Clinical Coverage Guideline

Easy Choice Health Plan

Missouri Care

‘Ohana Health Plan, a plan offered by WellCare Health Insurance of Arizona

OneCare (Care1st Health Plan Arizona, Inc.)

Staywell of Florida

WellCare (Arizona, Arkansas, Connecticut, Florida, Georgia, Illinois, Kentucky, Louisiana, Mississippi, Nebraska, New Jersey, New York, South Carolina, Tennessee, Texas)

WellCare Prescription Insurance

WellCare Texan Plus (Medicare – Dallas & Houston markets)

CAR-T Therapy

Policy Number: 338

Original Effective Date: 9/6/2018

Revised Date(s): N/A

APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

DISCLAIMER

The Clinical Coverage Guideline (CCG) is intended to supplement certain standard WellCare benefit plans and aid in administering benefits. Federal and state law, contract language, etc. take precedence over the CCG (e.g., Centers for Medicare and Medicaid Services [CMS] National Coverage Determinations [NCDs], Local Coverage Determinations [LCDs] or other published documents). The terms of a member’s particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this CCG. Additionally, CCGs relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. Providers are responsible for the treatment and recommendations provided to the member. The application of the CCG is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations, and any state-specific Medicaid mandates. Links are current at time of approval by the Medical Policy Committee (MPC) and are subject to change. Lines of business are also subject to change without notice and are noted on www.wellcare.com. Guidelines are also available on the site by selecting the Provider tab, then "Tools" and "Clinical Guidelines".

BACKGROUND

Acute Lymphocytic Leukemia - Acute lymphocytic leukemia (ALL) is a cancer that develops from early forms of lymphocytes in the bone marrow. In ALL bone marrow produces too many immature lymphocytes. ALL can originate from B cells or T cells These immature cells, or leukemia cells, are aggressive and can invade the blood quickly and easily spread to other parts of the body including lymph nodes, liver, spleen, central nervous system and the testicles (in males).1

Although ALL can develop at any age, incidence is highest in children between two and five years of age with 6 out of 10 cases of ALL being in children. ALL is the most common form of cancer in children and comprises approximately 30 percent of all childhood malignancies. It occurs more often in males than in females and is more prevalent in Whites and Hispanics than it in Black Americans. Children with certain genetic and immunodeficiency syndromes such as Down syndrome and neurofibromatosis are also at higher risk for developing the disease. The
American Cancer Society's estimates that 5,970 new cases of ALL were diagnosed in 2017. This number includes both adults and children, male and female.\textsuperscript{1,3}

Because of sequential collaborative standardized research protocols, survival rates have increased greatly since the 1980s and the National Cancer Institute (NCI) estimates that 85% of patients achieve a complete remission. Even though most cases of ALL are in children, the death rate from the disease is higher amongst adults with 4 out of 5 deaths being occurring in adults. About 1,440 deaths occur annually from ALL.\textsuperscript{1,2,3}

The presenting symptoms of ALL tend to be nonspecific and difficult to differentiate from common symptoms or other diseases. Symptoms typically result from shortages blood cells and can include fatigue, weakness, dizziness, shortness of breath, recurrent infections and bleeding or bruising easily. UpToDate reports that in a meta-analysis, over half the children with childhood leukemia had at least one of the following on presentation: palpable liver, palpable spleen, pallor, fever, or bruising.\textsuperscript{1,3}

If leukemia is suspected, the patient should be referred and evaluated by specialty cancer center. Evaluation should include medical history and physical examination followed by a complete blood count and peripheral smear. A bone marrow aspiration and biopsy are done for definitive diagnosis and to determine the leukemia phenotype as well as the presence or absence of cytogenetic abnormalities. The initial laboratory evaluation will also include assessment for any possible disease complications.\textsuperscript{2,3}

Standard treatment regimens for newly diagnosed ALL include 3 phases of chemotherapy (induction, consolidation, and maintenance). Treatment usually last 2 to 3 years and patients are treated with various combinations and doses of drugs. The intensity of treatment required for a favorable outcome varies widely from one patient to the next. Risk-based treatment selection is done to reserve the more intensive and toxic treatments for those patients with the least favorable clinical and biological features. ALL recurs in an estimated 10% to 20% of patients who achieve an initial remission. Treatment for patients who are refractory to primary treatment and those who relapse may include newer or more intensive chemotherapy or hematopoietic stem cell transplants.\textsuperscript{2}

**CAR-T Therapy** - Refractory disease is defined as those patients who fail to obtain a CR with induction therapy. Relapsed disease describes the reappearance of leukemia cells in the bone marrow or peripheral blood after the attainment of a complete remission. Adult and pediatric patients with relapsed or refractory B-cell ALL may be candidates for treatment with CD19-directed CAR T cell therapy.\textsuperscript{2,4}

CAR-T (chimeric antigen receptor T) cells are a form of genetically modified autologous immunotherapy that can be directed at B cell precursor ALL. The genetically engineered cells are manufactured by collecting lymphocytes from a patient or donor and modifying them through gene transfer techniques. Viral vectors are introduced that express cell receptors that are highly specific for tumor antigens. CAR T and TCR T cells are then infused back into a patient's body, where they direct a targeted immune response to cancerous tissue.\textsuperscript{2,4}

This guideline contains criteria for the two available CAR-T drugs, Kyrmiah\textsuperscript{®} and Yescarta\textsuperscript{®}.

