Appeals Support Guide

Resources and information to help your patients access PROMACTA® (eltrombopag)

Novartis cannot guarantee insurance coverage or reimbursement. Coverage or reimbursement may vary significantly by payer, plan, patient, and setting of care. It is the sole responsibility of the health care provider to select the proper codes and ensure the accuracy of all statements made in seeking coverage and reimbursement for an individual patient.

Important Safety Information for PROMACTA® (eltrombopag)

WARNING: RISK FOR HEPATIC DECOMPENSATION IN PATIENTS WITH CHRONIC HEPATITIS C

In patients with chronic hepatitis C, PROMACTA in combination with interferon and ribavirin may increase the risk of hepatic decompensation.

RISK OF HEPATOTOXICITY

PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity. Monitor hepatic function and discontinue dosing as recommended.

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

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This kit has been created to provide information and sample letters that can be used to help you communicate with health plans about prior authorization (PA) or appeal issues related to PROMACTA® (eltrombopag). Incomplete submissions may delay the appeal process.

This kit includes:

- Checklist suggestions to help ensure you have provided all needed information; however, please confirm the information required by the respective health plans
- Examples of information that will usually be required in an appeal letter

Jump directly to any section by clicking the tabs on the right, or by clicking within the table of contents below.

PROMACTA FOR PERSISTENT OR CHRONIC IMMUNE THROMBOCYTOPENIA

Indication and Important Safety Information

Indication for PROMACTA® (eltrombopag)

PROMACTA is indicated for the treatment of thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. PROMACTA should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.

Limitations of Use

PROMACTA is not indicated for the treatment of patients with myelodysplastic syndromes (MDS).

Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Important Safety Information for PROMACTA® (eltrombopag)

WARNING: RISK FOR HEPATIC DECOMPENSATION IN PATIENTS WITH CHRONIC HEPATITIS C

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CLINICAL CONSIDERATIONS FOR PROMACTA IN SECOND-LINE PERSISTENT OR CHRONIC ITP

Once-daily oral
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12.5mg, 25mg oral suspension

Adults

Efficacy

PERCENTAGE OF PATIENTS WHO ACHIEVED A PLATELET COUNT ≥50,000/mcL[1]

	PROMACTA® (eltrombopag)	Placebo
Day 8	44%	7%
Week 2	88%	7%

The primary end point—response at Day 43—was 70% for the 50-mg starting dose. Response rates for the 30-mg and 75-mg doses were 28% and 81%, respectively.

Study Design[1,2]

- TRA100773A was a phase 2, 12-week, double-blind, placebo-controlled trial of 117 adult patients with previously treated persistent or chronic ITP
- Response was defined as a shift from baseline platelet count <30,000/mcL to ≥50,000/mcL at any time during the study period up to 42 days of dosing with 30 mg, 50 mg, or 75 mg of eltrombopag
- Maximum response observed after 2 weeks of therapy

PERCENTAGE OF PATIENTS WITH REDUCTION IN BLEEDING EVENTS (DAY 15, ALL GRADES)[3]

	PROMACTA	Placebo
Baseline	73%	77%
Day 15	39%	68%

Study Design[3]

- The RAISE trial was a phase 3, 6-month, double-blind, randomized, placebo-controlled study of 197 patients with previously treated persistent or chronic ITP and baseline platelet counts <30,000/mcL
- The primary end point was the odds of response, defined as a platelet count ≥50,000/mcL and ≤400,000/mcL, during treatment

Safety

ADVERSE REACTIONS IN 3 PLACEBO-CONTROLLED STUDIES[2,a]

Adverse Reactions (≥3%)	PROMACTA (n=241)	Placebo (n=128)
Nausea	9%	3%
Diarrhea	9%	7%
Upper Respiratory Tract Infection	7%	6%
Vomiting	6%	<1%
Urinary Tract Infection[b]	5%	4%
Increased ALT	5%	3%
Myalgia	5%	2%
Oropharyngeal Pain	4%	3%
Increased AST	4%	2%
Pharyngitis	3%	2%
Back Pain	3%	2%
Influenza	3%	2%
Paresthesia	3%	2%
Rash	3%	2%

[a]All adverse events (AEs) reported were less than 10%. [b]Includes urinary tract infection, cystitis, urinary tract infection bacterial, and bacteriuria.
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

PERCENTAGE OF PATIENTS WITH REDUCTION IN BLEEDING EVENTS (YEAR 1)[4]

	PROMACTA
Baseline	57%
Year 1	16%

Study Design[2,4,5]

- The open-label, single-arm EXTEND trial enrolled patients who completed any prior clinical trial with PROMACTA to evaluate the safety and efficacy of long-term treatment of persistent or chronic ITP with PROMACTA. Attempts were made to decrease the dose or eliminate the need for any concomitant ITP medications
- Interim results showed that treatment with eltrombopag was effective in maintaining platelet counts up to 3 years. This study reviewed more than 8 years of continuous treatment
- Of 302 patients enrolled, 135 (45%) completed the study; 60% were treated at least 2 years and 35% at least 3 years. The "n" value represents the total number of patients, with median platelet counts ≥50,000/mcL by Week 2 and at least that throughout
- In the primary end point of the EXTEND study, no new or increased adverse reactions were identified at 6 years of therapy

EFFECT ON CONCOMITANT THERAPY, INCLUDING RESCUE THERAPY[5,c]

	PROMACTA
Permanently Stopped ≥1 Medications, Usually Corticosteroids	34% (n=34 of 101)
Maintained Levels ≥50,000/mcL for ≥25 Weeks Without a Change in Treatment	52% (n=133 of 257)
Maintained Levels ≥30,000/mcL for ≥25 Weeks Without a Change in Treatment	71% (n=183 of 257)

[c]Defined as the need for a new medication, increased dose of any concomitant medication, platelet transfusion, or splenectomy.[5]

ADVERSE REACTIONS IN THE LONG-TERM STUDY[2,d]

Adverse Reactions (≥3%)	PROMACTA (n=302)
Headache	10%
ALT Increased	5%
AST Increased	5%
Cataracts	5%
Fatigue	5%
Blood Bilirubin Increased	4%
Nausea	4%
Hyperbilirubinemia	3%
Diarrhea	3%

[d]All AEs reported were less than 10%.

