for help
- Posture
  - Change positions frequently
  - Keep activities/work within easy range using correct body alignment
  - Avoid bending and lifting
- Proficiency
  - Use labour saving devices (e.g. elevator) to maximize efficiency and minimize workload
- Encourage self-monitoring of fatigue levels and patterns and times of peak energy
### Sleep Hygiene
- **Encourage:**
  - Comfortable sleep surroundings
  - Soothing activities at bed time
  - Limiting naps to less than 1hr
- **Avoid:**
  - Lying in bed at times other than sleep
  - Distracting noise (e.g. television, radio) during sleep
  - Caffeine and exercise near bedtime

### Dietary Management
- Encourage adequate hydration (e.g. 8 – 12 cups of fluid throughout the day). Caution in patients with co-morbidities that affect fluid balance (e.g. Congestive heart failure)
- Encourage adequate nutrition (e.g. high-protein diet)

### Pharmacological Management
- Avoid/discontinue any medications that may cause or exacerbate fatigue in collaboration with physician and pharmacist
- Medications may be prescribed to correct causative factors (e.g. iron supplement)

### Distraction and Relaxation
- Consider stress management, relaxation, distraction (e.g. music, games, reading, socializing)

### Follow-Up
- Re-assess at each visit and modify strategies as necessary
- Advise patient to contact healthcare providers if fatigue level increases or does not improve

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### GRADE 2 – GRADE 3

#### URGENT:
Requires medical attention within 24 hours

### Patient Care and Assessment
- Collaborate with physician:
  - To rule out other causes or concomitant causes of fatigue
  - Need for further patient assessment at cancer centre or with GP
  - Special consideration for patients receiving Immunotherapy. Fatigue may not be a direct side effect of Immunotherapy, rather a product of immune mediated side effects. Refer to protocol specific algorithms for management.
- Monitor vital signs as clinically indicated
- Lab tests that may be ordered:
  - Complete blood count (CBC), electrolyte profile, transferrin, total iron-binding capacity, ferritin, iron levels, folic acid, B12 level, thyroid function tests,
  - AST / ALT, total bilirubin and evaluate endocrine function if patient on Immunotherapy

### Pharmacological Management
- Avoid/discontinue/reduce any medications that may cause or exacerbate fatigue in collaboration with physician and pharmacist
- Medications that may be prescribed:
  - Iron supplement
  - Psychostimulants (e.g. methylphenidate {Ritalin®} )
  - Sleep-enhancing medications (e.g. Benzodiazapines)
  - Blood transfusion or Erythropoiesis- Stimulating Agents (ESAs) such as Epoetin alfa or Darbepoetin alfa **See Appendix A: Cancer and Treatment-related Anemia below**
  - Corticosteroids (Refer to protocol specific algorithm if patient is on Immunotherapy)

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### RESOURCES & REFERRALS

<table>
<thead>
<tr>
<th>Referrals</th>
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</thead>
<tbody>
<tr>
<td>Patient Support Centre or Telephone Care Management</td>
</tr>
<tr>
<td>Oncology Nutrition Services (Dietitian)</td>
</tr>
<tr>
<td>Pain and Symptom Management/Palliative Care (PSMPC) - if multiple symptoms</td>
</tr>
<tr>
<td>Physiotherapist</td>
</tr>
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Appendix A: Cancer and Treatment-Related Anemia

**Definitions**

- **Anemia**: Reduction in red blood cell mass, leading to a decrease in the hemoglobin concentration in the blood and reduced oxygen carrying capacity of the blood.
- **Erythropoietin**: Hormone primarily made by the kidneys which stimulates the bone marrow to produce red blood cells.
- **Epoetin alfa and Darbepoetin alfa**: Erythropoiesis-stimulating agents produced by recombinant DNA technology.