**POSITION STATEMENT**

**Applicable To:**
- Medicaid – All Markets
- Medicare – All Markets

Please select criteria sets for Kyrmiah\textsuperscript{®} or Yescarta\textsuperscript{®}.

**Kyrmiah\textsuperscript{®}**

**Exclusions**

Kyrmiah\textsuperscript{®} is not considered medically necessary and not a covered benefit when any of the following apply:

1. Member has a diagnosis of any disorder other than Relapsed/Refractory B-cell Precursor Acute Lymphoblastic Leukemia (ALL); OR,
2. Member has Relapsed/Refractory Adult Diffuse Large B-Cell Lymphoma (DLBCL); OR,
3. Member has been previously treated with chimeric antigen receptor (CAR) T-cell therapy.

**Coverage**

**Treatment of Relapsed/Refractory B-cell Precursor**

*Kymria*® is considered medically necessary and a covered benefit for treatment of Relapsed/Refractory B-cell Precursor ALL when all of the following criteria are met:

**Initial Authorization:**
1. Pathology confirms the diagnosis of B-cell precursor acute lymphoblastic leukemia; **AND**,  
2. Member is 25 years old or younger; **AND**,  
3. Tumor demonstrates CD19 (+) tumor expression; **AND**,  
4. Disease is refractory or member has experienced 2 or more relapses on prior chemotherapy; **AND**,  
5. Member has no active infection or inflammatory disorders; **AND**,  
6. Actemra (tocilizumab) is available on site prior to infusion; **AND**,  
7. Treatment facility is enrolled and complies with Kymria® REMS requirements; **AND**,  
8. Member's ECOG Performance Status is rated as 2 or less or KPS is greater than or equal to 70.

**Treatment of Relapsed/Refractory DLBCL**

*Kymria*® is considered medically necessary for treatment of Relapsed/Refractory DLBCL when all of the following criteria are met:

**Initial Authorization:**
1. Pathology confirms the diagnosis of Diffuse large B-cell lymphoma (DLBCL), not otherwise specified; **AND**,  
2. Member is 18 years old or greater; **AND**,  
3. Tumor demonstrates CD19 (+) tumor expression; **AND**,  
4. Disease is refractory or member has experienced 2 or more relapses on prior chemotherapy; **AND**,  
5. Member has no active infection or inflammatory disorders; **AND**,  
6. Actemra (tocilizumab) is available on site prior to infusion; **AND**,  
7. Treatment facility is enrolled and complies with Kymria® REMS requirements; **AND**,  
8. Member's ECOG Performance Status is rated as 2 or less or KPS is greater than or equal to 70.

**Yescarta®**

**Exclusions**

Coverage for *Yescarta*® is not considered medically necessary and not a covered benefit when any of the following apply:
1. Member has a diagnosis of any disorder other than Relapsed/Refractory Adult Diffuse Large B-Cell Lymphoma (DLBCL) **OR**,  
2. Member has been previously treated with chimeric antigen receptor (CAR) T-cell therapy; **OR**,  
3. Member has been diagnosed with primary central nervous system lymphoma.

**Coverage**

*YESCARTA*® is considered medically necessary for treatment of Relapsed/Refractory DLBCL when all of the following criteria are met:

**Initial Authorization:**
1. Pathology confirms the diagnosis of Diffuse large B-cell lymphoma (DLBCL); **AND**,  
2. Member is age 18 years old or greater; **AND**,  
3. Tumor demonstrates CD19 (+) tumor expression; **AND**,  
4. Disease is refractory or member has experienced 2 or more relapses on prior chemotherapy; **AND**,
5. Member has no active infection or inflammatory disorders; **AND**, 
6. Actemra (tocilizumab) is available on site prior to infusion; **AND**, 
7. Treatment facility is a certified Yescarta healthcare facility; **AND**, 
8. Patient's ECOG Performance Status is rated as 2 or less.

**CODING**

**Covered CPT Codes** – None.

**Covered HCPCS Codes**

- **Q2040** Tisagenlecleucel, up to 250 Million CAR-Positive Viable T Cells, Including Leukapheresis And Dose Preparation Procedures, Per Infusion
- **Q2041** Axicabtagene Ciloleucel, up to 200 Million Autologous Anti-CD19 CAR T Cells, Including Leukapheresis and Dose Preparation Procedures, Per Infusion

**Covered ICD-10 Codes** – None.

Coding information is provided for informational purposes only. The inclusion or omission of a CPT, HCPCS, or ICD-10 code does not imply member coverage or provider reimbursement. Consult the member's benefits that are in place at time of service to determine coverage (or non-coverage) as well as applicable federal / state laws.

**REFERENCES**

5. Kymriah PI. Novartis Pharmaceuticals Corp., Morris Plains, NJ; May 2018
6. Yescarta PI. Kite Pharma, Inc., Santa Monica, CA 90404

**MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS**

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