Marqibo® (vincristine sulfate liposomal)
(Intravenous)

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Document Number: IC-0429

Last Review Date: 02/04/2020
Date of Origin: 02/04/2019
Dates Reviewed: 02/2019, 02/2020

I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Marqibo 5 mg/31 mL liposome injection: 8 vials every 28 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 40 billable units every 28 days

III. Initial Approval Criteria[1,2,3]

Coverage is provided in the following conditions:

- Patient is at least 18 years old; **AND**
- Patient does not have any pre-existing demyelinating conditions (e.g., Charcot-Marie-Tooth Syndrome); **AND**

Acute Lymphoblastic Leukemia (ALL) †

- Used as single agent therapy; **AND**
- Used for second or greater relapse, or refractory disease after 2 or more anti-leukemia therapies (e.g., regimens containing doxorubicin, daunorubicin, cyclophosphamide, cytarabine, vincristine, asparaginase, clofarabine, etc.); **AND**
- Patient's disease is Philadelphia chromosome-negative (Ph-)

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s)

IV. Renewal Criteria[1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: peripheral motor and sensory neuropathy, central and autonomic neuropathy, myelosuppression (e.g., neutropenia, thrombocytopenia, or anemia), tumor lysis syndrome, elevated liver function tests (ALT, AST, and bilirubin), etc.; **AND**
- Stabilization of disease and/or absence of progression of disease

V. Dosage/Administration

Indication	Dose
Acute Lymphocytic Leukemia (ALL)	Administer 2.25 mg/m^2 intravenously over 1 hour once every 7 days • NOT for intrathecal use *(intravenous use only)*

VI. Billing Code/Availability Information

HCPCS Code:

- J9371 – Injection, vincristine sulfate liposome, 1 mg; 1 mg = 1 billable unit

NDC:

- Marqibo 5 mg/31 mL liposome injection kit: 72893-0008-xx

VII. References

1. Marqibo [package insert]. Irvine, CA; Talon Therapeutics; September 2019. Accessed January 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for vincristine sulfate liposomal. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2020.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Acute Lymphoblastic Leukemia 2.2019. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2020.
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5. Kantarjian H, et al. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. N Engl J Med 2017; 376:836-847.
6. Kantarjian H, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. N Engl J Med 2016; 375:740-753.
7. Maude SL, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. N Engl J Med 2018; 378:439-448.
8. Berg SL, et al. Phase II Study of Nelarabine (compound 506U78) in Children and Young Adults With Refractory T-Cell Malignancies: A Report From the Children's Oncology Group. Journal of Clinical Oncology 2005 23:15, 3376-3382.
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10. Faderl S, et al. Augmented hyper-CVAD based on dose-intensified vincristine, dexamethasone, and asparaginase in adult acute lymphoblastic leukemia salvage therapy. Clin Lymphoma Myeloma Leuk. 2011 Feb;11(1):54-9.
11. Jeha S, et al. Phase II Study of Clofarabine in Pediatric Patients With Refractory or Relapsed Acute Lymphoblastic Leukemia. Journal of Clinical Oncology 2006 24:12, 1917-1923.
12. Hijiya N, Thomson B, Isakoff MS, et al. Phase 2 trial of clofarabine in combination with etoposide and cyclophosphamide in pediatric patients with refractory or relapsed acute lymphoblastic leukemia. Blood. 2011;118(23):6043-9.
13. Pigneux A, et al. Clofarabine Combinations in Adults with Refractory/Relapsed Acute Lymphoblastic Leukemia (ALL): A GRAALL Report. Blood. 2011;118:2586.
14. Weiss MA, et al. A single, high dose of idarubicin combined with cytarabine as induction therapy for adult patients with recurrent or refractory acute lymphoblastic leukemia. Cancer. 2002;95(3);581-587.
15. Martinelli G, et al. Complete Hematologic and Molecular Response in Adult Patients With Relapsed/Refractory Philadelphia Chromosome–Positive B-Precursor Acute Lymphoblastic Leukemia Following Treatment With Blinatumomab: Results From a Phase II, Single-Arm, Multicenter Study. Journal of Clinical Oncology 2017 35:16, 1795-1802.
16. Benjamini O, Dumlao TL, Kantarjian H, et al. Phase II trial of hyper CVAD and dasatinib in patients with relapsed Philadelphia chromosome positive acute lymphoblastic leukemia or blast phase chronic myeloid leukemia. Am J Hematol. 2014;89(3):282-7.
17. Magellan Health, Magellan Rx Management. Marqibo Clinical Literature Review Analysis. Last updated January 2020. Accessed January 2020.
18. CGS Administrators, Inc. Local Coverage Article: Billing and Coding: MARQIBO (VinCRIStine Sulfate Liposome) -J9371 (A57261). Updated on 9/18/2019 with effective date 9/26/2019. Accessed December 2019.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description

