Kansas City

An Independent Licensee of the Blue Cross and Blue Shield Association

Tibsovo (ivosidenib)

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Policy

Blue Cross and Blue Shield of Kansas City (Blue KC) will provide coverage for **Tibsovo (ivosidenib)** when it is determined to be medically necessary because the criteria shown below are met.

When Policy Topic is covered

Tibsovo (ivosidenib) may be considered **medically necessary** when all of the following criteria are met:

FDA-Approved Indications

1. **Acute Myeloid Leukemia (AML).** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patients have relapsed or refractory disease; AND
   B) The disease is isocitrate dehydrogenase-1 (IDH1) mutation positive

Tibsovo is indicated for the treatment of adult patients with relapsed or refractory AML with an IDH` mutation as detected by an FDA-approved test.[1] This mutation occurs in approximately 6% to 9% of patients with AML.

When Policy Topic is not covered

Tibsovo has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions and may be considered **investigational**. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Considerations

Tibsovo (ivosidenib) requires prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy statement was developed using available resources such as, but not limited to: Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, local medical policies of other health plans, Medicare (CMS), local providers.

Description of Procedure or Service

Tibsovo, an isocitrate dehydrogenase-1 (IDH1) inhibitor, is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test.[1] The recommended dose is 500 mg orally once daily (QD) with or without food until disease progression or unacceptable toxicity. Do not administer with a high-fat meal.

Disease Overview

AML is a heterogeneous hematologic malignancy hallmarked by clonal expansion of myeloid blasts in the peripheral blood, bone marrow, and/or other tissues.[2] Undifferentiated blast cells proliferate in bone marrow instead of maturing into normal blood cells. Among adults, it is the most common form of acute leukemia and accounts for the largest number of annual deaths from leukemias in the US. An estimated 21,380 individuals will be diagnosed with AML in 2017 and 10,590 are projected to die from the condition. The median age at diagnosis is 67 years. Diagnosis occurs at ≥ 65 years of age for 54% of patients with around one-third of patients diagnosed at ≥ 75 years of age. The incidence of AML increases as the population ages. Environmental factors such as prolonged exposure to petrochemicals, solvents such as benzene, pesticides, and ionizing radiation have been established to increase the risks for AML, as well as myelodysplastic syndrome (MDS).[2] The cure rates of AML have improved with this outcome noted in 35% to 40% of adult patients who are ≤ 60 years of age and 5% to 15% for patients who are > 60 years of age.[3] However, among patients who are older and unable to receive intensive chemotherapy the survival rates are dismal with a median survival of only 5 to 10 months.[3] Various gene mutations are present in adults with AML.[2,3] The incidence of IDH1 mutations have been reported in 6% to 9% of AML cases.[2]

Clinical Efficacy

The efficacy of Tibosovo was assessed in an open-label, single-arm, multicenter, clinical study involving 174 adult patients with relapsed or refractory AML that had an IDH1 mutation.[1,4] Patients were assigned to receive Tibosovo 500 mg QD. The median patient age was 67 years.[1,4] The most common types of IDH1 mutation were R132C and R132H.[1] Patients had received a median of two prior therapies (range, 1 to 6).[4] Approximately 70% and 64% of patients had received prior intensive chemotherapy and non-intensive chemotherapy, respectively.[4] Efficacy was based on the rate of complete remission (CR) plus complete remission with partial hematologic recovery (CRh), the duration of CR+CRh, and the rate of conversion from transfusion dependence to transfusion independence.[1] The median follow-up was 8.3 months (range, 0.2 to 39.5 months) and the median

treatment duration was 4.1 months (range, 0.1 to 39.5 months). CR (defined as < 5% blasts in the bone marrow, no evidence of disease and full recovery of peripheral blood counts [platelets > 100,000/microliter and absolute neutrophil counts > 1,000/microliter]) was achieved by 24.7% of patients (n = 43/174). Approximately 8% of patients (n = 14/174) obtained complete remission with partial hematological recovery (defined as < 5% of blasts in the bone marrow, no evidence of disease, and partial recovery of peripheral blood counts [platelets > 50,000/microliter and absolute neutrophil count > 500/microliter]). For patients who obtained CR or CRh, the median time first response was 2 months (range, 0.6 to 5.6 months). For the 110 patients who were dependent upon red blood cell (RBC) and/or platelet transfusions at baseline, 37.3% of patients (n = 41/110) became independent of RBC and platelet transfusions during any 56-day post-baseline period.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines on AML (version 1.2018), have not yet included Tibsovo.[2] Therapy for AML is usually divided into induction chemotherapy and postremission (e.g., consolidation) therapy and is based on age and several other factors (e.g., mutation status, performance status, concomitant disease).[2] Idhifa® (enasidenib tablets) is recommended, as well as indicated, for IDH2-mutated AML in adults.[2,5] Other oral agents may also be considered (e.g., Rydapt® [midostaurin capsules]).[2] Hematopoietic stem cell transplantation can be an option for selected patients. Refer to the guidelines regarding specific treatment modalities for the management of this complex condition.

Safety

Tibsovo has a Boxed Warning regarding differentiation syndrome.[1] Other more common adverse events (AEs) were fatigue (39%), leukocytosis (38%), arthralgia (36%), diarrhea (34%), dyspnea (33%), edema (32%), nausea (31%), mucositis (28%), electrocardiogram QT prolongation (26%), rash (26%), pyrexia (23%), cough (22%), and constipation (20%). Warnings and precautions include QTc interval prolongation and Guillain-Barre Syndrome.

Rationale

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Tibsovo (ivosidenib) while maintaining optimal therapeutic outcomes.

References

1. Tibsovo® tablets [prescribing information]. Cambridge, MA: Agios; July 2018.
2. The NCCN Acute Myeloid Leukemia Clinical Practice Guidelines in Oncology (Version 1.2018 – February 7, 2018). © 2017 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 24, 2018.
3. Dohner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. *N Engl J Med*. 2015;373(12):1136-1152.
4. DiNardo CD, Stein EM, De Botton S, et al. Durable remissions with ibosidenib in IDH1-mutated relapsed or refractory AML. *N Engl J Med*. 2018;378(25):2386-2398.
5. Idhifa® tablets [prescribing information]. Cambridge, MA and Summit, NJ: Agios and Celegene; August 2017.

Billing Coding/Physician Documentation Information

NA – Oral Tibsovo is a pharmacy benefit

Additional Policy Key Words

N/A

Policy Implementation/Update Information

12/2018 New policy titled Vibsovo (ivosidenib)

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.