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

CLINICAL CONSIDERATIONS FOR PROMACTA IN SECOND-LINE PERSISTENT OR CHRONIC ITP (continued)

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12.5mg, 25mg oral suspension

Pediatric

Efficacy

PERCENTAGE OF RESPONDERS IN 2 PIVOTAL TRIALS IN PEDIATRIC PATIENTS 1 YEAR AND OLDER[2]

	PROMACTA	Placebo
PETIT Study	62% (n=28 of 45)	32% (n=7 of 22)
PETIT 2 Study	41% (n=26 of 63)	3% (n=1 of 29)

Study Design[2,6]
- PETIT was a phase 2, 7-week, double-blind trial in children ≥1 year of age with relapsed or refractory persistent or chronic ITP followed by a 17- or 24-week open-label extension phase for patients from the PROMACTA and placebo arms of the double-blind phase, respectively
- Sixty-seven patients were randomized 2:1 to PROMACTA (n=45) or placebo (n=22) and permitted to use maintenance therapy, including (but not limited to) steroids, azathioprine, danazol, CsA, and mycophenolate mofetil. Platelet response was evaluated for 3 age cohorts: 1) 12 to 17 years, 2) 6 to 11 years, and 3) 1 to 5 years

PERCENTAGE OF PEDIATRIC PATIENTS REQUIRING RESCUE THERAPY IN 2 PIVOTAL TRIALS IN PEDIATRIC PATIENTS 1 YEAR AND OLDER[2]

	PROMACTA	Placebo
PETIT Study	13% (n=6 of 45)	50% (n=11 of 22)
PETIT 2 Study	19% (n=12 of 63)	24% (n=7 of 29)

Study Design[2,7]
- PETIT 2 was a phase 3, 13-week, double-blind trial to assess the efficacy and safety of PROMACTA in children ≥1 year of age with relapsed or refractory persistent or chronic ITP, followed by a 24-week open-label extension phase
- Ninety-two patients were randomized 2:1 to PROMACTA (n=63) or placebo (n=29) and permitted to use maintenance therapy, including steroids, IVIg, CsA, mycophenolate, azathioprine, and dapsone. Platelet response was evaluated for 3 age cohorts: 1) 12 to 17 years, 2) 6 to 11 years, and 3) 1 to 5 years

Safety

ADVERSE REACTIONS FROM 2 PLACEBO-CONTROLLED TRIALS IN PEDIATRIC PATIENTS 1 YEAR AND OLDER WITH PERSISTENT OR CHRONIC ITP[2]

Adverse Reactions (≥3%)	PROMACTA (n=107)	Placebo (n=50)
Upper Respiratory Tract Infection	17%	6%
Nasopharyngitis	12%	4%
Cough	9%	0%
Diarrhea	9%	2%
Pyrexia	9%	8%
Abdominal Pain	8%	4%
Oropharyngeal Pain	8%	2%
Toothache	6%	0%
ALT Increased[a]	6%	0%
Rash	5%	2%
AST Increased	4%	0%
Rhinorrhea	4%	0%

[a]Includes adverse reactions or laboratory abnormalities >3 x ULN.
CsA, cyclosporine A; TPO-RAs, thrombopoietin receptor agonists; ULN, upper limit of normal.

American Society of Hematology (ASH) 2019 guidelines for persistent or chronic ITP suggest treatment decisions should be individualized based on patient values and preferences.[8]

In adults with ITP ≥3 months who are corticosteroid dependent or have no response to corticosteroids, the ASH guidelines panel suggests:
- TPO-RAs for patients who place a high value on achieving a durable response*
- Rituximab for patients who want to avoid long-term medication and surgery
- Splenectomy should be delayed at least 1 year after diagnosis

*The 2019 ASH guidelines define durable response as platelet count ≥30 × 10^9/L and at least doubling of the baseline count at 6 months.

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

FILING A PA REQUEST

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All prior authorization (PA) forms should be completed and submitted to the plan by your office.

Benefits verifications performed by the customer service center of the patient's plan and specialty pharmacies can identify PA requirements, step therapies, and form requirements.

Please consult directly with the health plan regarding the relevant forms and information required.

Suggested Steps for Filing a PA for PROMACTA® (eltrombopag)

1. **COMPLETE** the clinical rationale, sign all documents, and submit the PA form and other required information to the health insurance plan.

2. **FOLLOW UP** regularly with the health insurance plan until a decision is made.

3. While the PA is under review, you might consider:
   - Telling the patient that the health insurance plan's review usually takes a few days
   - Providing samples so the patient can begin taking PROMACTA immediately
   - Contacting your Novartis Sales Rep to get access to a Sample bottle of 14 PROMACTA tablets for your patient, or providing the patient with a Day-1 PROMACTA Voucher (only eligible for patients new to PROMACTA)

Once the health insurance plan approves the PA, call the specialty pharmacy to ensure the prescription is filled and notify the patient.

4. **IF THE PA IS DENIED or a formulary exception request is required, the steps and sample letters on the following pages may help your patients receive therapy.**

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

SAMPLE LETTER FOR REQUESTING PRIOR AUTHORIZATION FOR PROMACTA

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

It is recommended that you also include a Letter of Medical Necessity (*see page 12*) and the patient's relevant medical records with the appeal letter.

Click here to download the Sample Letter for Requesting Prior Authorization for PROMACTA (ITP).

[Physician Practice letterhead]
[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

This letter is being submitted for the prior authorization of PROMACTA® (eltrombopag) for [insert patient's name]. The authorization requested is for the current date of [date] through the date of [future date].

[If patient is already taking PROMACTA, consider including information outlining the severity of persistent or chronic immune thrombocytopenia at the time of PROMACTA prescription. Medical records may need to be pulled from past dates to capture information relevant to PROMACTA treatment.

If you are addressing a step edit requirement, add a statement about why the required step therapies are not feasible for this patient and why you are requesting the step therapy requirement be eliminated.]

Listed below are my patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and other supporting information

[Insert information regarding the patient's diagnosis; history of persistent or chronic immune thrombocytopenia, including previous therapies and results if applicable; treatment plan; and other supporting information.]

The ordering physician is [physician name, NPI #]. The PA decision may be faxed to [fax #] or mailed to [physician business office address]. Please also send a copy of the coverage determination decision to [patient name].

