POLICY NUMBER UM ONC_1244	SUBJECT Promacta™ (eltrombopag)		DEPT/PROGRAM UM Dept.	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 07/10/13, 07/22/14, 12/18/15, 12/21/16, 11/08/17, 10/05/18, 07/10/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 07/10/13, 07/22/14, 12/18/15, 12/21/16, 11/08/17, 10/05/18, 07/10/19, 12/11/19	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1	NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Promacta (eltrombopag) usage in the treatment of cancer

II. DEFINITIONS

Promacta (eltrombopag): is an oral non-peptide thrombopoietin (TPO) receptor agonist that interacts with the transmembrane domain of the TPO receptor to increase platelet production. Specifically, eltrombopag binds to the TPO receptor and causes proliferation and differentiation of the megakaryocytes from bone marrow progenitor cells. Additionally, it may bind to a location that is distinct from where endogenous TPO binds to the receptor; in vitro data suggest that eltrombopag's effects may be additive to TPO.

Promacta (eltrombopag) is FDA approved for the following indications:

- Treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenia (ITP) who had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
- Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy.
- Treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.
- In combination with standard immunosuppressive therapy for the first-line treatment of adult and pediatric patients 2 years and older with severe aplastic anemia.

Promacta (eltrombopag) is available as 12.5 mg, 25 mg, 50 mg, and 75 mg oral tablets.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Promacta (eltrombopag) may be considered medically necessary when any of the following selection criteria is met:

1. **Chronic Idiopathic Thrombocytopenic Purpura (ITP)**
    a. The member has a diagnosis of relapsed/refractory chronic ITP of more than 6 months duration **AND**
    b. The member is at increased risk of bleeding and has a clear downward trend in platelet count after the last treatment **AND**
    c. Platelet count is less than 30,000/mm^3 (levels are obtained within the last 4 weeks) **AND**
    d. The member has insufficient response to prior splenectomy **OR**
    e. The member has insufficient response, intolerance, or contraindications to corticosteroids and immunoglobulins (IVIG) **AND**
    f. Insufficient response to prior therapy is defined as a platelet count < 50,000/mm^3.

Exclusion Criteria: Promacta (eltrombopag) is not considered medically necessary when any of the following selection criteria is met:

1. Promacta (eltrombopag) is not used to normalize platelet counts.
2. The member has insufficient response after 4 weeks of therapy OR with appropriate dosage adjustment. Response is defined as a platelet count between 50,000/mm^3 and 400,000/mm^3.
3. A platelet count > 400,000/mm^3, therapy should be discontinued.
4. Concurrent use with other TPO receptor agonist such as Nplate (romiplostim).
5. Member has thrombocytopenia due to myelodysplastic syndrome (MDS), chemotherapy, or any cause of thrombocytopenia other than chronic ITP.
6. Dosing exceeds single dose limit of Promacta (eltrombopag) 75 mg (for ITP).
7. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Promacta (eltrombopag) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**
    a. Chronic ITP (initial dose): 50 mg ORALLY once daily on an empty stomach for most adult and pediatric patients 6 years and older and at 25 mg once daily for pediatric patients aged 1 to 5 years. Dose reductions are needed for patients with hepatic impairment and some patients of East Asian ancestry. Adjust to maintain platelet count greater than or equal to 50 x 10 9/L. Do not exceed 75 mg per day.
    b. Chronic ITP (maintenance dose): after 2 weeks, increase dose by 25 mg daily to achieve and maintain a platelet count of 50,000 or more; if the platelet count fails to increase after 4 weeks at the maximum dose then discontinue Promacta (eltrombopag).
    c. Chronic Hepatitis C-associated Thrombocytopenia: Initiate at 25 mg once daily for all patients. Adjust to achieve target platelet count required to initiate antiviral therapy. Do not exceed a daily dose of 100 mg.

d. Severe Aplastic Anemia: Initiate at 50 mg once daily for most patients. Reduce initial dose in patients with hepatic impairment or patients of East Asian ancestry. Adjust to maintain platelet count greater than 50 x 10 9/L. Do not exceed 150 mg per day.

