

Supplementary Table 1 Exclusion criteria by system

Cardiac
Prolonged QTc, with corrected QTc >450 msec
Clinically significant cardio-vascular disease (e.g., uncontrolled hypertension, history of labile hypertension)
Known structural abnormalities (e.g. cardiomyopathy)
History or current diagnosis of cardiac disease indicating significant risk of safety for patients participating in the study such as uncontrolled or significant cardiac disease ^a
Gynecologic
Pregnant, breastfeeding, or unwilling to practice birth control during participation in the study. ^b
Hematology
Evans Syndrome: positive direct Coombs with evidence of active hemolysis (elevated LDH or reticulocyte count not attributable to recent treatment or bleeding)
Anticoagulant or anti-platelet agents
Thrombophilic risk factors ^c
Hepatic
AST or ALT > 2 x upper limit of normal (ULN)
Total bilirubin > 1.5 x ULN
Liver cirrhosis (as determined by the investigator)
Immunology
Known immediate or delayed hypersensitivity reaction to eltrombopag or its excipient
Infectious
HIV (or history of positivity)
Hepatitis C (screening not required if no clinical suspicion)
Active or uncontrolled infections not responding to appropriate therapy
Oncology
Any malignancy
History of stem cell transplant or solid organ transplant
Ophthalmic
Baseline problems that may potentiate cataract development
Psychologic
History of alcohol and drug abuse
Renal
Creatinine > 2.5 x ULN

Abbreviations: LDH, lactate dehydrogenase; AST, aspartate transaminase; ALT, alanine transaminase; ULN, upper limit of normal; HIV, human immunodeficiency virus

^aDefined as recent myocardial infarction (within last 6 months), uncontrolled congestive heart failure, unstable angina (within last 6 months), clinically significant (symptomatic) cardiac arrhythmias (e.g., sustained ventricular tachycardia, and clinically significant second or third degree AV block without a pacemaker), long QT syndrome, family history of idiopathic sudden death, congenital long QT syndrome or additional risk factors for cardiac repolarization abnormality, as determined by the investigator.

^bWomen of childbearing potential (have achieved menarche) must have a negative serum or urine pregnancy test and agree to use basic methods of contraception (if sexually active) or maintain abstinence for the duration of the study until 7 days after the last dose of study treatment. Basic contraception methods include: total abstinence, female sterilization, male sterilization,

barrier methods, or use of oral, injected, or implanted hormonal methods of contraception or placement of an intrauterine device or intrauterine system, or other hormonal contraception with similar efficacy. Male patients who are sexually active and do not agree to abstinence or to use a condom during intercourse while taking eltrombopag, and for 7 days after the last dose of study treatment.

†Subjects for whom the potential benefits of participating in the study outweigh the potential risks of thromboembolic events, as determined by the investigator

Supplementary Table 2 Dose adjustment nomogram for eltrombopag

PLATELET COUNT RESULT	DOSE ADJUSTMENT OR RESPONSE
Weeks 1-12	
< 50 x 10⁹/L following at least 2 weeks of eltrombopag	Increase daily dose by 25 mg to a maximum of 75 mg/day. For patients taking 12.5 mg once daily, increase the dose to 25 mg daily before increasing the dose amount by 25 mg.
≥ 50 x 10⁹/L to < 200 x 10⁹/L	Continue current dose
≥ 200 x 10⁹/L to ≤ 400 x 10⁹/L at any time	Decrease the daily dose by 25 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments. For patients taking 25 mg once daily, decrease the dose to 12.5 mg once daily.
> 400 x 10⁹/L at any time	Hold eltrombopag; increase the frequency of platelet monitoring to twice weekly. Once the platelet count is < 200 x 10 ⁹ /L, reinstitute therapy at a daily dose reduced by 25 mg. For patients taking 25 mg once daily, reinstitute therapy at a daily dose of 12.5 mg. If platelets remain ≥ 200 x 10 ⁹ /L to <400 x 10 ⁹ /L after 2 weeks, decrease frequency of platelet checks to weekly.
> 400 x 10⁹/L after 2 weeks of therapy at lowest dose of eltrombopag	Discontinue eltrombopag. If platelets drop to <50 x 10 ⁹ /L after discontinuing eltrombopag, restart at the last effective dose (lowest dose that achieved platelet count ≥ 50 x 10 ⁹ /L)
Weeks 13-52	
< 30 x 10⁹/L 2 weeks after dose adjustment	Increase dose to last effective dose (to attain platelet count ≥ 30 x 10 ⁹ /L)
≥ 30 x 10⁹/L to < 100 x 10⁹/L	Continue current dose.
≥ 100 x 10⁹/L to < 200 x 10⁹/L	Decrease daily dose by 12.5 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments. If platelets remain ≥ 100 x 10 ⁹ /L after 2 weeks at lowest dose, discontinue eltrombopag.
≥ 200 x 10⁹/L to ≤ 400 x 10⁹/L	Decrease the daily dose by 25 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments. For patients taking 25 mg once daily, decrease the dose to 12.5 mg once daily.
> 400 x 10⁹/L	Discontinue eltrombopag

< 30 x 10⁹/L after weaning off eltrombopag	Restart at the last effective dose (lowest dose prior to weaning). If platelets remain < 30 x 10 ⁹ /L, increase per initial dose adjustment.
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