Sincerely,

[Sign and print your name here]

Attachments: [Enclose supporting documentation]

APPEALING A PA DENIAL

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Suggestions for a letter appealing a PA denial

This type of letter may be helpful if a PA request for PROMACTA® (eltrombopag) has been denied. There may be multiple levels of appeal. Please refer to the plan's specific appeal guidelines and use the plan's PA form where applicable.

This letter comes from the **patient** and the **physician**. It is recommended that the letter be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (*see page 12*).

Checklist suggestions

General information

- ☐ Include the patient's information: name, date of birth, policy information
- ☐ Include prescriber information: specialty, contact details

History of persistent or chronic ITP treatment

- ☐ Provide evidence that the patient has an increased risk for bleeding related to persistent or chronic ITP
- ☐ List previous therapies, their durations, and reasons why the patient could not tolerate them, with supporting clinical evidence of the severity and duration of the reaction, if applicable
- ☐ Provide evidence that the patient had an insufficient response to previous therapies, including splenectomy, if applicable
- ☐ If other treatments are not appropriate for this patient, explain why they have not been tried previously
- ☐ Provide a clinical rationale for initiating PROMACTA

Laboratory values and other requirements

- ☐ Platelet count: <30,000/mcL
- ☐ After at least 1 week of PROMACTA therapy, the patient must respond with a platelet count of at least 50,000/mcL, but less than 200,000/mcL
- ☐ Attestation that prescriber will obtain baseline serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels and monitor these levels

Other supporting evidence

- ☐ ASH 2019 guidelines for persistent or chronic ITP

Other information required by the relevant health plan

SAMPLE LETTER FOR APPEALING PA DENIAL FOR PROMACTA

It is recommended that an appeal include a Letter of Medical Necessity (*see page 12*) and the patient's relevant medical records with the appeal letter.

Click here to download the Sample Letter for Appealing a PA Denial for PROMACTA (ITP).

[Physician Practice letterhead]
[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing to request that you reconsider your denial of coverage for PROMACTA® (eltrombopag) [dose and frequency] that I prescribed for my patient, [patient's full name]. Your reason for denial was [insert health insurance plan's reason for denying coverage].

I still believe PROMACTA is appropriate for my patient. Listed below are my patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and other supporting information

[Insert information regarding the patient's diagnosis; history of persistent or chronic immune thrombocytopenia, including previous therapies and results; treatment plan; and other supporting information.]

I hope you will agree PROMACTA is appropriate and medically necessary for [patient's name] and provide coverage for this treatment. Enclosed in support of this appeal are [insert description of supporting documents. Refer to page 8 of this guide for examples of documentation that may help support an appeal for PROMACTA coverage].

Thank you in advance for your consideration. Please contact me at [office phone number] for any additional information you may require regarding this request. I look forward to your timely approval of this appeal.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose denial letter and supporting documentation]

HELPING A PATIENT APPEAL A PA DENIAL

Once-daily oral PROMACTA® (eltrombopag) 12.5mg, 25mg, 50mg, 75mg tablets 12.5mg, 25mg oral suspension

A patient or caregiver may wish to appeal a PA denial for PROMACTA® (eltrombopag). There may be multiple levels of appeal. Please refer to the plan's specific appeal guidelines.

This letter comes from the **patient**. It is recommended that the letter be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (*see page 12*).

Checklist suggestions

- ☐ Talk to your patient and offer to help with writing the letter
- ☐ Provide a Letter of Medical Necessity (*see page 12*) and the patient's relevant medical records
- ☐ This sample letter can be modified for caregivers to write an appeal on behalf of the patient
- ☐ Other information required by the relevant health plan

SAMPLE LETTER FOR YOUR PATIENT TO APPEAL A PA DENIAL FOR PROMACTA

Once-daily oral
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12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Consider giving this sample letter to a patient who wants to file an appeal when the initial PA request has been denied.

Click here to download the Sample Letter for a Patient to Appeal a PA Denial for PROMACTA (ITP).

[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing to request that you reconsider your denial of coverage for PROMACTA® (eltrombopag) for [insert patient's name]. I understand the reasons for the denial are [include the reasons from the letter you received from the insurance company].

Listed below are the reasons why [my/his/her] doctor prescribed PROMACTA:

[Insert information the doctor gave you about the diagnosis; history of persistent or chronic immune thrombocytopenia, including previous therapies and results; the treatment plan; and other supporting information.]

I have also enclosed [insert descriptions of supporting documents the doctor gave you] outlining why [my/his/her] doctor believes [I/he/she] should be treated with PROMACTA.

Please approve this request so [I/he/she] can start treatment with PROMACTA as prescribed by [my/his/her] doctor.

[My/His/Her] doctor may be contacted at [insert the doctor's phone number] for any additional information you may require regarding this request. You can also contact me at [insert your phone number]. I look forward to your timely approval of this appeal.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose denial letter and supporting documentation]

WRITING A LETTER OF MEDICAL NECESSITY

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Suggestions for a Letter of Medical Necessity

Health insurance plans often request this letter to justify the need to prescribe PROMACTA® (eltrombopag). It is usually submitted to support a PA denial appeal or formulary exception request.

This letter comes from the **physician**.

Checklist suggestions

General information

- ☐ Include the patient's information: name, date of birth, policy information
- ☐ Include the prescribing physician's name and NPI #
- ☐ Include phone numbers for the prescribing physician and patient if the health plan requires any additional information to support the appeal
- ☐ Include specific billing codes where appropriate
- ☐ Clearly state the rationale for treatment with PROMACTA and why it is appropriate for your patient

Clinical information

- ☐ Support your recommendations with the following:
  - ☐ Patient history, diagnosis of persistent or chronic ITP, and risk of bleeding
  - ☐ Include copies of relevant medical records and laboratory results (payers may want to review the patient's platelet count and see if any infections, allergies, or comorbidities are present)

Other requirements

- ☐ Be sure to include all the listed documents with the letter when you send it to your patient's insurance provider
- ☐ Prescribing physician and patient should each sign the letter
- ☐ Explain why formulary-preferred agents are not appropriate
- ☐ Provide rationale for prescribing PROMACTA and clinical support for your recommendation. This can be:
  - ☐ Persistent or chronic ITP clinical trial data from the PROMACTA package insert
  - ☐ ASH 2019 guidelines for persistent or chronic ITP[6]
- ☐ To close the letter, summarize your recommendation and provide a phone number should any additional information be required

Other information required by the relevant health plan

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

SAMPLE LETTER OF MEDICAL NECESSITY

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12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Click here to download the Sample Letter of Medical Necessity for PROMACTA (ITP).

