SUPPLEMENTARY MATERIALS

Supplementary Methods

Supplementary Table 1. Additional Sources Assessed During the Review

Conference	Years
ASH	2019–2023
EHA	2020–2023[a]
ISTH	2020–2023[a]
BIC[b]	2021 + 2023
WFH[b]	2020 + 2023
EAHAD	2020–2023
GTH[b]	2020
IHEA Annual	2019–2023
ISPOR Europe	2020–2023
ISPOR Annual	2020–2024
HTAi[b] Annual	2020–2023
HTA bodies searched	
NICE	Since inception
CADTH	Since inception
SMC	Since inception
AWMSG	Since inception
PBAC	Since inception
HAS	Since inception
IQWiG	Since inception
INAHTA	Since inception
ICER	Since inception

[a]Conference search years conducted for both original and update SLR on different dates; [b]The proceedings from the following conferences were either not published or not retrievable: BIC 2020, BIC 2022, WFH 2021, WFH 2022, GTH 2021, GTH 2022, and GTH 2023.

ASH, American Society of Hematology; AWMSG, All Wales Medicines Strategy Group; BIC, Bari International Conference; CADTH, Canadian Agency for Drugs and Technologies in Health; EAHAD, European Association for Haemophilia and Allied Disorders; EHA, European Haematology Association; GTH, German Haemostasis and Thrombosis Conference; HAS, Haute Autorité de Santé; HTAi, Health Technology Assessment International; ICER, Institute for Clinical and Economic Review; IHEA, International Health Economics Association; INAHTA, International Network of Agencies for Health Technology Assessment; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesenin; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; ISTH, International Society on Thrombosis and Haemostasis; NICE, National Institute for Health and Care Excellence; PBAC, Pharmaceutical Benefits Advisory Committee; SMC, Scottish Medicines Consortium; WFH, World Federation of Hemophilia.

Supplementary Table 2. Full Study Eligibility Criteria and Rationale for Exclusion From Economic Evaluation Review

Category	Inclusion criteria	Exclusion criteria
Population	• Patients of any age with cTTP, irrespective of their prior treatment status, including on-demand treatment for acute events or ongoing prophylactic treatment • Patients of any age with iTTP • Patients of any age with broad TTP without subgroup data for cTTP or iTTP	Healthy volunteers Diseases other than TTP
Study type	Full economic evaluations: • Cost-consequence • Cost-minimization • Cost-effectiveness • Cost-utility • Cost-benefit • Budget impact • SLRs and meta-analyses conducted on relevant populations[a]	In vitro studies Preclinical studies or clinical studies reporting efficacy or safety information only Reviews, comments, letters, and editorials Case reports, case series Studies not reporting economic evaluation outcomes
Interventions	• No restrictions • All economic evaluations in the populations defined above were included in the review	None
Comparators	No restrictions	None
Outcomes	• Incremental costs • ICER/ICUR • Incremental QALYs/LYs • Model inputs (eg, transition probabilities) • Sensitivity analyses results • Type of model, time horizon, health states, cycle length, cost categories included, etc	Studies not reporting outputs from economic evaluations
Language	English language only	Not applicable
Time limit	Original SLR: September 28, 2021 Updated SLR: September 2021–January 16, 2024	Not applicable

Category	Inclusion criteria	Exclusion criteria
Countries	No limits	Not applicable

cTTP, congenital thrombotic thrombocytopenic purpura; ICER, incremental cost-effectiveness ratio; ICUR, incremental cost utility ratio; iTTP, immune-mediated thrombotic thrombocytopenic purpura; LY, life year; QALY, quality-adjusted life year; SLR, systematic literature review; TTP, thrombotic thrombocytopenic purpura.
[a]SLRs were included for bibliography searches only.

Supplementary Table 3. Full Study Eligibility Criteria and Rationale for Exclusion From HCRU and Cost Studies Review

Category	Inclusion criteria	Exclusion criteria
Population	• Patients of any age with cTTP, irrespective of their prior treatment status, including on-demand treatment for acute events or ongoing prophylactic treatment[a]	• Healthy volunteers • Diseases other than TTP

Study design	• Cost and resource use studies:
	• Cost studies
	  ○ Resource use studies
	  ○ Economic evaluations reporting costs or resource use
	• SLRs conducted on relevant populations[b]
		• In vitro studies
		• Preclinical studies or clinical studies reporting efficacy or safety information only
		• Reviews, comments, letters, and editorials
		• Case reports, case series
		• Studies not reporting cost or resource use data

Interventions	• No restrictions	• None
Comparators	• No restrictions	• None
Outcomes	• Resource use data • Cost data: Direct (medical/non-medical), indirect cost, drug acquisition cost, administration cost, treatment cost, adverse event cost, health state related costs, terminal care costs etc • Productivity losses (presenteeism, absenteeism) • Supportive care medication use	• Studies not reporting cost and resource use data
Language	• English only	• Not applicable
Time limit	• Original SLR: September 28, 2021 • Updated SLR: September 2021–January 16, 2024	• Not applicable
Country	• No limit	• Not applicable

[a]Studies reporting HCRU and cost data for patients with cTTP were included, even if these studies also reported data for patients with iTTP, or TTP of unspecified subtype. However, for the HCRU and cost studies review—which focused solely on cTTP—only data for patients with cTTP were extracted. [b]Systematic reviews conducted in the last 3 years were included for bibliography searches only.

cTTP, congenital thrombotic thrombocytopenic purpura; HCRU, healthcare resource use; iTTP, immune-mediated thrombotic thrombocytopenic purpura; SLR, systematic literature review; TTP, thrombotic thrombocytopenic purpura.

