Care Step Pathway – Pneumonitis (inflammation of lung alveoli)

Assessment

Look:
- Does the patient appear uncomfortable?
- Did the patient have difficulty walking to the exam room? Or going up stairs?
- Does the patient appear short of breath?
- Is the patient tachypneic?
- Does the patient appear to be in respiratory distress?

Listen:
- Has the patient noted any change in breathing?
- Does the patient feel short of breath?
- Does the patient note new dyspnea on exertion?
- Does the patient notice a new cough? Or a change in an existing cough?
  - Is it a dry cough or a productive cough?
- Have symptoms worsened?
- Are symptoms limiting ADLs?
- Associated symptoms?
  - Fatigue
  - Wheezing

Recognize:
- Is the pulse oximetry low? Is it lower than baseline or compared with last visit? Is it low on ambulation?
- Is there a pre-existing pulmonary autoimmune condition (e.g., sarcoidosis)?
- Does patient have lung metastases?
- History of radiation to the lung?
- Is there a history of prior respiratory compromise (e.g., asthma, COPD, congestive heart failure)?
- Has the patient experienced other immune-related adverse effects?

Grading Toxicity

Pneumonitis

Definition: A disorder characterized by inflammation focally or diffusely affecting the lung parenchyma

Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grade 4 (Potentially Life-Threatening)	Grade 5 (Death)
Asymptomatic; Confined to one lobe of lung;clinical or diagnostic observations only; intervention not indicated	Symptomatic; medical intervention indicated; limiting instrumental ADLs	Severe symptoms; limiting self-care ADLs; oxygen indicated	Life-threatening respiratory compromise; urgent intervention indicated (tracheostomy, intubation)	

Management

Overall Strategy:
- Assess for other etiologies such as infection (e.g., nasal swab for viral pathogens; sputum culture), pulmonary embolism, progressive lung metastases, pleural effusion, or lung disease
- Early intervention to maintain or improve physical function and impact on QOL
- Assess pulse oximetry (resting & on exertion) at baseline and at each visit to assist in identifying a decrease at early onset
- Consider chest CT or X-ray for assessment of efficacy of steroids/monitor for new lung metastases
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence, including adherence with medication, physical activity

Prevention
- Decrease or cease smoking; preventive vaccinations for flu and pneumonia

Grade 1 (Mild)
- Anticipate immunotherapy to continue
- Continue to monitor via radiology testing (q 2–4 weeks, as needed)
- Review symptoms to watch for with patient & family, and remember to assess at every subsequent visit
- Continue monitoring pulse oximetry (resting and with ambulation)
- Assess patient & family understanding of recommendations and rationale
- Identify barriers to adherence

Grade 2 (Moderate)
- Immunotherapy to be withheld for Grade 2 events (resume when Grade 0/1)
- Immunotherapy to be discontinued for recurrent (pembrolizumab, nivolumab) or persistent Grade 2 events (ipilimumab, pembrolizumab, nivolumab)
- Monitor pulse oximetry (resting and with ambulation) q 3–7 days
- Anticipate treatment with:
  - Corticosteroids* (e.g., prednisone 1–2 mg/kg/day or equivalent) until symptoms improve to baseline, and then slow taper over at least 1 month
  - If symptoms do not improve within 48–72 hours, corticosteroid* dose will be escalated. IV corticosteroids* may be considered if no improvement in 72 hours, treat as Grade 3
  - Additional supportive care medications may also be initiated
- Anticipatory guidance on proper administration of IV corticosteroids
- Anticipate the use of empiric antibiotics until infection is excluded
- Anticipate that bronchoscopy may be ordered by provider

Grades 3/4 (Severe or Life-Threatening)
- Permanently discontinue immunotherapy for Grade 3/4 events
- Obtain Respiratory and Infectious Diseases opinion
- Patient will likely need to be admitted to the hospital for further management and supportive care ITU assessment maybe necessary for Non-Invasive ventilation
- Anticipate the use of high-dose IV corticosteroids* (e.g., methylprednisolone 1–4 mg/kg/day or equivalent)
- Once symptoms have resolved to baseline or Grade 1, convert to equivalent oral corticosteroid dose and then taper slowly over at least 1 month
- Anticipate the use of empiric antibiotics until infection is excluded
- Anticipate the use of additional immunosuppressive agents if symptoms do not improve in 48–72 hours (e.g., infliximab, mycophenolate, cyclophosphamide, IVIG)
- Assess patient & family understanding of rationale for treatment discontinuation
- Identify barriers to adherence, specifically compliance with medication, physical activity

*Administering Corticosteroids:

Steroid taper instructions/calendar as a guide but not an absolute
- Taper should consider patient's current symptom profile
- Close follow-up in person or by phone, based on individual need & symptomatology
- Steroids cause indigestion; provide antacid therapy daily as gastric ulcer prevention while on steroids (e.g., proton pump inhibitor or H2 blocker if prednisone dosage is >20 mg/day)
- Review steroid medication side effects: mood changes (angry, reactive, hyperaware, euphoric, manic), increased appetite, interrupted sleep, oral thrush, fluid retention
- Be alert to recurring symptoms as steroids taper down & report them (taper may need to be adjusted)

Long-term high-dose steroids:
- Consider antimicrobial prophylaxis (sulfamethoxazole/trimethoprim double dose M/W/F; single dose if used daily) or alternative if sulfa-allergic (e.g., atovaquone [Mepron®] 1500 mg po daily)
- Consider additional antiviral and antifungal coverage
- Avoid alcohol/acetaminophen or other hepatoxins
- If extended steroid use, risk for osteoporosis; initiate calcium and vitamin D supplements

Implementation:
- Identify high-risk individuals (e.g., asthma, COPD, prior thoracic radiation therapy) and those with cardiopulmonary symptoms prior to initiating immunotherapy. Establish a thorough baseline, including pulse oximetry (resting & with ambulation)
- Educate patients that new or worsening/changing pulmonary symptoms should be reported immediately
- Anticipate that the steroid requirements to manage pneumonitis are high (1–2 mg/kg/day) and patient will be on corticosteroid therapy for at least 1 month
- Educate patients & family about the rationale for discontinuation of immunotherapy in patients who do develop moderate or severe pneumonitis
- For severe/life-threatening pneumonitis, treat patient as immunocompromised, so ID workup to include nasal swab (viral), sputum, blood, and urine cultures

RED FLAGS:
- **Risk of acute onset**
- **Risk of mortality if pneumonitis treatment is delayed**
- **Risk of pneumonitis is greater in patients receiving combination immunotherapy regimens**

ADLs = activities of daily living; COPD = chronic obstructive pulmonary disease; IVIG = intravenous immunoglobulin; po = by mouth