[Physician Practice letterhead]
[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing on behalf of my patient, [patient's name], to document the medical necessity of PROMACTA® (eltrombopag) for treatment of persistent or chronic immune thrombocytopenia and provide information about the patient's medical history and treatment.

Listed below are my patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and other supporting information

[Insert information regarding the patient's diagnosis; history of persistent or chronic immune thrombocytopenia, including previous therapies and results; treatment plan; and other supporting information.]

Enclosed in support of this matter are [insert description of supporting documents. Refer to page 12 of this guide for examples of documentation that may help support a Letter of Medical Necessity]. Please contact me at [insert office phone number] for any additional information you may need to ensure prompt approval of PROMACTA for my patient.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose supporting documentation]

FILING A FORMULARY EXCEPTION REQUEST

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Suggestions for a filing a formulary exception request

This type of letter may be used when PROMACTA® (eltrombopag) is not listed on a formulary or if it has a National Drug Code (NDC) block. While the plan may provide a form on its website that can be used to apply for an exception, the sample provided in this kit may be helpful regarding the type of information that is typically required.

This letter comes from the **patient** and is also signed by the **physician**. It is recommended that the letter be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (*see page 12*). Consider requesting a peer-to-peer review for the prescribing physician to discuss the necessity of providing a formulary exception.

Checklist suggestions

General information

- ☐ Include the patient's information: name, date of birth, policy information
- ☐ Include the prescribing physician's name and NPI #
- ☐ Include phone numbers for the prescribing physician and patient if the health plan requires any additional information to support the appeal

Clinical information

- ☐ Patient's medical records:
  - ☐ History, diagnosis, and list previous therapies (if applicable)
  - ☐ Include copies of relevant medical records and laboratory results

Other requirements

- ☐ Explain the main reasons supporting a formulary exemption for PROMACTA for this patient
- ☐ Provide rationale for prescribing PROMACTA and clinical support for your recommendation. This can be clinical trial data from the PROMACTA package insert
- ☐ If this is a second- or third-level appeal, include the letter of denial and medical notes in response to the denial
- ☐ Include a Letter of Medical Necessity (*see page 12*)

Other information required by the relevant health plan

SAMPLE FORMULARY EXCEPTION REQUEST LETTER

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12.5mg, 25mg oral suspension

Consider giving this sample letter to a patient when PROMACTA is not listed on a formulary or if it has a National Drug Code (NDC) block.

Click here to download the Sample Formulary Exception Request Letter for PROMACTA (ITP).

[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing to request an exception to your formulary for PROMACTA® (eltrombopag) [dose, frequency] that I prescribed for my patient, [patient's full name].

Listed below are the patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and supporting information

[Insert information regarding the patient's diagnosis; history of persistent or chronic immune thrombocytopenia, including previous therapies and results; treatment plan; and other supporting information.]

I hope you will agree PROMACTA is appropriate and medically necessary to treat my patient's condition and will support this request for a formulary exception. Enclosed in support of this request are [insert description of supporting documents. Refer to page 14 of this guide for examples of documentation that may help support a formulary exception request].

Thank you in advance for your consideration. Please contact me at [office phone number] for any additional information you may require regarding this matter. I look forward to your timely approval of this formulary exception request.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose supporting documentation]

PROMACTA FOR SEVERE APLASTIC ANEMIA

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Indications and Important Safety Information

Indications for PROMACTA® (eltrombopag)

PROMACTA is indicated 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 is indicated for the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.

Limitations of Use

PROMACTA is not indicated for the treatment of patients with myelodysplastic syndromes (MDS).

Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Important Safety Information for PROMACTA® (eltrombopag)

WARNING: RISK FOR HEPATIC DECOMPENSATION IN PATIENTS WITH CHRONIC HEPATITIS C

In patients with chronic hepatitis C, PROMACTA in combination with interferon and ribavirin may increase the risk of hepatic decompensation.

RISK OF HEPATOTOXICITY

PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity. Monitor hepatic function and discontinue dosing as recommended.

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

CLINICAL CONSIDERATIONS FOR PROMACTA IN SAA

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

In First Line: PROMACTA in Combination With Immunosuppressive Therapy From Day 1

Efficacy

RESPONSE RATES AT 6 MONTHS (COHORT 3 + EXTENSION COHORT)[2,9]

	PROMACTA® (eltrombopag)	Historical Cohort
Complete Hematologic Response[a]	44% (n=38 of 87; 95% CI, 33-55)	17% (n=102)
Overall Response[b]	79% (n=69 of 87; 95% CI, 69-87)	66% (n=102)

[a]Complete response was defined as hematologic parameters meeting all 3 of the following values on 2 consecutive serial blood count measurements at least 1 week apart: ANC >1000/mcL, platelet count >100,000/mcL, and Hb count >10 g/dL.[2]
[b]Overall response rate was defined as the number of partial responses (blood counts no longer meeting the standard criteria for severe pancytopenia in SAA) plus complete responses.[2]

DURATION OF RESPONSE[2,10]

	PROMACTA
Median Duration of Response	24.3 months
Overall Survival at 2 Years	96.7% (n=89 of 92)

Study Design[2]
- Single-arm, open-label, sequential cohort trial in patients 2 years of age or older (N=153)
- All cohorts received h-ATG Days 1 to 4 and CsA for 6 to 24 months
- Cohort 3 + extension cohort patients received PROMACTA Day 1 to 6 months (n=92). Of these patients, 5 were not included in analyses of hematologic response at Month 6, as they had neither reached the 6-month assessment nor withdrawn earlier
- 66 patients were ≥17 years of age; 26 patients were 2 to 16 years of age

Safety

ADVERSE REACTIONS IN FIRST-LINE SAA (COHORT 3 + EXTENSION COHORT)[2]

Adverse Reactions (≥5%)	PROMACTA (n=92)
ALT Increased	29%
AST Increased	17%
Blood Bilirubin Increased	17%
Rash	8%
Skin Discoloration Including Hyperpigmentation	5%

COMPARISON OF ADVERSE REACTIONS IN PEDIATRIC VS ADULT PATIENTS (COHORT 3 + EXTENSION COHORT)[2]

Adverse Reactions (≥10%)	PROMACTA Pediatric: Aged 2 to 16 (n=26)	PROMACTA Adult: Aged 17 and Older (n=66)
ALT Increased	23%	32%
AST Increased	12%	20%
Blood Bilirubin Increased	12%	20%
Rash[c]	12%	6%

[c]Rash and upper respiratory tract infection were the only serious adverse drug reactions experienced by ≥10% of pediatric patients.
ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CsA, cyclosporine A; h-ATG, horse antithymocyte globulin; Hb, hemoglobin; IST, immunosuppressive therapy; SAA, severe aplastic anemia.