Supplementary Table 4. Full Study Eligibility Criteria and Rationale for Exclusion From Utility and HRQoL Review

Category	Inclusion criteria	Exclusion criteria
Population	• Patients of any age with cTTP, irrespective of their prior treatment status, including on-demand treatment for acute events or ongoing prophylactic treatment • Patients of any age with broad TTP without subgroup data for cTTP or iTTP • Patients of any age with iTTP • Carers for patients with any of the conditions above	• Healthy volunteers • Diseases other than TTP
Study design	• Studies reporting HRQoL and/or utility/disutility data (regardless of treatment) • Systematic reviews and meta-analysis conducted on relevant population[a]	• In vitro studies • Preclinical studies • Reviews, comments, letters, and editorials • Case reports, case series • Clinical studies reporting only efficacy and safety data
Interventions	No restrictions	None
Comparators	No restrictions	None

Outcomes	• All types of utilities or disutilities data including but not limited to EQ-5D®, SF-6D, Health Utility Index, Assessment of Quality of Life
	• Studies reporting mapped utilities values from disease-specific instruments
	• HRQoL outcomes reported using:
	  ○ SF-36 (and others like SF-12)
	  ○ EQ-5D
	  ○ EQ-5D-Y
	  ○ PedsQL
	  ○ TSQM-9
	  ○ cTTP-PEQ
		Studies not reporting utility values

Language	English only	Non-English

Category	Inclusion criteria	Exclusion criteria
Time limit	Original SLR: September 28, 2021 Updated SLR: September 2021–January 16, 2024	None
Country	No limit	None

[a]SLRs conducted in the last 3 years were included for bibliography searches only.
cTTP, congenital thrombotic thrombocytopenic purpura; cTTP-PEQ, congenital thrombotic thrombocytopenic purpura–patient experience questionnaire; EQ-5D, EuroQol-5-Dimension; EQ-5D-Y, The Youth version of EuroQol-5 dimension; HRQoL, Health-Related Quality of Life; iTTP, immune-mediated thrombotic thrombocytopenic purpura; PedsQL, Pediatric Quality of Life Inventory; SLR; systematic literature review; SF-36, 36-Item Short Form Survey; SF-6D, Short-Form 6 Dimensions; SF-12, 12-Item Short Form Survey; TSQM-9, Treatment Satisfaction Questionnaire for Medication - 9 Items.

Supplementary Table 5. Key Characteristics of Included Economic Evaluation Studies

Study	Type of TTP	Study country	Model details	Time horizon	Perspective	Cost year(s)	Currency	Cycle length	Discount rate for cost and benefits (per annum)	Willingness-to-pay threshold
NICE 2020	iTTP	UK	Decision tree model for the acute iTTP episode followed by Markov model for patients in remission and following relapse	Decision tree model: 3 months Markov model: lifetime (55 years)	National Health Service and personal social services	2017–18	Pounds Sterling (£)	Markov model[a]: 3 months	3.5% and an alternate discount rate of 1.5% also used for outcomes	NR
SMC 2020	iTTP	Scotland	Decision tree model for the acute episode while a cohort-level Markov model used to model iTTP in remission.	55 years	Healthcare system	NR	Pounds Sterling (£)	Markov model: 3 months	NR	NR

Study	Type of TTP	Study country	Model details	Time horizon	Perspective	Cost year(s)	Currency	Cycle length	Discount rate for cost and benefits (per annum)	Willingness-to-pay threshold
CADTH 2023	iTTP	Canada	Decision tree followed by Markov model	Lifetime (53 years)	Canadian public health care payer	NR	Canadian dollars ($)	3 months	1.5% per cycle	$50,000
Di Minno 2020	iTTP	Italy	Markov model	Lifetime (60 years)	Italian healthcare	NR	Euros (€)	NR	3.5%	NR
Di Minno 2021	iTTP	Italy	Markov model	Lifetime	Healthcare	2020	Euros (€)	3 months	3%	€60,000
Goshua 2021	iTTP	USA	Markov model Decision tree model	Markov model: 5 years	Health system	2019	US dollars ($)	Markov model: 12 months (5 cycles)	3%	$195,330
Butt 2022	iTTP	USA	Markov model	At least 1 year	US healthcare	NR	US dollars ($)	NR	NR	$195,300

Study	Type of TTP	Study country	Model details	Time horizon	Perspective	Cost year(s)	Currency	Cycle length	Discount rate for cost and benefits (per annum)	Willingness-to-pay threshold
Sullivan 2023	iTTP	USA	Markov model Decision tree model	Markov model: lifetime (55 years) Decision tree model: 3 months	US healthcare	2022	US dollars ($)	3 months	3%	$150,000 to $200,000

[a]Half-cycle correction is also applied.
CADTH, Canadian Agency for Drugs and Technologies; HTA, health technology assessment; iTTP, immune thrombocytopenic purpura; NICE, National Institute for Health and Care Excellence; NR, not reported; SMC, Scottish Medicines Consortium.