

BC Cancer Protocol Summary for Management of Immune-Mediated Adverse Reactions to Checkpoint Inhibitors Immunotherapy

Protocol Code	SCIMMUNE
Tumour Group	Supportive Care
Contact Physician	Dr. Kerry Savage

Eligibility

Patients treated with immunotherapy agents with checkpoint inhibition, including:

- CTLA-4 inhibitors (e.g., ipilimumab)
- PD-1 inhibitors (e.g., nivolumab, pembrolizumab)
- PD-L1 inhibitors (e.g., atezolizumab, avelumab, durvalumab)

These agents are associated with immune-mediated adverse reactions, although the incidence may vary from agent to agent. Reactions can be severe to fatal and usually occur during the treatment course. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications. For specific toxicities management, see the following flow diagrams.

Serious immune-mediated reactions

These can be severe to fatal and usually occur during the treatment course. They may include enterocolitis, intestinal perforation or hemorrhage, hepatitis, dermatitis, neuropathy, endocrinopathy, as well as toxicities in other organ systems. Early diagnosis and appropriate management are essential to minimize life-threatening complications. For specific toxicities management, see the following flow diagrams.

Infusion-related reactions

Isolated cases of severe reaction have been reported. In case of a severe reaction, infusion of checkpoint inhibitors should be discontinued and appropriate medical therapy administered. Patients with mild or moderate infusion reaction may receive checkpoint inhibitors with close monitoring. Premedications with acetaminophen and anti-histamine may be considered.

Other immune-mediated adverse reactions

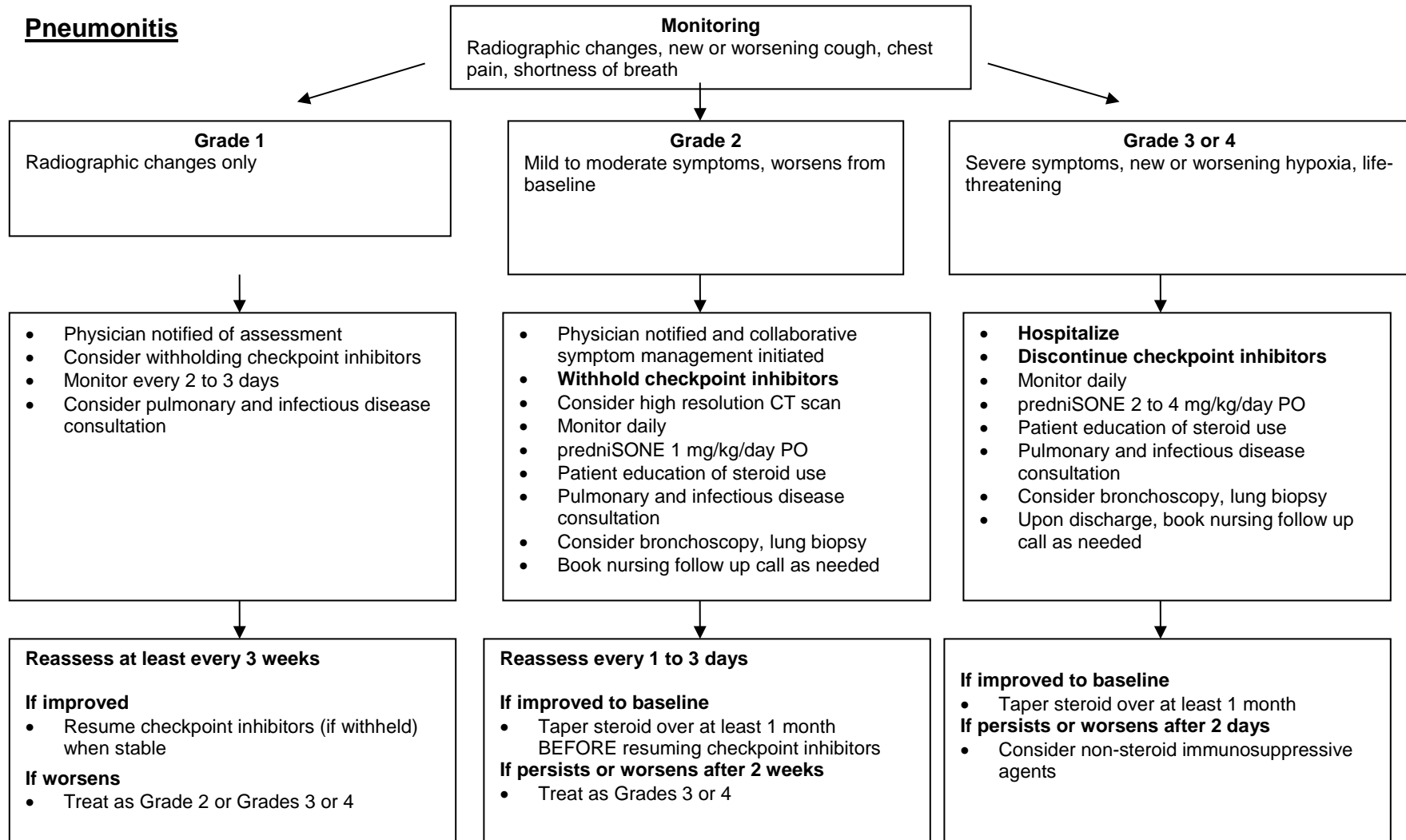
If severe or clinically significant:

- **Discontinue the checkpoint inhibitors.**
 - predniSONE 1 to 2 mg/kg/day PO
 - Corticosteroid eye drops for uveitis, iritis or episcleritis
 - Consider referring to a specialist
1. **Blood and lymphatic:** hemolytic anemia
 2. **Cardiovascular:** angiopathy, myositis, myocarditis, pericarditis, temporal arteritis, vasculitis
 3. **Endocrine:** autoimmune thyroiditis
 4. **Eye:** blepharitis, conjunctivitis, episcleritis, iritis, scleritis, uveitis
 5. **Gastrointestinal:** pancreatitis
 6. **Infectious:** meningitis
 7. **Musculoskeletal:** arthritis, polymyalgia rheumatica
 8. **Renal and urinary:** nephritis
 9. **Respiratory:** pneumonitis
 10. **Skin:** psoriasis, leukocytoclastic vasculitis

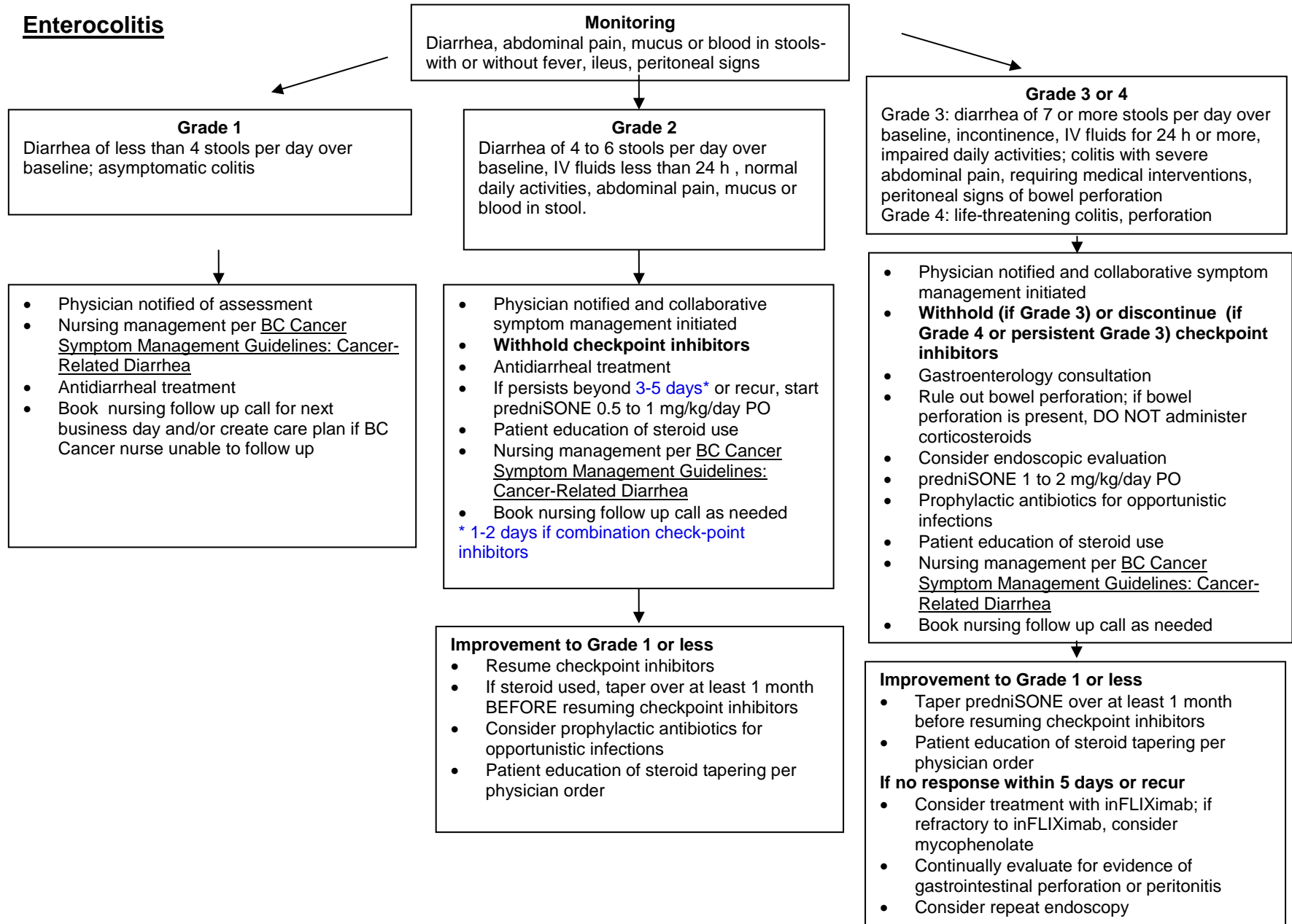
References:

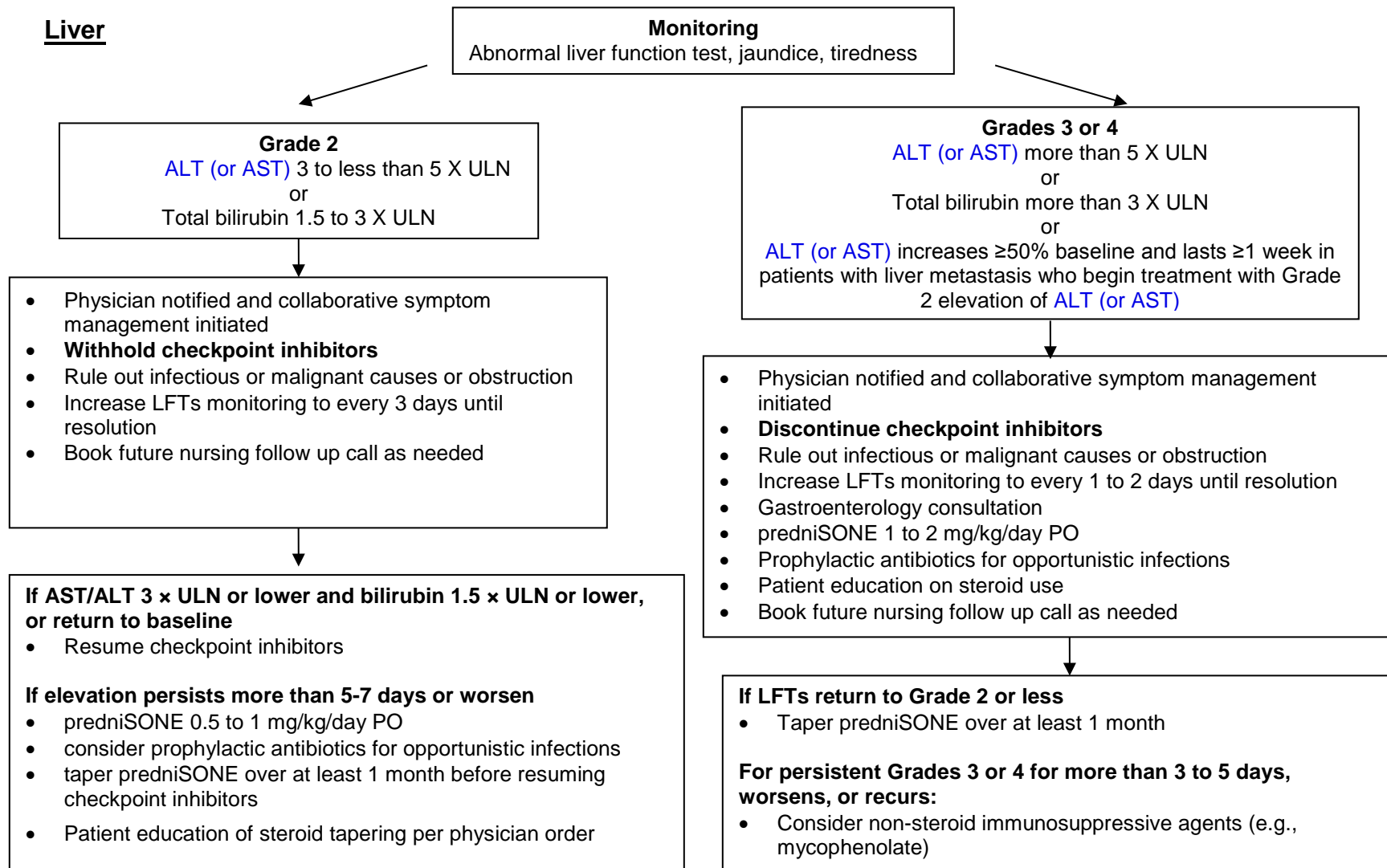
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2. Bristol-Myers Squibb Pharma: YERVOY (ipilimumab) summary of product characteristics. Uxbridge, United Kingdom: 2 July 2012.
3. Bristol-Myers Squibb: YERVOY (ipilimumab): Serious and fatal immune-mediated adverse reactions - YERVOY Risk Evaluation and Mitigation Strategy (REMS). <http://www.yervoy.com/hcp/remr.aspx> (Accessed in October, 2012)
4. Momtaz P, Park V, Panageas KS, et al. Safety of infusing ipilimumab over 30 minutes. *J Clin Oncol* (ePub 29 June 2015).
5. Bristol-Myers Squibb: OPDIVO (nivolumab) product monograph. Montreal, Quebec: 26 October 2016.
6. Bristol-Myers Squibb: OPDIVO prescribing information. Princeton, NJ: November 2016.
7. Weber JS, et al. Management of adverse events following treatment with anti-programmed death-1 agents. *Oncologist* 2016;21:1-11.