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

CLINICAL CONSIDERATIONS FOR PROMACTA IN SAA (continued)

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Relapsed/Refractory: PROMACTA Monotherapy After an Insufficient Response to Immunosuppressive Therapy

Efficacy

HEMATOPOIESIS MAINTAINED AFTER DISCONTINUATION[2,11]

	PROMACTA
Achieved Hematologic Response (Initial Phase)	40% (n=17 of 43)
Responders Who Achieved a Multilineage Response (Extension Phase)[a,b]	57% (n=8 of 14)
Achieved a Trilineage Response (Extension Phase)	50% (n=4 of 8)

[a]Three of the 17 eligible patients did not enter the extension phase.[11]
[b]A multilineage response is defined as an increase in production in ≥2 of the following hematologic markers: platelets, white blood cells, and red blood cells.[11,12]

All 4 patients who achieved a trilineage response were able to maintain this response after discontinuing PROMACTA[2,11]

RESPONSE LED TO TRANSFUSION INDEPENDENCE[2]

	PROMACTA
Median Red Blood Cell Transfusion-Free Period	208 days (range, 15-1082 days)
Median Platelet Transfusion-Free Period	200 days (range, 8-1096 days)

Study Design

- Prospective, open-label, nonrandomized, single-arm, dose-modification, investigator-sponsored study conducted by the National Institutes of Health to assess the safety and efficacy of PROMACTA in patients with SAA and IST-refractory thrombocytopenia (N=43)[2,11,12]
- Primary end point was hematologic response at Week 12 or Week 16, defined by meeting 1 or more of the following criteria: platelet count increase to 20,000/mcL above baseline or stable platelet counts with transfusion independence for a minimum of 8 weeks; Hb count increase >1.5 g/dL for patients with pretreatment Hb count <9 g/dL or a reduction in ≥4 units of red blood cell transfusions for 8 consecutive weeks; ANC increase of 100% or >500/mcL[2,12]
- Patients who responded in the initial phase were eligible to continue therapy in an extension phase[2,11]
- Patients had a median age of 45 years and either had an insufficient response to at least 1 prior course of IST or were relapsed/refractory and had responded to at least 1 prior cycle of IST, but were refractory to the most recent course of IST[2,12]

Safety

ADVERSE REACTIONS IN RELAPSED/REFRACTORY SAA[2]

Adverse Reactions (≥10%)	PROMACTA (n=43)
Nausea	33%
Fatigue	28%
Cough	23%
Diarrhea	21%
Headache	21%
Pain in Extremity	19%
Pyrexia	14%

Adverse Reactions (≥10%)	PROMACTA (n=43)
Dizziness	14%
Oropharyngeal Pain	14%
Abdominal Pain	12%
Muscle Spasms	12%
Transaminases Increased	12%
Arthralgia	12%
Rhinorrhea	12%

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

FILING A PA REQUEST

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Your office is responsible for completing and submitting all forms required by the relevant health plan.

Benefits verifications performed by the customer service center of the patient's plan and specialty pharmacies can identify prior authorization (PA) requirements, step therapies, and form requirements.

Please consult directly with the health plan regarding the relevant forms and information required.

Suggested Steps for Filing a PA for PROMACTA® (eltrombopag)

1. **COMPLETE** the clinical rationale, sign all documents, and submit the PA form and other required information to the health insurance plan.

   For patients who are going to receive PROMACTA first line, in combination with inpatient-administered IST, it is important to submit the PA request in a timely manner to ensure continuity of care in the outpatient setting.

2. **FOLLOW UP** regularly with the health insurance plan until a decision is made.

3. While the PA is under review, you might consider:

   - Telling the patient that the health insurance plan's review usually takes a few days
   - Providing samples so the patient can begin taking PROMACTA immediately
   - Contacting your Novartis Sales Rep to get access to a Sample bottle of 14 PROMACTA tablets for your patient, or providing patient with a Day-1 PROMACTA Voucher (only eligible for patients new to PROMACTA)

Once the health insurance plan approves the PA, call the specialty pharmacy to ensure the prescription is filled and notify the patient.

4. **IF THE PA IS DENIED or a formulary exception request is required, the steps and sample letters on the following pages may help your patients receive therapy.**

SAMPLE LETTER FOR REQUESTING PRIOR AUTHORIZATION FOR PROMACTA

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Consider including a Letter of Medical Necessity *(see page 25)* and the patient's relevant medical records with the appeal letter.

Click here to download the Sample Letter for Requesting Prior Authorization for PROMACTA (SAA).

[Physician Practice letterhead]
[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

This letter is being submitted for the prior authorization of PROMACTA® (eltrombopag) for [insert patient's name]. The authorization requested is for the current date of [date] through the date of [future date].

[If patient is already taking PROMACTA or has discontinued PROMACTA after achieving a multilineage response, consider including information outlining the severity of severe aplastic anemia at the time of PROMACTA prescription. Medical records may need to be pulled from past dates to capture information relevant to PROMACTA treatment.

If you are addressing a step edit requirement, add a statement about why the required step therapies are not feasible for this patient and why you are requesting the step therapy requirement be eliminated.]

Listed below are my patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and other supporting information

[Insert information regarding the patient's diagnosis; history of SAA, including previous therapies and results if applicable; treatment plan; and other supporting information.]

The ordering physician is [physician name, NPI #]. The PA decision may be faxed to [fax #] or mailed to [physician business office address]. Please also send a copy of the coverage determination decision to [patient name].

