ZYNTEGLO is a one-time gene therapy that expands treatment options for patients with TDT who meet these criteria:

- Diagnosed with transfusion-dependent β-thalassaemia
- NON-β/β: do not have a β/β genotype
- ≥12 years of age
- Appropriate for haematopoietic stem cell transplant
- No human leukocyte antigen-matched related donor available

Treatment relies on close collaboration with haematologists and transfusion medicine professionals at ZYNTEGLO Qualified Treatment Centres. ZYNTEGLO is manufactured and delivered through a highly coordinated and regulated process that involves close collaboration with the referring physician, ZYNTEGLO Qualified Treatment Centre, and bluebird bio.

ZYNTEGLO is intended for autologous use. No dose adjustment is required.

Interactions:

Anti retroviral medications and/or hydroxyurea should be stopped ≥1 month prior to mobilization and ≥7 days after Zynteglo infusion. Monitor for thrombocytopenia and managed with rescue treatment from back-up collection. Delayed neutrophil engraftment failure should be managed with rescue treatment from back-up collection. Delayed neutrophil engraftment failure as measured by neutrophil engraftment positivity. Engraftment failure as measured by neutrophil engraftment:

- Patients who experience neutrophil engraftment failure should be administered a reliable treatment as soon as possible, and ≥4 hours after thawing. Each bag should be confirmed with the Lot Information Sheet. Complete myeloablative conditioning must be administered before infusion of Zynteglo. Full myeloablative conditioning must be administered before infusion of Zynteglo. Prophylaxis for veno-occlusive liver disease should be considered. Patients treated with Zynteglo who do not experience neutrophil engraftment should be administered a reliable treatment as soon as possible, and ≥4 hours after thawing. Each bag should be confirmed with the Lot Information Sheet. Complete myeloablative conditioning must be administered before infusion of Zynteglo. Prophylaxis for veno-occlusive liver disease should be considered. Patients treated with Zynteglo who do not experience neutrophil engraftment should be administered a reliable treatment as soon as possible, and ≥4 hours after thawing. Each bag should be confirmed with the Lot Information Sheet. Complete myeloablative conditioning must be administered before infusion of Zynteglo. Prophylaxis for veno-occlusive liver disease should be considered.

Effects on the ability to drive or use machines. The effects of the individual agents and the myeloablative conditioning agent on the ability to drive or use machines must be considered.

Legal Category: Prescription Only Medicine

Marketing Authorisation Number: C12579/071071

Expiration date: 26 April 2020 Reference: ZYNTEGLO EU SmPC U2

For additional information on a Qualified Treatment Centre, please contact your local gene therapy representative at bluebird bio.
TREATMENT PATHWAY

Treatment with ZYNTEGLO is managed through a highly coordinated process

By using a patient’s own cells, ZYNTEGLO gives patients the potential to achieve transfusion independence without the need for a donor.1

CONSULTATION
- Haematologist or other referring physician identifies a potential and appropriate patient for treatment with ZYNTEGLO
- After contacting a Qualified Treatment Centre, the referring physician will schedule a consultation and, if appropriate, schedule an intake time for the patient

COLLECTION1
(Approximately 2 months prior to ZYNTEGLO infusion)
- Cell collection is required for treatment, since ZYNTEGLO uses the patient’s own haematopoietic stem cells
- Includes mobilisation followed by apheresis
- Mobilisation and apheresis may be repeated to ensure collection of sufficient stem cells for treatment

MANUFACTURING1
- Collected patient cells are shipped to licensed manufacturing facilities and genetically modified with copies of the βA-T87Q-globin-globin gene in order to manufacture ZYNTEGLO
- ZYNTEGLO is then cryopreserved and stored until ready to be shipped to a ZYNTEGLO Qualified Treatment Centre

CONDITIONING1
(At least 6 days before ZYNTEGLO infusion). In clinical trials, a 4-day regimen of busulfan was the only myeloablative conditioning tested with ZYNTEGLO
- Full myeloablative conditioning (a chemotherapy given over 4 days) must be administered before infusion of ZYNTEGLO

INFUSION AND MONITORING1
(Approximately 3 to 6 weeks in the hospital setting)
- ZYNTEGLO is administered to the patient via intravenous infusion at a Qualified Treatment Centre
- Per clinical judgement, patients will remain in hospital until they are ready to be discharged

REGISTRY1
(For 15 years following administration of ZYNTEGLO)
- The possibility of enrolling in the product registry for up to 15 years should be discussed with patients receiving ZYNTEGLO
- The registry collects data on safety and efficacy of treatment
- NOTE: Restarting iron chelation after ZYNTEGLO infusion may be necessary and should be based on clinical practice; phlebotomy can be used in lieu of iron chelation, when appropriate

PATHWAY KEY
- These steps take place outside of a Qualified Treatment Centre
- These steps take place at a Qualified Treatment Centre
- This step takes place at a licensed manufacturing facility

(zynteglo™ (betibeglogene autotemcel))