2. **Dosage Adjustments**

a. Platelet counts < 50,000/mm^3 after at least 2 weeks: Increase daily dose by 25 mg to MAX 75 mg/day for idiopathic thrombocytopenia patients and 100 mg/day for chronic hepatitis C patients; for patients taking 12.5 mg/day, increase the dose to 25 mg daily before increasing the dose amount by 25 mg.

b. Platelet counts 200,000/mm^3 to 400,000/mm^3: Decease the daily dose by 25 mg; subsequent dose adjustments should occur after 2 weeks.

c. Platelet counts > 400,000/mm^3: Stop eltrombopag, then increase the frequency of platelet monitoring to twice weekly; may restart at a dose reduced by 25 mg/day once the platelet count is less than 150,000/mm^3; for patients taking 25 mg/day, may restart at 12.5 mg/day.

d. Platelet counts > than 400,000/mm^3 after 2 weeks at the lowest dose: permanently discontinue eltrombopag .

e. Hepatic impairment, idiopathic thrombocytopenia: initial dose 25 mg/day; wait 3 weeks before increasing the dose.

f. Hepatic impairment, in idiopathic thrombocytopenia patients of East Asian ethnicity (i.e., Japanese, Chinese, Taiwanese, Korean); initial dose 12.5 mg/day; wait 3 weeks before increasing the dose.

g. East Asian ethnicity (i.e., Japanese, Chinese, Taiwanese, Korean), idiopathic thrombocytopenia: initial dose 25 mg/day.

h. Concomitant idiopathic thrombocytopenia medications should be adjusted to avoid excessive increases in platelet counts.

i. Discontinue if liver function test abnormalities increase to 3 or more times the ULN and are progressive, persistent for 4 weeks or more, accompanied by increased direct bilirubin, or are accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation; manufacturer recommends against reintroduction of eltrombopag; if the potential benefits outweigh the risk for hepatotoxicity, then reinitiate with caution and monitor serum liver tests weekly during the dose-adjustment phase; permanently discontinue eltrombopag if liver test abnormalities persist, worsen, or recur.

3. **Monitoring**

a. Black box warning: Hepatic decompensation may occur in patients with chronic hepatitis C concomitantly receiving interferon and ribavirin; increased risk with low albumin levels or Model for End-Stage Liver Disease (MELD) score of 10 or greater at baseline; monitoring recommended

b. Black box warning: Increased risk of severe and potentially life-threatening hepatotoxicity; monitoring recommended; discontinuation may be required

c. Progression of myelodysplastic syndrome to acute myeloid leukemia and increased risk of death has been reported.

d. A rise in platelet count may indicate efficacy.

e. Chronic ITP

i. Obtain CBC with differential, including platelet count, weekly during the dose adjustment phase until a stable platelet count (50,000/mm^3 or greater) has been established, then monthly thereafter during treatment.

f. Monitor ALT, AST, and bilirubin prior to initiation of treatment, every 2 weeks during dose adjustment phase, then monthly thereafter.

g. Monitor for signs and symptom of hepatic decompensation in patients with chronic hepatitis C with cirrhosis and low albumin levels (less than 3.5 g/dL) or Model for End-Stage Liver Disease (MELD) score of 10 or greater at baseline.

h. Perform baseline ocular examination at baseline, and monitor for signs and symptoms of cataracts during therapy

i. Pregnancy: Based on animal data, may cause fetal harm..

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Promacta prescribing information. SKF Triangle Park, NC. 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.

VIII. ADDENDUM

1. Preferred product(s) for Arizona Health Care Cost Containment System (AHCCCS), Arizona's Medicaid agency: Nplate/oral Promacta

For AHCCCS members: when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy for a list of NON-preferred products.