Sincerely,

[Sign and print your name here]

Attachments: [Enclose supporting documentation]

APPEALING A PA DENIAL

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Suggestions for a letter appealing a PA denial

This type of letter may be helpful if a PA request for PROMACTA® (eltrombopag) has been denied. There may be multiple levels of appeal. Please refer to the plan's specific appeal guidelines and use the plan's PA form where applicable.

This letter comes from the **patient** and the **physician**. It is recommended that the letter be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (*see page 25*).

Checklist suggestions

General information

- ☐ Include the patient's information: name, date of birth, policy information
- ☐ Include prescriber information: specialty, contact details

History of SAA treatment

- ☐ Provide evidence that the patient has pancytopenia (if patient is treatment naive) or has demonstrated an incomplete response to immunosuppressive therapy
- ☐ List previous therapies, their durations, and reasons why the patient could not tolerate them, with supporting clinical evidence of the severity and duration of the reaction if applicable
- ☐ If other treatments are not appropriate for this patient, explain why they have not been tried previously
- ☐ Provide a clinical rationale for initiating PROMACTA

Laboratory values and other requirements

- ☐ Bone marrow cellularity
- ☐ Peripheral blood count
  - ☐ Neutrophils
  - ☐ Platelets
  - ☐ Reticulocytes
- ☐ Note if patient is transfusion dependent
- ☐ Attestation that prescriber will obtain baseline serum alanine aminotransferase, aspartate aminotransferase, and bilirubin levels and monitor these levels
- ☐ If patient is receiving PROMACTA first line, provide a treatment plan that includes inpatient initiation of PROMACTA with IST, followed by outpatient treatment continuation

Other information required by the relevant health plan

SAMPLE LETTER FOR APPEALING A PA DENIAL FOR PROMACTA

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Consider including a Letter of Medical Necessity and the patient's relevant medical records *(see page 25)* with the appeal letter.

Click here to download the Sample Letter for Appealing a PA Denial for PROMACTA (SAA).

[Physician Practice letterhead]
[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing to request that you reconsider your denial of coverage for PROMACTA® (eltrombopag) [dose and frequency] that I prescribed for my patient, [patient's full name]. Your reason for denial was [insert health insurance plan's reason for denying coverage].

I still believe PROMACTA is appropriate for my patient. Listed below are my patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and other supporting information

[Insert information regarding the patient's diagnosis; history of severe aplastic anemia including previous therapies and results; treatment plan; and other supporting information.]

I hope you will agree PROMACTA is appropriate and medically necessary for [patient's name] and provide coverage for this treatment. Enclosed in support of this appeal are [insert description of supporting documents. Refer to page 21 of this guide for examples of documentation that may help support an appeal for PROMACTA coverage].

Thank you in advance for your consideration. Please contact me at [office phone number] for any additional information you may require regarding this request. I look forward to your timely approval of this appeal.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose denial letter and supporting documentation]

HELPING A PATIENT APPEAL A PA DENIAL

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

A patient or caregiver may wish to appeal a PA denial for PROMACTA® (eltrombopag). There may be multiple levels of appeal. Please refer to the plan's specific appeal guidelines.

This letter comes from the **patient**. It is recommended that the letter be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (*see page 25*).

Checklist suggestions

- ☐ Talk to your patient and offer to help with writing the letter
- ☐ Provide a Letter of Medical Necessity (*see page 25*) and the patient's relevant medical records
- ☐ This sample letter can be modified for caregivers to write an appeal on behalf of the patient
- ☐ Other information required by the relevant health plan

SAMPLE LETTER FOR YOUR PATIENT TO APPEAL A PA DENIAL FOR PROMACTA

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Consider giving this sample letter to a patient who wants to file an appeal when the initial PA request has been denied.

Click here to download the Sample Letter for a Patient to Appeal a PA Denial for PROMACTA (SAA).

[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing to request that you reconsider your denial of coverage for PROMACTA® (eltrombopag) for [insert patient's name]. I understand the reasons for the denial are [include the reasons from the letter you received from the insurance company].

Listed below are the reasons why [my/his/her] doctor prescribed PROMACTA:

[Insert information the doctor gave you about the diagnosis; history of severe aplastic anemia, including previous therapies and results; the treatment plan; and other supporting information.]

I have also enclosed [insert descriptions of supporting documents the doctor gave you] outlining why [my/his/her] doctor believes [I/he/she] should be treated with PROMACTA.

Please approve this request so [I/he/she] can start treatment with PROMACTA as prescribed by [my/his/her] doctor.

[My/His/Her] doctor may be contacted at [insert the doctor's phone number] for any additional information you may require regarding this request. You can also contact me at [insert your phone number]. I look forward to your timely approval of this appeal.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose denial letter and supporting documentation]

WRITING A LETTER OF MEDICAL NECESSITY

Once-daily oral PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Suggestions for a Letter of Medical Necessity

Health insurance plans often request this letter to justify the need to prescribe PROMACTA® (eltrombopag). It is usually submitted to support a PA denial appeal or formulary exception request.

This letter comes from the **physician**.

Checklist suggestions

General information

- ☐ Include the patient's information: name, date of birth, policy information
- ☐ Include the prescribing physician's name and NPI #
- ☐ Include phone numbers for the prescribing physician and patient if the health plan requires any additional information to support the appeal
- ☐ Include specific billing codes where appropriate
- ☐ Clearly state the rationale for treatment with PROMACTA and why it is appropriate for your patient

Clinical information

- ☐ Support your recommendations with the following:
  - ☐ Patient history, diagnosis of SAA, transfusion dependence, and list previous therapies (if applicable)
  - ☐ Include copies of relevant medical records and laboratory results (payers may want to review the patient's bone marrow cellularity and peripheral neutrophil, platelet, and reticulocyte information, and see if any infections, allergies, or comorbidities are present)

Other requirements

- ☐ Be sure to include all the listed documents with the letter when you send it to your patient's insurance provider
- ☐ Prescribing physician and patient should each sign the letter
- ☐ Explain why formulary-preferred agents are not appropriate
- ☐ Provide rationale for prescribing PROMACTA and clinical support for your recommendation. This can be SAA clinical trial data from the PROMACTA package insert
- ☐ To close the letter, summarize your recommendation and provide a phone number should any additional information be required

Other information required by the relevant health plan

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

SAMPLE LETTER OF MEDICAL NECESSITY

Once-daily oral PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Click here to download the Sample Letter of Medical Necessity for PROMACTA (SAA).