C83.50	Lymphoblastic (diffuse) lymphoma, unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma, lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma, intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma, lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma, lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma, intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma, spleen
C83.58	Lymphoblastic (diffuse) lymphoma, lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma, extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia, not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): 15	**NCD/LCD Document (s):** A57261
https://www.cms.gov/medicare-coverage-database/search/document-id-search-results.aspx?DocID=A57261&bc=gAAAAAAAAAAA&	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.

J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; TKI = tyrosine kinase inhibitor; HCT = hematopoietic cell transplantation; AE = adverse event

Acute Lymphoblastic Leukemia (ALL) – Adult patients

Philadelphia chromosome-negative (Ph-) relapsed or refractory disease (ALL-D 4 of 6)							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Vincristine sulfate liposome	2A	Yes (for Ph-negative ALL in second or greater relapse or disease that has progressed after 2 or more therapies)	Phase 2 (RALLY), multi-center, open-label	N/A	CR	Second or greater relapse or whose disease had progressed following two or more anti-leukemia therapies	• Vincristine sulfate liposome injection resulted in durable responses with n ORR of 35% and also allowed bridging to HCT in advanced ALL settings.
Blinatumomab	1 for relapsed/ refractory Philadelphia-chromosome negative B-ALL	Yes (Not restrictive of Ph-status)	Phase 3 (TOWER), randomized	Standard of care: • FLAG ± anthracycline-based regimen • HiDAC-based regimen • High-dose methotrexate-	OS	Relapsed or refractory disease	• Treatment with blinatumomab resulted in significantly longer OS than chemotherapy

				based regimen • Clofarabine-based regimen			
Inotuzumab ozogamicin	1 for relapsed/ refractory Philadelphia-chromosome negative B-ALL	Yes (Not restrictive of Ph-status)	Phase 3 (INO-VATE), randomized, open-label	Standard of care: • FLAG • HiDAC-based regimen	CR and OS	Relapsed or refractory CD22-positive Ph+ or Ph-negative ALL in patients due for first or second salvage treatment. Ph+ patients were required to have failed treatment with at least 1 TKI and standard chemotherapy	• Patients receiving inotuzumab ozogamicin versus standard care achieved higher response, MRD-negativity rates, and prolonged PFS and OS
Tisagenlecleucel	2A for relapsed/ refractory Philadelphia-chromosome negative B-ALL in patients < 26 years and with refractory	Yes for patients up to 25 years of age with B-cell ALL that is refractory or in second or later relapse (Not restrictive of Ph-status)	Phase 2 (ELIANA), single-cohort	N/A	ORR	Relapsed or refractory disease Excluded patients with previous anti-CD19 therapy	• Tisagenlecleucel provided durable remission with long-term persistence in pediatric and young adult patients with relapsed or refractory B-cell ALL, with transient high-grade toxic effects

