

Care Step Pathway - Pyrexia (elevated body temperature in the absence of clinical or microbiological evidence of infection)

Nursing Assessment

Look:

- Does the patient appear unwell?
 - o Diaphoretic?
 - o Pale?
- Does the patient appear dehydrated?
- Is the patient currently febrile?
- If febrile, are rigors present?

Listen:

- Onset and duration of fevers
- Associated symptoms (chills, rigors, decreased urine output, hypotension, malaise, fatigue, GI or respiratory symptoms)
- Method of temperature assessment (oral, axillary, temporal)
- Self-management of fevers (OTC agents, medications, tepid baths)
- Adequacy of fluid intake in the last 24 hours (how much, types, etc)
- How the patient has been taking BRAF/MEKi medications
- Potential infectious causes
 - o Symptoms suggestive of infectious etiology (e.g., upper respiratory, urinary)
 - o Recent sick contacts?
 - o Recent exposure to animals?
 - o Recent international or national travel?

Recognize:

- Other treatment-related adverse events
- Grade of fever and chills if present
- Other symptoms, such as dehydration, rigors, hypotension (complex pyrexia syndrome)
- Potential infectious causes (via urinalysis, urine culture, throat cultures, blood cultures, etc)
- Impact of symptoms on QOL/performance status

Grading Toxicity

Grade 1 (Mild)

Asymptomatic; mild, low-grade fevers (99.0°F–101.2°F [37.2°C–38.4°C])

Grade 2 (Moderate)

Fevers (101.3°F–104.0°F [38.5°C–40.0°C]); mildly symptomatic (chills, etc) affecting ADLs

Grade 3 (Severe)

Any fever >104.0°F (>40.0°C) or fever of 101.3°F–104.0°F (38.5°C–40.0°C) that is moderately symptomatic (rigors, chills, decreased urinary output, hypotension); limiting self-care ADLs

Grade 4 (Potentially Life-Threatening)

Any fever >101.3°F (38.5°C) that is **highly** symptomatic (acute renal insufficiency, hypotension requiring hospitalization, prompt supportive care)

Grade 5 (Death)

Management

Grade 1 (Mild)

- Acetaminophen or ibuprofen q4-6 hrs until fever resolves (<99°F [37.2°C]) for at least 24 hours
 - o Monitor renal and hepatic function during antipyretic treatment
 - o Do not exceed 3000 mg/d acetaminophen or 2400 mg/d ibuprofen
- Increase oral hydration to minimize insensible losses. Suggested fluids: water, juice, sports drinks (e.g., Gatorade®, Powerade®, Pedialyte®)
- Review medication profile with patient and family, including prescriptions, OTCs, herbals, supplements, or other complementary therapies
 - o Determine if concomitant medications contain antipyretics
 - o Assess for potential drug-drug interactions
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence

Grade 2 (Moderate)

- For temperatures >101.3°F (38.5°C), dabrafenib to be held/trametinib to be continued
- Acetaminophen or ibuprofen q4-6 hrs until fever resolves (<99°F [37.2°C]) for at least 24 hours
 - o Monitor renal and hepatic function during antipyretic treatment
 - o Do not exceed 3000 mg/d acetaminophen or 2400 mg/d ibuprofen
- Institute re-hydration strategies, particularly if patient is hypotensive or there is other clinical concern. Set hydration goals
 - o Oral, advise fluids: water, rehydration drinks (Pedialyte), juice, sports drinks (Gatorade, Powerade), popsicles
 - o Intravenous, as needed
- For pyrexia refractory to antipyretics, CS with prednisone or equivalent will be used (25 mg/d, with downward titration); consider change in targeted therapy, if clinically appropriate (eg, switch from dabrafenib to vemurafenib if fever persists and refractory to antipyretics or prednisone treatment, causing moderate changes in the patient's ADLs)
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence
- Upon symptom and fever resolution (<99°F [37.2°C]) for 24 hours, possible treatment restart with appropriate dose reduction
- For recurrent pyrexia, CS with prednisone or equivalent will be used (10 mg/day for at least 5 days); In the unresectable/metastatic setting, consider change in targeted therapy, if clinically appropriate (e.g., switch from dabrafenib to vemurafenib if fever persists)

Grades 3-4 (Severe or Potentially Life-Threatening)

- For fevers >104°F (>40.0°C), or any fever accompanied by chills, hypotension, dehydration, or renal failure, **both** dabrafenib and trametinib will be held
- For intolerable temperatures 102.3°F–104.0°F (39.1°C–40.0°C) and all temperatures >104°F (40.0°C), both vemurafenib and cobimetinib will be held
- Targeted therapy will be held (Grade 3) or discontinued (Grade 4)
- Prompt medical and supportive care interventions
 - o Hospitalization, if clinically indicated
- Acetaminophen or ibuprofen q4-6 hrs until fever resolves (<99°F; 37.2°C) for at least 24 hours
 - o Monitor renal and hepatic function during antipyretic treatment
 - o Do not exceed 3000 mg/d acetaminophen or 2400 mg/d ibuprofen
- Aggressive hydration management to address hypotension, etc
- For pyrexia refractory to antipyretics, CS with prednisone or equivalent will be used, 25 mg/d, with downward titration; consider change in targeted therapy, if clinically appropriate (e.g., dabrafenib to vemurafenib)
- Grade 3: Upon symptom and fever resolution for (<99°F [37.2°C]) for 24 hours, possible treatment restart
 - o Same agents with appropriate dose reductions
 - o Oral corticosteroid premedication (10 mg/d) to be used for second or subsequent pyrexia with dabrafenib if prolonged (>3 days) or with complications
- In the unresectable/metastatic setting, change to different targeted therapy regimen, if clinically appropriate (e.g., switch from dabrafenib to vemurafenib if fever persists)
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence

ADL = activities of daily living; CS = corticosteroid; GI = gastrointestinal; OTC = over the counter; QOL = quality of life