[Physician Practice letterhead]
[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing on behalf of my patient, [patient's name], to document the medical necessity of PROMACTA® (eltrombopag) for treatment of severe aplastic anemia and provide information about the patient's medical history and treatment.

Listed below are my patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and other supporting information

[Insert information regarding the patient's diagnosis; history of severe aplastic anemia, including previous therapies and results; treatment plan; and other supporting information.]

Enclosed in support of this matter are [insert description of supporting documents. Refer to page 25 of this guide for examples of documentation that may help support a Letter of Medical Necessity]. Please contact me at [insert office phone number] for any additional information you may need to ensure prompt approval of PROMACTA for my patient.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose supporting documentation]

FILING A FORMULARY EXCEPTION REQUEST

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Suggestions for filing a formulary exception request

This type of letter may be helpful when PROMACTA® (eltrombopag) is not listed on a formulary or if it has a National Drug Code (NDC) block. While the plan may provide a form on its website that can be used to apply for an exception, the sample provided in this kit may be helpful regarding the type of information that is typically required.

This letter comes from the **patient** and is also signed by the **physician**. It is recommended that the letter be submitted along with a copy of the patient's relevant medical records and a Letter of Medical Necessity (*see page 25*). Consider requesting a peer-to-peer review for the prescribing physician to discuss the necessity of providing a formulary exception.

Checklist suggestions

General information

- ☐ Include the patient's information: name, date of birth, policy information
- ☐ Include the prescribing physician's name and NPI #
- ☐ Include phone numbers for the prescribing physician and patient if the health plan requires any additional information to support the appeal

Clinical information

- ☐ Patient's medical records:
  - ☐ History, diagnosis, and list of previous therapies (if applicable)
  - ☐ Include copies of relevant medical records and laboratory results

Other requirements

- ☐ Explain the main reasons supporting a formulary exemption for PROMACTA for this patient
- ☐ Provide rationale for prescribing PROMACTA and clinical support for your recommendation. This can be clinical trial data from the PROMACTA package insert
- ☐ If this is a second- or third-level appeal, include the letter of denial and medical notes in response to the denial
- ☐ Include a Letter of Medical Necessity (*see page 25*)

Other information required by the relevant health plan

SAMPLE FORMULARY EXCEPTION REQUEST LETTER

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Consider giving this sample letter to a patient when PROMACTA is not listed on a formulary or if it has a National Drug Code (NDC) block.

Click here to download the Sample Formulary Exception Request Letter for PROMACTA (SAA).

[Date]

[Name of insurance company]
[Address]
[City, State, ZIP code]

Re: [Patient's name]
[Policy number]
[Date of birth]

To whom it may concern:

I am writing to request an exception to your formulary for PROMACTA® (eltrombopag) [dose, frequency] that I prescribed for my patient, [patient's full name].

Listed below are the patient's diagnosis, medical history, treatment plan, and other supporting information, which confirm the medical necessity and appropriateness of PROMACTA.

Patient's diagnosis, medical history, treatment plan, and supporting information

[Insert information regarding the patient's diagnosis; history of severe aplastic anemia, including previous therapies and results; treatment plan; and other supporting information.]

I hope you will agree PROMACTA is appropriate and medically necessary to treat my patient's condition and will support this request for a formulary exception. Enclosed in support of this request are [insert description of supporting documents. Refer to page 27 of this guide for examples of documentation that may help support a formulary exception request].

Thank you in advance for your consideration. Please contact me at [office phone number] for any additional information you may require regarding this matter. I look forward to your timely approval of this formulary exception request.

Sincerely,

[Sign and print your name here]

Attachments: [Enclose supporting documentation]

SEVERE APLASTIC ANEMIA AND PERSISTENT OR CHRONIC ITP

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Indications and Important Safety Information

Indications for PROMACTA® (eltrombopag)

PROMACTA is indicated for the treatment of thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. PROMACTA should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding.

PROMACTA is indicated 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 is indicated for the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.

Limitations of Use

PROMACTA is not indicated for the treatment of patients with myelodysplastic syndromes (MDS).

Safety and efficacy have not been established in combination with direct-acting antiviral agents used without interferon for treatment of chronic hepatitis C infection.

Important Safety Information for PROMACTA® (eltrombopag)

WARNING: RISK FOR HEPATIC DECOMPENSATION IN PATIENTS WITH CHRONIC HEPATITIS C

In patients with chronic hepatitis C, PROMACTA in combination with interferon and ribavirin may increase the risk of hepatic decompensation.

RISK OF HEPATOTOXICITY

PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity. Monitor hepatic function and discontinue dosing as recommended.

Hepatotoxicity

PROMACTA may increase the risk of severe and potentially life-threatening hepatotoxicity.

Treatment of ITP, chronic hepatitis C, and refractory severe aplastic anemia

- Measure serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin prior to initiation of PROMACTA, every 2 weeks during the dose-adjustment phase, and monthly following establishment of a stable dose
- PROMACTA inhibits UGT1A1 and OATP1B1, which may lead to indirect hyperbilirubinemia. If bilirubin is elevated, perform fractionation
- Evaluate abnormal serum liver tests with repeat testing within 3 to 5 days. If the abnormalities are confirmed, monitor serum liver tests weekly until resolved or stabilized
- Discontinue PROMACTA if ALT levels increase to ≥3 times the upper limit of normal in patients with normal liver function or ≥3 times baseline in patients with pretreatment elevations in transaminases and are progressively increasing; or persistent for ≥4 weeks; or accompanied by increased direct bilirubin; or accompanied by clinical symptoms of liver injury or evidence for hepatic decompensation
- If the potential benefit for reinitiating treatment with PROMACTA outweighs the risk for hepatotoxicity, then consider cautiously reintroducing PROMACTA and measure serum liver tests weekly during the dose-adjustment phase. Hepatotoxicity may reoccur if PROMACTA is reinitiated. If liver test abnormalities persist, worsen, or recur, then permanently discontinue PROMACTA

First-line treatment of severe aplastic anemia

- ALT, AST, and bilirubin should be measured prior to initiation of PROMACTA
- During treatment, increases in ALT levels should be managed based on recommendation in Dosing and Administration section for hepatic impairment

