Oxbryta

I. Generic Name:
- a. Voxelotor

II. Brand Name:
- a. Oxbryta

III. Medication Class:
- a. Hemoglobin S (HbS) Polymerization inhibitor : pathological polymerization of deoxygenated HbS is essential to the phenomena of vaso-occlusive crises (VOCs), where rope-like fibers elongate and align with other fibers resulting in distortion of erythrocytes into crescent or sickle shape

IV. FDA Approved Uses:
- a. Sickle cell disease (SCD): Treatment of sickle cell disease in adults and pediatric patients at least 12 years of age or older

V. Application of Criteria:
- a. The following criteria apply to Illinois Medicaid, Michigan Medicaid, and Meridian Choice (HIX)

VI. Criteria for Use:
- a. Member must be 12 years of age or older
- b. Prescribed by a hematologist/oncologist
- c. Current chart notes with plan of care recommending treatment with Oxbryta
- d. Clear documentation of severity and frequency of vaso-occlusive pain crises (VOCs)
- e. Documentation that the patient has had 2 or more episodes of VOCs requiring an emergent intervention (ED visit or admission) within the past 12 months
- f. Documentation of adequate trial and failure and compliance to appropriate maximum tolerated dose of Hydroxyurea
- g. Documentation of adequate trial and failure and compliance to appropriate maximum tolerated dose of Endari (L-Glutamine)
- ~~h. Documentation of adequate trial and failure and compliance to combination treatment with Hydroxyurea and Endari at maximum tolerated doses~~
- ~~i.~~h. Current CBC documenting Hemoglobin (Hgb) level greater than or equal to 5.5 but less than or equal to 10.5 g/dL
- ~~j.~~i. Current hepatic function lab/test results

~~k.~~j. Related lab work/test results such as neonatal genetic screening, high-performance liquid chromatography (HPLC), iso-electric focusing (IEF), direct DNA testing, or gel electrophoresis, supporting the diagnosis of one of the following genotypes:
   A. (Refer to Table 1): Please note that hemoglobin electrophoresis testing after transfusion of red cells can result in an incorrect diagnosis. In such cases, sickle cell diagnosis should utilize DNA testing or be postponed for at least four months after transfusion.
   B. Homozygous sickle cell (HbSS) disease
   C. Sickle-cell Beta+ thalassemia (SC-Beta+)
   D. Sickle-cell Beta0 thalassemia (SC-Beta0)
   E. Hemoglobin SC (HbSc) disease

VII. Required Medical Information:

a. Proper diagnosis and documentation of an FDA approved indication
b. Current progress notes detailing the diagnosis with plan of care
c. Documentation of dose, date ranges of therapy, and clinical outcomes for all medications previously tried and failed
d. Complete chart notes documenting disease history
e. Related lab work/test results
f. Charts showing compliance to previous therapy and office visits

VIII. Contraindications:

a. Hypersensitivity to Oxbryta or any component of the formulation

IX. Not Approved If:

a. Request is for Oxbryta as combination therapy used concurrently with either Endari (L-Glutamine) or Adakveo (crizanlizumab)
b. Patient shows non-compliance with previous treatment based on progress notes and/or pharmacy claims/fill history for required step therapies
c. Patient shows any contraindications to the use of Oxbryta as outlined in the FDA approved prescribing information
d. Request is for a non-FDA approved indication or dose

X. Length of Authorization:

a. Initial: 3 months
b. Continuation: up to 6 months

XI. Dosing:

a. Sickle cell disease (adults and children greater than or equal to 12 years of age used with or without Hydroxyurea):

A. Usual maximum dose: 1500mg once daily
B. Avoid strong or moderate CYP3A4 inducers, inhibitors, or fluconazole, if use is necessary adjust Oxbryta dose
   i. CYP3A4 strong or moderate inducer: increase dose to 2500mg once daily
   ii. CYP3A4 inhibitor or fluconazole: reduce dose to 1000mg once daily
C. Hepatic impairment (Child Pugh class C): reduce dose to 1000mg once daily
D. Renal impairment: no dose adjustment

XII. Criteria for Continuation of Therapy:

a. Initial therapy was tolerated
b. Demonstrated improvement in disease (reduction in the number of frequent VOCs; response in Hgb level from baseline of at least 1 g/dL)
c. Patient must be compliant with taking all medication as prescribed
d. Patient must not be experiencing any severe adverse reaction while taking the medication
e. Office visit every 3-6 months with verified compliance and improvement or stability on drug

XII. Criteria for Discontinuation of Therapy:

a. Patient is non-compliant with pharmacologic or non-pharmacologic therapy
b. No demonstrable clinically significant improvement after initiation and stabilization of drug therapy
c. Patient is non-responsive to FDA-approved usual maximum dosing

XIII. References:

1. Voxelotor: Facts and Comparisons. Wolters Kluwer Health. March 2020
2. Oxbryta (voxelotor) Prescribing Information. South San Francisco, CA: Global Blood Therapeutics Inc.; November 2019.
3. Yawn BP, Buchanan GR, Afenyi-annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. JAMA. 2014; 312(10):1033-48.
4. Ryan K, Bain BJ, Worthington D, et al. Significant haemoglobinopathies: guidelines for screening and diagnosis. Br J Haematol. 2010; 149(1):35-49.
5. Vichinsky E, Hoppe CC, Ataga KI, et al. A Phase 3 Randomized Trial of Voxelotor in Sickle Cell Disease. N Engl J Med. 2019;

6. Torres L, Conran N. Emerging pharmacotherapeutic approaches for the management of sickle cell disease. Expert Opin Pharmacother. 2019; 20(2):173-186.

Table 1. Hemoglobin patterns in common hemoglobinopathies

				Older children (>5 years, adolescents, and adults)				
Phenotype	**Genotype**	Neonatal Screen	Age = 6 weeks screening	**HbA (%)**	**HbA2 (%)**	**HbF (%)**	**HbS (%)**	**HbC (%)**
Normal	AA	FA	FA or AF	95 – 98	2 – 3	< 2	0	0
HbSS disease	**SS**	**FS**	**FS**	**0**	**< 3.5**	**5 - 15 (or higher)**	**85 – 95**	**0**
SC-Beta+	**SBeta+**	**FSA or FS**	**FSA**	**3 – 30**	**> 3.5**	**2- 10**	**65 – 90**	**0**
SC-Beta0	**SBeta0**	**FS**	**FS**	**0**	**> 3.5**	**2 - 15**	**80 – 92**	**0**
HbSc disease	**SC**	**FSC**	**FSC**	**0**	**< 3.5**	**1 – 5 (or higher)**	**45 – 50**	**45 – 50**
Beta thalassemia trait	A/(Beta or Beta+)	FA	FA	90 – 95	> 3.5	1 – 3	0	0
Sickle cell trait	AS	FAS	FAS	50 – 60	< 3.5	< 2	35 – 45 (lower if concomitant alpha thalassemia)	0

PHARMACY BENEFITS MANAGER

meridianRx

P.259 Approval Criteria

Oxbryta

Approved by: _____ Date: _____
CMO

Initial Approval:	
Revised:	
Annual Review:	
Next Review Date:	