SmartPA Criteria Proposal

Drug/Drug Class:	Zynteglo Clinical Edit
First Implementation Date:	TBD
Proposed Date:	December 15, 2022
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☐Revision of Existing Criteria ☒New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Zynteglo® (betibeglogene autotemcel)

Why Issue Selected: Zynteglo® (betibeglogene autotemcel), approved by the FDA in August of 2022, is the first cell-based gene therapy indicated for the treatment of adult and pediatric patients with beta-thalassemia who require regular red blood cell (RBC) transfusions. Beta-thalassemia is an inherited blood disorder caused by pathogenic variants in the beta-globin gene leading to impaired production of beta-globin, an important component of hemoglobin. Transfusion-dependent thalassemia (TDT) is one of the more severe forms of thalassemia. Clinical manifestations include severe anemia, skeletal and growth deficits, and iron overload resulting in reduced life expectancy. Hematopoietic stem cell transplant (HSCT) offers a potential cure for TDT however it is associated with toxicities and transplant-related mortality, even for patients considered to be very good candidates. According to the FDA Cellular, Tissue, and Gene Therapies Advisory Committee only 25% of TDT patients have a matched sibling donor. Zynteglo, a one-time therapy, consists of an intravenous infusion containing a frozen suspension of genetically modified autologous cells, enriched for CD34+ cells. Zynteglo was shown to achieve 89% transfusion independence for a continuous period of ≥ 12 months.

Due to the high cost and specific approved indication, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Zynteglo.

Program-Specific Information:

Drug	Cost per unit (WAC)
ZYNTEGLO INFUSION BAG-CASSETTE	$2,800,000.00

Type of Criteria:

☐ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources:

☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Zynteglo® (betibeglogene autotemcel)
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Prescribed by or in consultation with a hematologist or other specialist in the treated disease state **AND**
- For participants aged < 5 years:
  - Participant weighs ≥ 6 kg **AND**
  - Documentation of prescriber attestation that participant is reasonably anticipated to be able to provide at least the minimum number of cells required to initiate manufacturing process **AND**
- Documented diagnosis of beta-thalassemia confirmed by genetic testing **AND**
- Participant considered to be transfusion-dependent defined by:
  - Documented history of ≥ 100 mL/kg/year of pRBCs in the past two years **OR**
  - For participants aged ≥ 12 years: ≥ 8 transfusions of pRBCs per year in the past two years **AND**
- Prescriber attestation that participant is clinically stable and eligible to undergo HSCT **AND**
- Participant must be evaluated for availability of matched donors for hematopoietic stem cell transplantation (HSCT)

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Participant is currently pregnant
- Participant has known and available HLA-matched family donor for HSCT
- History of HSCT
- Previous therapy with Zynteglo or any other gene therapy approved for TDT at any time

Required Documentation

Laboratory Results:	X	Progress Notes:	X
MedWatch Form:		Other:	X

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

3 months

References

- Zynteglo® (betibeglogene autotemcel) [package insert]. Somerville, MA: bluebird bio, Inc.; August 2022.
- IPD Analytics: New Drug Review: Zynteglo (betibeglogene autotemcel). Accessed 10 September 2022.
- Beaudoin F, Richardson M, et al. Betibeglogene Autotemcel for Beta Thalassemia: Effectiveness and Value; Final Evidence Report. Institute for Clinical and Economic Review. https://icer.org/wp-content/uploads/2021/11/ICER_Beta-Thalassemia_Final-Report_071922.pdf. Accessed 10 September 2022.
- Thalassemia International Federation. 2021 Guidelines for the Management of Transfusion Dependent Thalassemia (TDT). https://www.thalassemia.org/wp-content/uploads/2021/06/TIF-2021-Guidelines-for-Mgmt-of-TDT.pdf. Accessed 10 September 2022.
- Kasamon K. Treatment of patients with β-Thalassemia who require regular red blood cell (RBC) transfusions. U.S. Food & Drug Administration. June 10, 2022. https://www.fda.gov/media/159128/download. Accessed 10 September 2022.