Clinical Tool

Rash/Inflammatory Dermatitis	
G1 (symptoms not affecting quality of life or controlled with topical regimen and/or oral antipruritic)	Continue ICIs; treat with topical emollients and/or mild-moderate potency topical corticosteroids; patients should avoid skin irritants and sun exposure
G2 (inflammatory reaction affecting quality of life and requiring intervention based on diagnosis)	Consider holding ICIs and monitor weekly for improvement; if not resolved, interrupt treatment until AE reverts to G1; consider initiating prednisone (or equivalent) at dosing 1 mg/kg, tapering over ≥ 4 weeks; additionally, treat with topical emollients, oral antihistamines, and medium- to high-potency topical corticosteroids
G3 (as grade 2 but refractory to indicated grade 2 interventions)	Hold ICIs and consult with dermatology to determine appropriateness of resuming; treat with topical emollients, oral antihistamines, and high-potency topical corticosteroids; initiate (methyl)prednisolone (or equivalent) 1-2 mg/kg, tapering over ≥ 4 weeks
G4 (severe/intolerable symptoms refractory to prior interventions)	Immediately hold ICIs and consult dermatology to determine appropriateness of resuming therapy upon resolution of skin toxicity and once corticosteroids are reduced to prednisone (or equivalent) ≤ 10 mg
Colitis	
G1 (increase of ≥ 3 stools/d over baseline; mild increase in ostomy output over baseline)	Continue ICIs; alternatively, hold ICIs temporarily and resume if toxicity does not exceed grade 1; monitor for dehydration and recommend modified diet; set up expedited phone contact with patient/caregiver; for prolonged cases, consider gastroenterology consult
G2 (increase of 4-6 stools per d over baseline; moderate increase in ostomy output over baseline)	Hold ICIs temporarily until symptoms abate to G1; concurrent immunosuppressant maintenance therapy (< 10 mg prednisone equivalent dose) may be offered only if clinically indicated in individual cases (when symptoms improve to grade 1 or less, taper corticosteroids over at least 4-6 weeks before resuming treatment, although resuming treatment while on low-dose corticosteroid may also be an option after an evaluation of the risks and benefits); assuming infection has been ruled out, consider including supportive care with loperamide; consult with gastroenterology; recommended EGD/colonoscopy, endoscopy evaluation to stratify patients for early treatment with infliximab based on the endoscopic findings and to determine the safety of resuming PD-1/PD-L1 therapy; consider stool inflammatory markers (lactoferrin and calprotectin) testing to differentiate functional vs inflammatory diarrhea, and use calprotectin to monitor treatment response
G3 (increase of ≥ 7 stools/d over baseline, incontinence, severe increase in ostomy output compared with baseline)	Consider permanently discontinuing CTLA-4 therapy if symptoms do not abate to G1 or less; administer corticosteroids (initial dose of 1-2 mg/kg/d prednisone or equivalent); consider hospitalization or outpatient facility for patients with dehydration or electrolyte imbalance; if symptoms persist ≥ 3-5 days or recur after improvement, consider administering IV corticosteroid or infliximab; consider colonoscopy in patients who are immunosuppressed and may be at risk for opportunistic infections such as CMV colitis and those who are infliximab- or corticosteroid-refractory

G4 (life-threatening complications; urgent intervention indicated)	Permanently discontinue ICIs; admit patient when clinically indicated (patients managed as outpatients should be very closely monitored); administer 1-2 mg/kg/d methylprednisolone or equivalent until symptoms abate to G1, and then start taper over 4-6 weeks; consider early infliximab 5-10 mg/kg, if symptoms refractory to corticosteroid within 2-3 days; consider lower GI endoscopy, if symptoms are refractory despite treatment or there is concern of new infections
Pneumonitis	
G1 (asymptomatic, confined to 1 lobe or < 25% of lung parenchyma, clinical or diagnostic observations only)	Hold ICIs with radiographic evidence of pneumonitis progression; consider 1 repeat CT in 3-4 weeks (in patients who have had baseline testing, consider offering a repeat spirometry/DLCO in 3-4 weeks); consider resuming ICIs with radiographic evidence of symptom improvement or resolution; monitor weekly with history and physical examination and pulse oximetry; consider offering CXR
G2 (symptomatic, involves more than 1 lobe or 25%-50% of lung parenchyma, medical intervention indicated)	Hold ICIs until symptoms abate to G1 or less; prednisone 1-2 mg/kg/d and taper by 5-10 mg/wk over 4-6 weeks; consider bronchoscopy with BAL and empirical antibiotics; monitor every 3 days with history and physical examination and pulse oximetry, consider CXR; no clinical improvement after 48-72 hours of prednisone, treat as G3
G3 (severe symptoms, hospitalization required, involves all lobes or > 50% of lung parenchyma, oxygen indicated); G4 (life-threatening respiratory compromise, urgent intervention indicated)	Permanently discontinue ICIs; empirical antibiotics; (methyl)prednisolone IV 1-2 mg/kg/d; no improvement after 48 hours, may add infliximab 5 mg/kg or mycophenolate mofetil IV 1 g twice a day or IVIG for 5 days or cyclophosphamide; taper corticosteroids over 4-6 weeks; pulmonary and infectious disease consults if necessary; bronchoscopy with BAL $\pm$ transbronchial biopsy; patients should be hospitalized for further management
Inflammatory Arthritis	
G1 (mild pain with inflammation, erythema, or joint swelling)	Continue ICIs; initiate analgesia with acetaminophen and/or NSAIDs
G2 (moderate pain associated with signs of inflammation, erythema, or joint swelling)	Hold ICIs and resume upon symptom control and on prednisone $\leq$ 10 mg/d; escalate analgesia and consider higher doses of NSAIDs as needed; if inadequately controlled, initiate prednisone or prednisolone 10-20 mg/d or equivalent for 4-6 weeks; if symptoms abate, slow taper according to response during the next 4-6 weeks (if no improvement after initial 4-6 weeks, treat as G3); if unable to lower corticosteroid dose to < 10 mg/d after 3 months, consider DMARD; consider intra-articular corticosteroid injections for large joints; refer to rheumatology
G3-4 (severe pain associated with signs of inflammation, erythema, or joint swelling; irreversible joint damage; disabling)	Hold ICIs temporarily and, if symptoms abate to G1 or less, consider resuming in consultation with rheumatology; initiate oral prednisone 0.5-1 mg/kg; if failure of improvement after 4 weeks or worsening in meantime, consider synthetic or biologic DMARD; test for viral hepatitis B, C, and latent/active TB test prior to DMARD treatment; refer to rheumatology

