

Table 7. Recommendations for steroid treatment

GENERAL PRINCIPLES	
Indications and timing	Therapeutic considerations
<p>First trial:</p> <ul style="list-style-type: none"> • Patient with chronic transfusions: Start ≥12 months old. Possible start at 15-18 months in children with failure to thrive. Earlier start (~9 months) if unable to provide safe venous access or safe transfusions <p>Second trial:</p> <ul style="list-style-type: none"> • In previous non-responders (1-2 years after first unsuccessful trial), recommended before planned HSCT <p>Additional trials: Not recommended</p>	<p>Before:</p> <ul style="list-style-type: none"> • Live viral vaccines (1st dose MMRV) given optimally ≥ 3 weeks before first steroid trial <p>Dosing:</p> <ul style="list-style-type: none"> • <u>Drug:</u> Oral prednisone or prednisolone (equal potency) • <u>Start dose:</u> 2mg/kg per day in children (max 80mg); 80mg per day in adults • <u>When to start:</u> one day or ~10-14 days after last transfusion • <u>Initial response assessment:</u> reticulocytes and Hb at day 10-14 <p>Tapering principles and stopping rule:</p> <ul style="list-style-type: none"> • Initial response: start taper after 2 weeks but not later than 4 weeks: reduce by 0.5mg/kg every ~2 weeks. • From 0.5mg/kg slow taper to arrive at maximum maintenance dose (0.3mg/kg per day or 0.6mg/kg alternate days) • Further passive/active taper to reach minimally effective dose • Non-response after 4 weeks: stop initial dose without unnecessarily extending therapy <p>Definitions of steroid response:</p> <ul style="list-style-type: none"> • <u>Initial response:</u> significant reticulocytosis (≥50-100x10⁹/L) and stable/increasing Hb (expected within 2-4 weeks). • <u>Long-term response:</u> maximum maintenance dose resulting in Hb ≥9g/dl without transfusions
CLINICAL SCENARIOS AND MANAGEMENT	
Loss of efficacy	<ul style="list-style-type: none"> • Acute Hb drop (e.g., viral illness): single RBC transfusion • Persistent Hb drop: consider increasing dose; if dose too high, declare non-response and switch to RBC transfusions
Estrogen-containing oral contraception	<ul style="list-style-type: none"> • May limit steroid response
Pregnancy, systemic disease (including cancer)	<ul style="list-style-type: none"> • Discontinue steroids and switch to RBC transfusions
Preadolescence/adolescence	<ul style="list-style-type: none"> • Consider steroid holiday (1-3 years) to improve growth
Immunosuppression, lymphopenia with risk of opportunistic infections	<ul style="list-style-type: none"> • Taper/discontinue steroids if clinically relevant infection • Avoid live vaccines during initial high dose steroids
Classic side effects: hypertension, diabetes, adrenal insufficiency, and others	<ul style="list-style-type: none"> • Monitoring toxicity with endocrinologist • Annual eye exam (cataracts?) • Annual bone densitometry scan (osteopenia?)
SUPPORTIVE CARE	
Vitamin D and calcium supplementation	<ul style="list-style-type: none"> • All patients on long-term steroids
Proton pump inhibitors or H2 antagonists	<ul style="list-style-type: none"> • During initial high dose of steroids or if symptomatic
Pneumocystis jirovecii pneumonia prophylaxis	<ul style="list-style-type: none"> • No consensus reached on antibiotic prophylaxis during initial high dose steroids (2mg/kg). Adapt to local standard

Abbreviations: HSCT, hematopoietic stem cell transplantation; Hb, hemoglobin; MMRV, mumps, measles, rubella, varicella; RBC, red blood cells