	disease or ≥ 2 relapses						
Nelarabine	2A for (T-cell ALL)	Yes (for unresponsive or relapsed disease after at least 2 regimens)	Phase 2	N/A	ORR	Relapsed or refractory T-cell ALL or T-cell NHL	• Nelarabine is active as a single agent in recurrent T-cell leukemia in children and young adults, with a response rate more than 50% in first bone marrow relapse.
Nelarabine	2A for (T-cell ALL)	Yes (for unresponsive or relapsed disease after at least 2 regimens)	Phase 2, multi-center, open-label	N/A	CR	Relapsed or refractory T-cell ALL or T-cell lymphoblastic leukemia (LBL)	• Nelarabine demonstrated anti-tumor activity in relapsed or refractory T-cell ALL or T-cell LBL with an ORR of 41%.
Augmented Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone, pegaspargase; alternating with methotrexate and cytarabine)	2A	No	Phase 2	N/A	----------	Relapsed or refractory ALL	• Augmented hyper-CVAD may be a suitable treatment option for patients with relapsed or refractory ALL based on a CR of 47%.
Clofarabine	2A	Yes (for pediatric patients aged 1-21 years with relapsed or	Phase 2, open-label, multi-center	N/A	ORR	Relapsed or refractory ALL	• Clofarabine is active as a single agent in pediatric patients with multiple relapsed or refractory ALL with an ORR of 20%

		refractory ALL after at least 2 prior regimens)					
Clofarabine + cyclophosphamide + etoposide	2A		Phase 2	N/A	ORR	Relapsed or refractory ALL	• Clofarabine combination therapy demonstrated a complete response rate of 44% with sustained remission in relapsed or refractory patients
Clofarabine (plus chemotherapy)	2A		GRAALL report	N/A	---------	Relapsed or refractory ALL	• Combination of clofarabine with standard chemotherapy is clinically active in adult patients with relapsing or refractory ALL with a CR of 41%-50%.
Cytarabine + idarubicin	2A		Phase 2, multicenter	N/A	---------	Recurrent or refractory ALL	• Cytarabine and idarubicin demonstrated moderate activity with 38% of patients achieving a complete response
Philadelphia chromosome-positive (Ph+) relapsed or refractory disease after prior tyrosine kinase inhibitor therapy (ALL-D 3 of 6)							
Regimen	**NCCN Category**	**FDA Approved**	**Trial Design**	**Comparator**	**Primary End-Point**	**Line of Therapy**	**Conclusion**
Liposomal vincristine	2A (refractory to TKIs)	No	No clinical trial data for Philadelphia chromosome-positive disease.				
Blinatumomab	2A	Yes	Phase 2 (ALCANTA	N/A	CR or CRh	After imatinib and at least one	• Blinatumomab demonstrated anti-

	for relapsed/ refractory Philadelphia chromosome-positive TKI intolerant/ refractory B-ALL	(Not restrictive of Ph-status)	RA), open-label, single-arm			second-generation or later TKI	leukemia activity in high-risk patients with Ph+ ALL who had relapsed or were refractory to TKIs
Inotuzumab ozogamicin	2A for relapsed/ refractory Philadelphia chromosome-positive TKI intolerant/ refractory B-ALL	Yes (Not restrictive of Ph-status)	Phase 3 (INO-VATE), randomized, open-label	SOC • FLAG • HiDAC-based regimen	CR and OS	Relapsed or refractory CD22-positive Ph+ or Ph-negative ALL in patients due for first or second salvage treatment. Ph+ patients were required to have failed treatment with at least 1 TKI and standard chemotherapy	• Patients receiving inotuzumab ozogamicin versus standard care achieved higher response, MRD-negativity rates, and prolonged PFS and OS
Tisagenlecleucel	2A for relapsed/ refractory Philadelphia-chromosome positive B-ALL in patients < 26 years and with	Yes for patients up to 25 years of age with B-cell ALL that is refractory or in second or later relapse (Not restrictive of Ph-status)	Phase 2 (ELIANA), single-cohort	N/A	ORR	Relapsed or refractory disease	• Tisagenlecleucel provided durable remission with long-term persistence in pediatric and young adult patients with relapsed or refractory B-cell ALL, with transient high-grade toxic effects

	refractory disease or ≥ 2 relapses						
Clofarabine	2A	Yes (for pediatric patients aged 1-21 years with relapsed or refractory ALL after at least 2 prior regimens)	Phase 2, open-label, multi-center	N/A	ORR	Relapsed or refractory ALL	• Clofarabine is active as a single agent in pediatric patients with multiple relapsed or refractory ALL with an ORR of 20%
Hyper-CVAD+ dasatinib (if not used for induction)	2A	Yes	Phase 2	N/A	---------	Relapsed disease	• HyperCVAD regimen with dasatinib is effective in patients with relapsed Ph-positive ALL and CML