Venous Thromboembolism	
G1 (superficial thrombosis)	Continue ICIs; warm compress; clinical surveillance
G2 (uncomplicated DVT); G3 (uncomplicated PE, non-embolic cardiac mural thrombus)	Continue ICIs; management according to CHEST, ACC, and/or AHA guidelines; consider consult from cardiology; LMWH is suggested over VKA, dabigatran, rivaroxaban apixaban, or edoxaban for initial and long-term treatment; IV heparin is an acceptable alternative for initial use, and oral anticoagulants are acceptable for the long-term use
G4 (life-threatening complications such as PE, cerebrovascular event, arterial insufficiency; urgent intervention indicated)	Permanently discontinue ICIs; admit patient and manage according to CHEST, ACC, and/or AHA guidelines and with guidance from cardiology; respiratory and hemodynamic support; LMWH is suggested over VKA, dabigatran, rivaroxaban, apixaban, or edoxaban for initial and long-term treatment; IV heparin is an acceptable alternative for initial use, and oral anticoagulants are acceptable for the long-term use
Uveitis/Iritis	
G1 (asymptomatic)	Continue ICIs; refer to ophthalmology within 1 week; artificial tears
G2 (anterior uveitis)	Hold ICIs temporarily until after ophthalmology consult; urgent ophthalmology referral; topical corticosteroids, cycloplegic agents, systemic corticosteroids; consider resuming ICIs once off systemic corticosteroids, which are purely indicated for ocular adverse effects or once corticosteroids for other concurrent systemic irAEs are reduced to $\leq$ 10 mg; continued topical/ocular corticosteroids are permitted when resuming therapy to manage and minimize local toxicity; re-treat after return to G1 or less
G3 (posterior or panuveitis)	Permanently discontinue ICIs; urgent ophthalmology referral; systemic corticosteroids and intravitreal/periocular/topical corticosteroids
G4 (20/200 or worse)	Permanently discontinue ICIs; emergent ophthalmology referral; systemic corticosteroids (IV prednisone 1-2 mg/kg or methylprednisolone 0.8-1.6 mg/kg) and intravitreal/periocular/topical corticosteroids per ophthalmologist opinion
Autoimmune Hemolytic Anemia	
G1 (Hgb < LLN to 10.0 g/dL; < LLN to 6.2 mmol/L; < LLN to 100 g/L)	Continue ICIs with close clinical follow-up and laboratory evaluation
G2 (Hgb < 10.0 to 8.0 g/dL; < 6.2 to 4.9 mmol/L; < 100 to 80 g/L)	Hold ICIs and strongly consider permanent discontinuation; administer 0.5-1 mg/kg/d prednisone equivalents
G3 (Hgb < 8.0 g/dL; < 4.9 mmol/L; < 80 g/L; transfusion indicated)	Permanently discontinue ICIs; hematology consult; prednisone 1-2 mg/kg/d; consider RBC transfusion per existing guidelines; do not transfuse more than the minimum number of RBC units necessary to relieve symptoms of anemia or to return a patient to a safe Hgb range (7-8 g/dL in stable, noncardiac inpatients); offer patients supplementation with folic acid 1 mg once daily
G4 (life-threatening complications, urgent intervention indicated)	Permanently discontinue ICIs; admit patient; hematology consult; IV prednisone corticosteroids 1-2 mg/kg/d (if no improvement or if worsening while on corticosteroids or severe symptoms on presentation, initiate other immunosuppressive drugs, such as rituximab, IVIG, cyclosporine A, and mycophenolate mofetil); RBC transfusion per existing guidelines; discuss the patient symptoms with blood bank team prior to transfusions