

MONITOR ADULT NON-TRANSFUSION-DEPENDENT PATIENTS WITH α- OR β-THALASSEMIA FROM THE TIME OF DIAGNOSIS

This assessment schedule is based on guidance from leading physicians* and recommendations from the Thalassaemia International Federation Guidelines for the Management of α -Thalassaemia and Non–Transfusion-Dependent β -Thalassaemia. Monitoring recommendations represent core health evaluations that allow healthcare providers to track disease progression over time in adult patients. The patient's physician will determine the actual frequency of necessary consultations and assessments based on disease course, clinical severity, and individual needs for medical care and routine follow-up. *The Monitoring Guidelines were written by a Steering Committee of leading physicians convened by Agios, and the physicians were compensated by Agios for their time.

RECOMMENDED SCHEDULE OF ROUTINE ASSESSMENTS AT EVERY VISIT^{1,2}

Medical history, including quality of life (which can be assessed as a change from previous visit)

Physical exam

Laboratory tests

Complete blood count⁺

Serum ferritin

Liver and kidney function test (CMP)[‡]

RECOMMENDED SCHEDULE OF MONITORING FOR LISTED COMPLICATIONS1-4						
	Baseline	Q6 Months	Q12 Months	Q24 Months		
Extramedullary hematopoiesis						
MRI C/T/L spine with contrast						
Splenomegaly (physical exam/ultrasound)	 As clinically indicated based on degree of anemia or symptoms 					
Iron overload						
Liver MRI for LIC [§]	•		●II			
Cardiac T2* MRI [¶]	•					
Cardiac function				_		
ECHO, including TRV			•			
Holter or equivalent	As clinically indicated					
Osteoporosis and bone disease						
DEXA scan	•			•#		
25-hydroxyvitamin D	•		•			
Endocrinopathy (Collect a baseline assessm	nent for every patient	. Perform exams annu	ually if there is evidence	of iron overload.)**		
Hypogonadism				-		
FSH, LH, testosterone, and estrogen	•		•			
Hypothyroidism						
Free thyroxine (FT4) and TSH	•		•			
Hypoparathyroidism						
PTH, calcium, phosphate, magnesium	٠		•			
Diabetes mellitus						
Fasting glucose or oral glucose tolerance test	•		•			

[†]Perform every 2 weeks if patient is on deferiprone.

[‡]Perform every month if patient is on chelation therapy. Perform a baseline liver MRI in patients with frequent transfusions or [¶]Perform cardiac MRI if LIC is ≥10 mg/g dry weight.

#Perform every 24 months or every 12 months with abnormality. **Exams may be referred out to an endocrinologist or performed independently.

serum ferritin ≥300 na/mL. Perform assessments every 12 months for patients on chelation therapy and every 24 months for patients who are not receiving iron chelation therapy.

C/T/L=cervical/thoracic/lumbar; CMP=comprehensive metabolic panel; DEXA=dual-energy X-ray absorptiometry; ECHO=echocardiogram; FSH=follicle-stimulating hormone;

LH=luteinizing hormone; LIC=liver iron concentration; MRI=magnetic resonance imaging; PTH=parathyroid hormone; TRV=tricuspid regurgitant jet velocity; TSH=thyroidstimulating hormone.

CONDITIONAL INTERVENTIONS BASED ON FINDINGS ^{1,2}					
Refer to a cardiologist	Refer to an endocrinologist or bone health specialist	Refer females to a reproductive endocrinologist			
 When ECHO or MRI indicates: Low ejection fraction Evidence of diastolic dysfunction Elevated TRV (ie, possible pulmonary hypertension) When monitoring indicates arrhythmias/abnormal Holter test results. 	 When monitoring indicates: Abnormal assessments (see previous page) 	To assess for fertility and need for reproductive assistance.			

CONSIDER ADDITIONAL POTENTIAL COMPLICATIONS AS CLINICALLY INDICATED ^{1,2,4}				
Complication and/or condition	Suggested interventions			
Hemolytic crisis	Counsel the patient on the risk of worsening anemia, which can commonly develop from infections resulting in fever. Hemolytic crisis presents with symptoms of worsening fatigue and signs of jaundice and/ or dark-colored urine and requires emergency management.			
Splenectomized individuals	Counsel patient on the risk of infections and course of action during emergency-related febrile events. Refer to the latest CDC guidelines and follow vaccination recommendations. Thrombocytosis following splenectomy may also contribute to thrombosis and vascular events.			
Thrombosis and vascular events	Counsel patient on classical symptoms of DVT (swelling, pain, warmth and tenderness to touch, and redness in the involved leg) and PE (dyspnea followed by chest pain, and cough).			
Liver fibrosis, cirrhosis, and HCC	Counsel patient on risk and consider obtaining a baseline AFP, ultrasound, and FibroScan in patients with chronic, severe iron overload or hepatitis.			
Choledocholithiasis	Counsel patient on right upper quadrant or epigastric pain, nausea, vomiting, and worsening jaundice. Perform laboratory tests for liver function and imaging (ultrasound) with clinical suspicion.			
HCV, HBV, and HIV	Screen annually (serology and, if positive, PCR) in patients who have received blood transfusions in the previous 12 months.			

ADDITIONAL ASSESSMENTS AT EVERY VISIT^{1,2}

Perform skin inspection at every visit.

ysical well-being	
eeling fatigue and/or tiredness	
eeling weak or washed out	
ack of energy	
nctional well-being	
bility to work	
bility to do usual activities	
bility to tolerate exercise (eg, walking up stairs)	
otional well-being	
Depression	
Anxiety and/or stress	

Additional Resources for Consideration:

Cooley's Anemia

Leg ulcers



References: 1. Amid A, Lal A, Coates TD, Fucharoen S, eds. *Cuidelines for the Management of α-Thalassaemia*. Thalassaemia International Federation; 2023. 2. Taher AT, Musallam KM, Cappellini MD. *Cuidelines for the Management of Non-Transfusion-Dependent β-Thalassaemia*. 3rd ed. Thalassaemia International Federation; 2023. 3. Musallam KM, Cappellini MD, Coates TD, et al. Alpha-thalassemia: a practical overview. *Blood Rev*. 2024;64:101165. doi:10.1016/j.blre.2023.101165 4. Taher AT, Musallam KM, Cappellini MD. β-Thalassemias. *N Engl J Med*. 2021;384(8):727-743. doi:10.1056/NEJMra2021838

AFP=alpha-fetoprotein; DVT=deep vein thrombosis; ECHO=echocardiogram; HBV=hepatitis B; HCC=hepatocellular carcinoma; HCV=hepatitis C; HIV=human immunodeficiency virus; MRI=magnetic resonance imaging; PCR=polymerase chain reaction; PE=pulmonary embolism; TRV=tricuspid regurgitant jet velocity.