Thrombotic/Thromboembolic Complications

- Thrombotic/thromboembolic complications may result from increases in platelet counts with PROMACTA
- Reported thrombotic/thromboembolic complications included both venous and arterial events, and were observed at low and at normal platelet counts
- Portal vein thrombosis has been reported in patients with chronic liver disease receiving PROMACTA
- To minimize the risk for thrombotic/thromboembolic complications, do not use PROMACTA in an attempt to normalize platelet counts. Follow the dose-adjustment guidelines to achieve and maintain target platelet counts

Please see Important Safety Information for PROMACTA continued on page 30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

SEVERE APLASTIC ANEMIA AND PERSISTENT OR CHRONIC ITP (continued)

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

Increased Risk of Death and Progression of Myelodysplastic Syndromes (MDS) to Acute Myeloid Leukemia (AML)

- In a clinical trial of patients with intermediate- to high-risk MDS and thrombocytopenia receiving PROMACTA, an increased number of progressions from MDS to AML and deaths have been observed compared to placebo
- PROMACTA is not indicated for the treatment of patients with MDS

Cataracts

- Development or worsening of cataracts with PROMACTA has been reported with a frequency of 5% to 11% in 6 clinical studies
- Perform a baseline ocular examination prior to initiating PROMACTA. Regularly monitor patients for signs and symptoms of cataracts while on PROMACTA

Laboratory Monitoring

Persistent or chronic ITP

- Monitor serum liver tests
- During therapy with PROMACTA, assess complete blood counts (CBCs) with differentials, including platelet counts, weekly until a stable platelet count has been achieved. Monitor platelet counts monthly thereafter
- Obtain CBCs with differentials, including platelet counts, weekly for at least 4 weeks following discontinuation of PROMACTA
- When switching between the oral suspension and tablet, assess platelet counts weekly for 2 weeks, then follow standard monthly monitoring

Severe aplastic anemia

- Monitor serum liver tests
- Monitor clinical hematology tests regularly throughout therapy with PROMACTA and modify the dosage regimen of PROMACTA based on platelet counts
- Hematologic response may take up to 16 weeks after starting PROMACTA. If no hematologic response has occurred after 16 weeks with PROMACTA, discontinue therapy

Drug/Drug and Drug/Food Interactions

- PROMACTA must be taken at least 2 hours before or 4 hours after any medications or products containing polyvalent cations such as antacids, calcium-rich foods, and mineral supplements
- Take PROMACTA without a meal or with a meal low in calcium (≤50 mg)

Adverse Reactions

Across all indications, the most common adverse reactions (≥20% in any indication) were anemia, nausea, pyrexia, ALT increased, cough, fatigue, headache, and diarrhea.

The most common adverse reactions in 3 placebo-controlled clinical trials in patients with persistent or chronic ITP (≥3% and greater than placebo) for PROMACTA were nausea (9%), diarrhea (9%), upper respiratory tract infection (7%), vomiting (6%), increased ALT (5%), myalgia (5%), urinary tract infection (5%), oropharyngeal pain (4%), increased AST (4%), pharyngitis (4%), back pain (3%), influenza (3%), paresthesia (3%), and rash (3%).

The most common adverse reactions in 2 placebo-controlled clinical trials in patients with persistent or chronic ITP 1 year and older (≥3% and greater than placebo) for PROMACTA were upper respiratory tract infection (17%), nasopharyngitis (12%), cough (9%), diarrhea (9%), pyrexia (9%), abdominal pain (8%), oropharyngeal pain (8%), toothache (6%), ALT increased (6%), rash (5%), AST increased (4%), and rhinorrhea (4%).

The most common adverse reactions (≥5%) in a single-arm trial of 92 patients 2 years and older with severe aplastic anemia (SAA) who had not received prior immunosuppressive therapy were increased ALT (29%) and AST (17%), blood bilirubin increased (17%), rash (8%), and skin discoloration including hyperpigmentation (5%). Upper respiratory infection, particularly in pediatric patients, was also reported. The most common adverse reactions (≥20%) in a single-arm, open-label trial in 43 patients with refractory SAA who received PROMACTA were nausea (33%), fatigue (28%), cough (23%), diarrhea (21%), and headache (21%). In this trial, patients had bone marrow aspirates evaluated for cytogenetic abnormalities. Eight patients had a new cytogenetic abnormality reported, including 5 patients who had complex changes in chromosome 7. If new cytogenetic abnormalities are observed, consider discontinuation of PROMACTA.

Please see full Prescribing Information for PROMACTA, including Boxed WARNING, and Medication Guide.

References: 1. Data on file. Study TRA100773A. Novartis Pharmaceuticals Corp; October 2007. **2.** Promacta [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2021. **3.** Data on file. Study TRA102537 (RAISE). Novartis Pharmaceuticals Corp; February 2009. **4.** Data on file. Study TRA105325 (EXTEND). Novartis Pharmaceuticals Corp; March 2016. **5.** Wong RSM, Saleh MN, Khelif A, et al. Safety and efficacy of long-term treatment of chronic/persistent ITP with eltrombopag: final results of the EXTEND study. *Blood*. 2017;130(23):2527-2536. **6.** Data on file. Study TRA108062 (PETIT). Novartis Pharmaceuticals Corp; July 2014. **7.** Data on file. Study TRA115450 (PETIT 2). Novartis Pharmaceuticals Corp; July 2014. **8.** Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829-3866. **9.** Townsley DM, Scheinberg P, Winkler T, et al. Eltrombopag added to standard immunosuppression for aplastic anemia. *N Engl J Med*. 2017;376(16):1540-1550, S1-S39. doi:10.1056/NEJMoa1613878. **10.** Data on file. Study ETB115AUS01T 120-day update. Novartis Pharmaceuticals Corp; July 2018. **11.** Data on file. Study ELT112523. Novartis Pharmaceuticals Corp; February 2014. **12.** Desmond R, Townsley DM, Dumitriu B, et al. Eltrombopag restores trilineage hematopoiesis in refractory severe aplastic anemia that can be sustained on discontinuation of drug. *Blood*. 2014;123(12):1818-1825.

Please see Important Safety Information for PROMACTA on pages 29-30 and click here for full Prescribing Information, including Boxed WARNING, and Medication Guide.

Once-daily oral
PROMACTA® (eltrombopag)
12.5mg, 25mg, 50mg, 75mg tablets
12.5mg, 25mg oral suspension

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