Pneumonitis

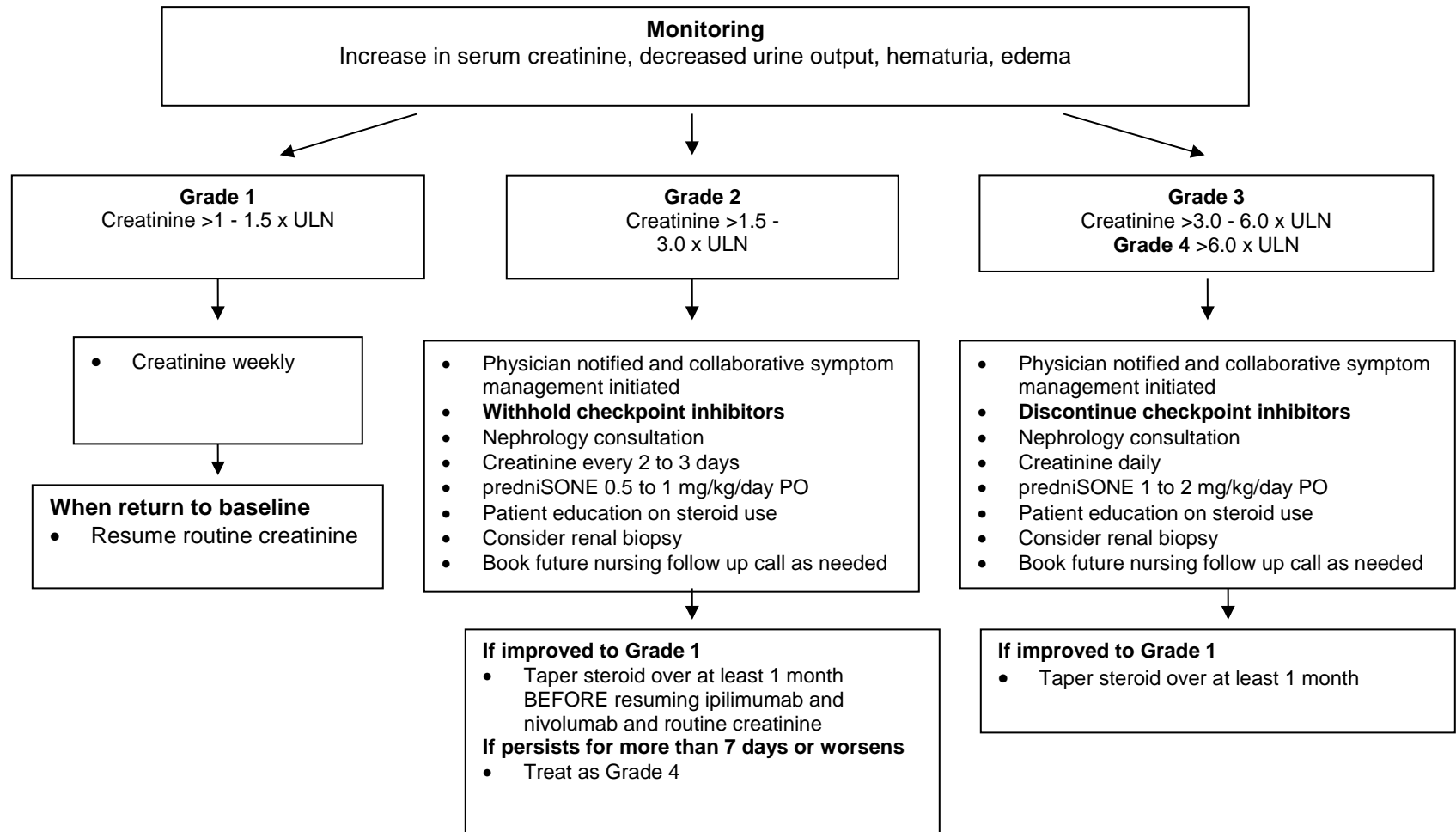


Enterocolitis





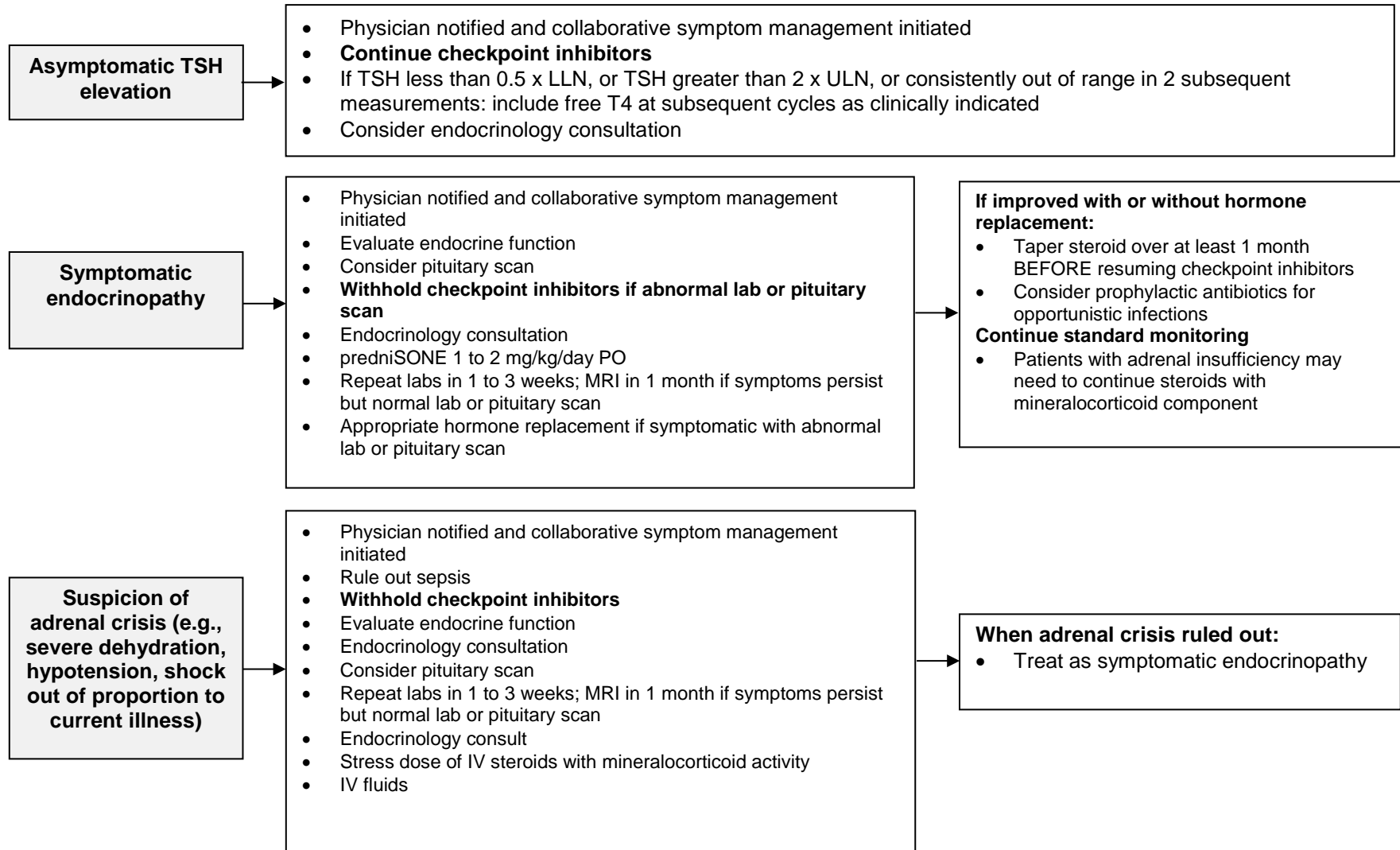
Renal



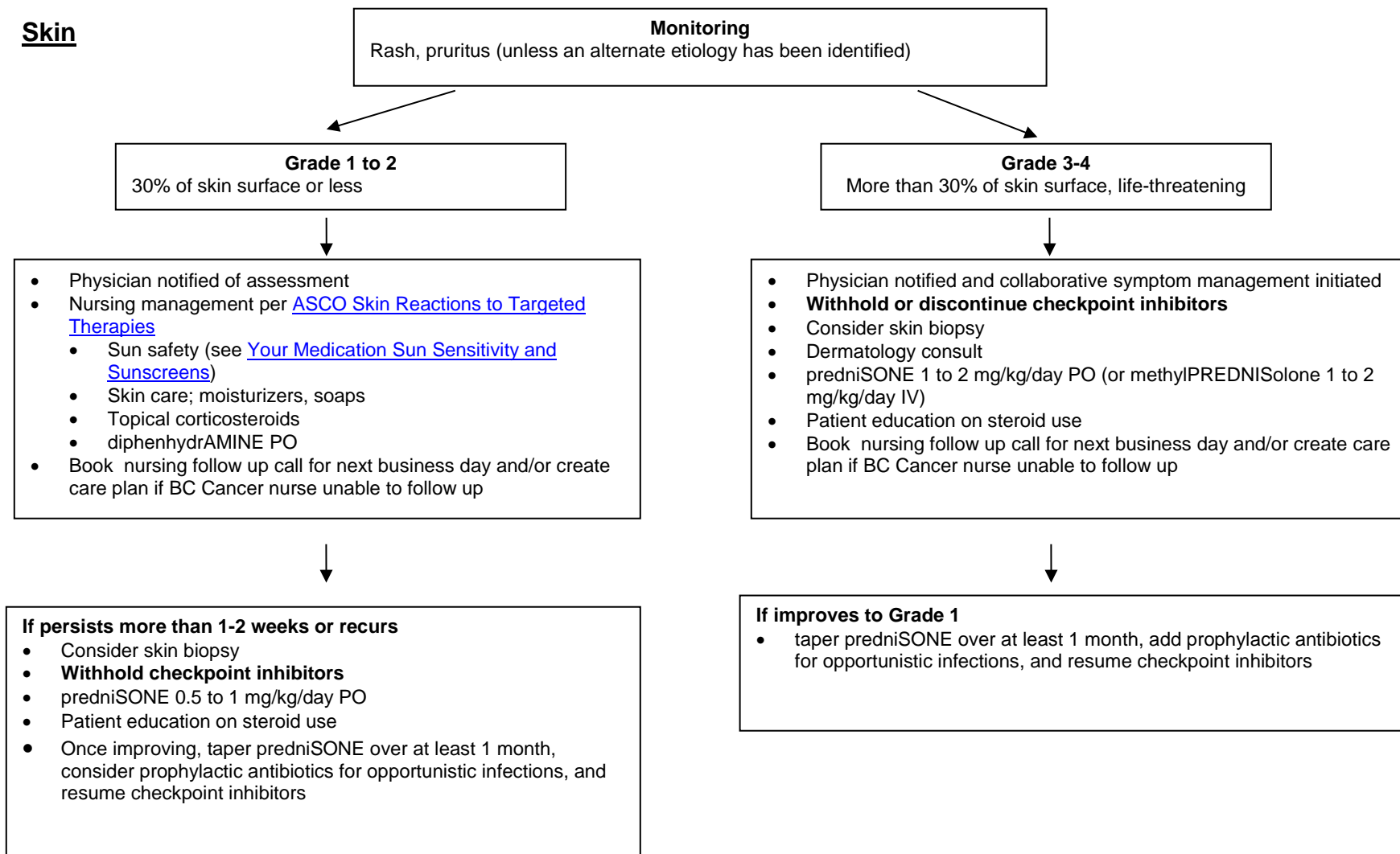
Endocrine

Monitoring

Persistent or unusual headaches, extreme tiredness, weight gain or loss, mood or behaviour changes (e.g., decreased libido, irritability, forgetfulness) dizziness or fainting, hair loss, feeling cold, constipation, voice gets deeper



Skin



Neurologic