**Contributing Factors**

- **Cancer – related**:  
  * Highest for lung and ovarian cancer  
  - Bone marrow infiltration  
  - Hemolysis, blood loss associated with tumor  
- **Cancer Treatment-related**:  
  - Radiation therapy targeted at large areas of bone marrow  
  - Myelosuppressive chemotherapy  
  - Nephrotic effects of chemotherapy (e.g. platinum containing agents - Cisplatin)  
  - Immunotherapy resulting in immune mediated hemolytic anemia  
- **Other**:  
  - Blood loss due to surgery, nutritional deficiencies, renal insufficiency, hypersplenism

**Consequences**

- Fatigue  
- Impact on quality of life  
- Impaired cognitive function  

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May cause treatment delays and dose modifications

### ANEMIA GRADING SCALE*

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<th>GRADE 4</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (Hgb)</td>
<td>Hgb &lt;10.0 g/dL;</td>
<td>Hgb &lt;8.0 g/dL;</td>
<td>Life threatening consequences; urgent intervention indicated</td>
<td>Death</td>
</tr>
<tr>
<td>LLN - 10.0 g/dL;</td>
<td>&lt;6.2 - 4.9 mmol/L;</td>
<td>&lt;4.9 mmol/L;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LLN - 6.2 mmol/L;</td>
<td>&lt;100 - 80 g/L</td>
<td>&lt;80 g/L; transfusion indicated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LLN -100 g/L</td>
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</tbody>
</table>

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### ANEMIA ASSESSMENT AND MANAGEMENT

#### Patient Care and Assessment
- Collaborate with physician to rule out other causes or concomitant causes of anemia (e.g. iron deficiency) and to determine need for further investigation
- Immunotherapy may result in hemolytic anemia via immune mediated side effects, collaborate with physician accordingly.
- Assess for:
  - Fatigue (focused assessment above)
  - Shortness of breath, dyspnea
  - Chest pain, rapid heart rate
  - Visible blood loss (e.g. urine, stool)
  - Previous blood transfusions. If so, note last date.
  - Headaches, dizziness, light headedness
  - Ankle swelling
  - Feeling cold, pale skin
  - Tinnitus
  - Activity level
- Monitor vital signs as clinically indicated
- Lab tests that may be ordered:
  - CBC, peripheral blood smear, vitamin B12 or folate levels, serum iron, transferrin and ferritin levels, reticulocyte count, erythropoietin level, direct and indirect Coombs test, and/or examination of a bone marrow aspirate and biopsy.

#### Transfusion Therapy
- Administer packed red blood cell transfusion as prescribed considering patient factors

#### Radiation Therapy
- May need urgent radiation if bleeding from a tumor

#### Pharmacological Management
- Medications may be prescribed to correct causative factors (e.g. iron supplement)

#### Erythropoiesis stimulating agents (ESA)
- Only recommended for anemic patients with cancer, who are receiving myelosuppressive chemotherapy and the intent of treatment is NOT curative
- Treatment should NOT be started until hemoglobin is LESS than 100 g/L
- The lowest dose needed to avoid RBC transfusions should be given
- ESAs should be discontinued at the end of chemotherapy treatment or if there is no response after 8 weeks of ESA therapy
- Iron supplementation may be considered to improve response to ESA therapy
- Risks of ESA include: increased mortality, tumor progression, thrombosis, cardiovascular events, hypertension, seizure and pure RBC aplasia
- Monitor iron levels before and during ESA treatment (majority of patients will eventually require supplemental iron therapy)
- Review with patient:
  - ESAs take at least 2 weeks to take effect
  - Ensure patient keeps appointment for blood work to monitor hemoglobin
  - Reinforce that BP needs to be measured and monitored
  - Importance of reporting symptoms (e.g. increased BP, headaches, confusion, seizures, weakness, edema, muscle aches, chest pain)

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Follow up

- Reassess symptoms and lab values at each visit
- Ask patient to contact healthcare providers if condition not improved or worsens and/or arrange a nurse-initiated telephone follow up

Date of Print:
Revised: October, 2014
Created: January, 2010

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