

## MONITOR ADULT NON-TRANSFUSION-DEPENDENT PATIENTS WITH $\alpha-$ OR $\beta-$ 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 \alpha-Thalassaemia* and *Non-Transfusion-Dependent \beta-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 <sup>1,2</sup>
Medical history, including quality of life (which can be assessed as a change from previous visit)
Physical exam
Laboratory tests
Complete blood count <sup>†</sup>
Serum ferritin
Liver and kidney function test (CMP) <sup>‡</sup>

RECOMMENDED SC	HEDULE OF MONITOR	RING FOR LISTED CON	MPLICATIONS1-4	
	Baseline	Q6 Months	Q12 Months	Q24 Months
Extramedullary hematopoiesis				
MRI C/T/L spine with contrast	As clinically indicated based on degree of anemia or symptoms			
Splenomegaly (physical exam/ultrasound)				
Iron overload				
Liver MRI for LIC§	•		•II	
Cardiac T2* MRI <sup>¶</sup>	•			
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	ment for every patient	. Perform exams annu	ally if there is evidence	of iron overload.)**
Hypogonadism				
FSH, LH, testosterone, and estrogen	•		•	
Hypothyroidism				
Free thyroxine (FT4) and TSH	•		•	
Hypoparathyroidism				
PTH, calcium, phosphate, magnesium	•		•	
Diabetes mellitus				
Fasting glucose or oral glucose tolerance test	•		•	

<sup>&</sup>lt;sup>†</sup>Perform every 2 weeks if patient is on deferiprone.

<sup>&</sup>lt;sup>‡</sup>Perform every month if patient is on chelation therapy.

<sup>§</sup>Perform a baseline liver MRI in patients with frequent transfusions or serum ferritin ≥300 ng/mL.

 $<sup>\| \</sup>text{Perform}$  assessments every 12 months for patients on chelation therapy and every 24 months for patients who are not receiving iron chelation therapy.

 $<sup>\</sup>P$ Perform cardiac MRI if LIC is ≥10 mg/g dry weight.

<sup>#</sup>Perform every 24 months or every 12 months with abnormality.

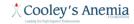
<sup>\*\*</sup>Exams may be referred out to an endocrinologist or performed independently.

CONDITIONAL INTERVENTIONS BASED ON FINDINGS <sup>1,2</sup>					
Refer to a cardiologist	Refer to an endocrinologist or bone health specialist	Refer females to a reproductive endocrinologist			
<ul> <li>When ECHO or MRI indicates:</li> <li>Low ejection fraction</li> <li>Evidence of diastolic dysfunction</li> <li>Elevated TRV (ie, possible pulmonary hypertension)</li> <li>When monitoring indicates arrhythmias/abnormal Holter test results.</li> </ul>	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.			
Leg ulcers	Perform skin inspection at every visit.			

ADDITIONAL ASSESSMENTS AT EVERY VISIT <sup>1,2</sup>				
Physical well-being				
Feeling fatigue and/or tiredness				
Feeling weak or washed out				
Lack of energy				
Functional well-being				
Ability to work				
Ability to do usual activities				
Ability to tolerate exercise (eg, walking up stairs)				
Emotional well-being				
Depression				
Anxiety and/or stress				

## **Additional Resources for Consideration:**







References: 1. Amid A, Lal A, Coates TD, Fucharoen S, eds. *Guidelines for the Management of α-Thalassaemia*. Thalassaemia International Federation; 2023. 2. Taher AT, Musallam KM, Cappellini MD. *Guidelines 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 immunode ficiency virus; MRI= magnetic resonance imaging; PCR= polymerase chain reaction; PE= pulmonary embolism; TRV= tricuspid regurgitant jet velocity.