

Optimizing aTTP/iTTP Diagnosis and Care Using Epic[®] Capabilities

This guide provides educational information to help emergency departments, hospitals, and health systems use BPAs and Order Sets to expedite aTTP/iTTP diagnosis and provide appropriate care.

INDICATIONS:

CABLIVI (caplacizumab-yhdp) is indicated for the treatment of adult patients with acquired thrombotic thrombocytopenic purpura (aTTP), in combination with plasma exchange and immunosuppressive therapy.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS:

CABLIVI is contraindicated in patients with a previous severe hypersensitivity reaction to caplacizumab-yhdp or to any of its excipients. Hypersensitivity reactions have included urticaria.

Please see additional [Important Safety Information](#) throughout and accompanying full [Prescribing Information](#).

Based on Epic's February 2022 version. Functions and features may change with software updates. This guide includes examples and hypothetical screenshots for consideration only. The information provided is not medical advice, which is solely the health system's responsibility.

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aTTP/iTTP=acquired or immune-mediated thrombotic thrombocytopenic purpura; BPA=best practice advisory.

Background Information

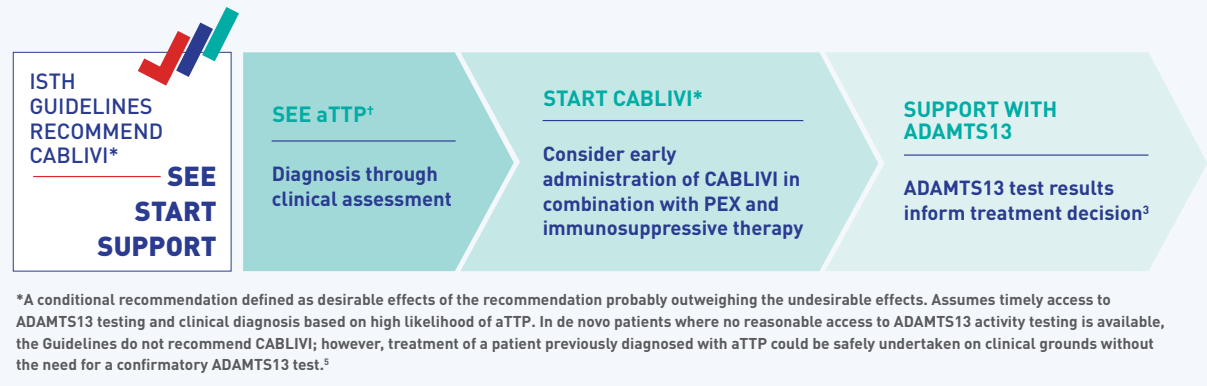
Support Timely Evaluation and Treatment of aTTP/iTTP Using Electronic Health Records (EHRs)

aTTP/iTTP is a rare and life-threatening blood disorder that often presents as a medical emergency.¹⁻⁴ Diagnosing aTTP /iTTP can be difficult because the complex presentation often includes symptoms that resemble other disorders; early treatment is essential.²

Who should not start CABLIVI?

- CABLIVI is contraindicated in patients with a previous severe hypersensitivity reaction to caplacizumab-yhdp or to any of its excipients
- Withhold CABLIVI treatment 7 days prior to elective surgery, dental procedures, or other invasive interventions

ISTH Guidelines recommend CABLIVI* in combination with PEX and immunosuppressive therapy for acute aTTP events—initial and relapsing^{3,5}



[†]The ISTH TTP Guidelines refer to aTTP as iTTP.

EHR capabilities such as BPAs and Order Sets can help a hospital/health system follow the ISTH guidelines by prompting actions such as medication orders and ADAMTS13 testing to support treatment decisions.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS:

Hemorrhage:

- CABLIVI increases the risk of bleeding. In clinical studies, severe bleeding adverse reactions of epistaxis, gingival bleeding, upper gastrointestinal hemorrhage, and metrorrhagia were each reported in 1% of subjects. Overall, bleeding events occurred in approximately 58% of patients on CABLIVI versus 43% of patients on placebo.

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PEX=plasma exchange

Using Best Practice Advisories to Promote aTTP/iTTP Evaluation

BPAs can help to proactively identify at-risk patients for further evaluation to standardize timely testing to differentiate aTTP/iTTP from other similarly presenting conditions.

Example criteria for configuring a BPA consistent with the ISTH TTP Diagnosis Guidelines and published blood reference ranges are shown here for illustrative purposes only.

Potential inclusion criteria:

Platelet count $<100 \times 10^9/L^5$ AND microangiopathic hemolytic anemia (MAHA)* defined as follows:

- If female adult, Hb <12 g/dl and hematocrit $<36\%^6$ OR
- If male adult, Hb <14 g/dl and hematocrit $<40\%^6$ AND
- Low haptoglobin <41 mg/dL⁷ AND
- Increased LDH >333 IU/L⁸ AND
- Schistocytes (presence in peripheral blood smear) $>1\%^9$ AND
- Relatively preserved renal function⁵

Display BPA for: Emergency department health care professionals, hospitalists, hematologists, nephrologists, transfusion medicine/blood bank, critical care physicians (ICU).

Timing for when to display: When the prior criteria are met.

Example message to display in BPA: Patient may be experiencing TTP based on thrombocytopenia and evidence of MAHA. Please refer to hematologist or nephrologist and use the recommended order set or indicate the reason for a different course of action.

Display values in BPA under message for the following:

- | | | |
|------------------------------------|--------------------------------------|---------------------------------------|
| <input type="checkbox"/> Platelets | <input type="checkbox"/> Hematocrit | <input type="checkbox"/> LDH |
| <input type="checkbox"/> Hb | <input type="checkbox"/> Haptoglobin | <input type="checkbox"/> Schistocytes |

Actions:

- | | |
|--|--|
| <input type="checkbox"/> Open TTP order set | <input type="checkbox"/> Refer to transfusion medicine/ blood bank |
| <input type="checkbox"/> Refer to hematology | <input type="checkbox"/> Reason: _____ |
| <input type="checkbox"/> Refer to nephrology | |

*Hb and hematocrit below reference range, low haptoglobin, elevated LDH, presence of schistocytes in peripheral blood smear.

Requesting BPAs

A physician or other authorized person for hospital EHR changes may provide specific information needed for BPA setup to the EHR support team. Necessary criteria include the categories listed below.

- Inclusion and exclusion criteria for BPAs
- Timing for when to display BPAs in the workflow
- Display restrictions
- Example of text to be displayed in BPAs
- Actions to take based upon the BPA recommendation

Best Practice Advisory

! Patient may be experiencing acquired Thrombotic Thrombocytopenic Purpura (TTP) based on thrombocytopenia and evidence of MAHA. Please refer to hematologist or nephrologist and use the recommended order set or indicate the reason for a different course of action.

Platelets	25 x 10 ⁹ /L	Haptoglobin	33 mg/dL
Hb	10 g/dL	LDH	275 IU/L
Hematocrit	34%	Schistocytes	1.1 (Schistocytes in peripheral blood smear)

acquired Thrombotic Thrombocytopenic Purpura (TTP) [Preview](#)

Reason for a different course of action.

Refer to hematology
 Refer to nephrology
 Refer to transfusion medicine

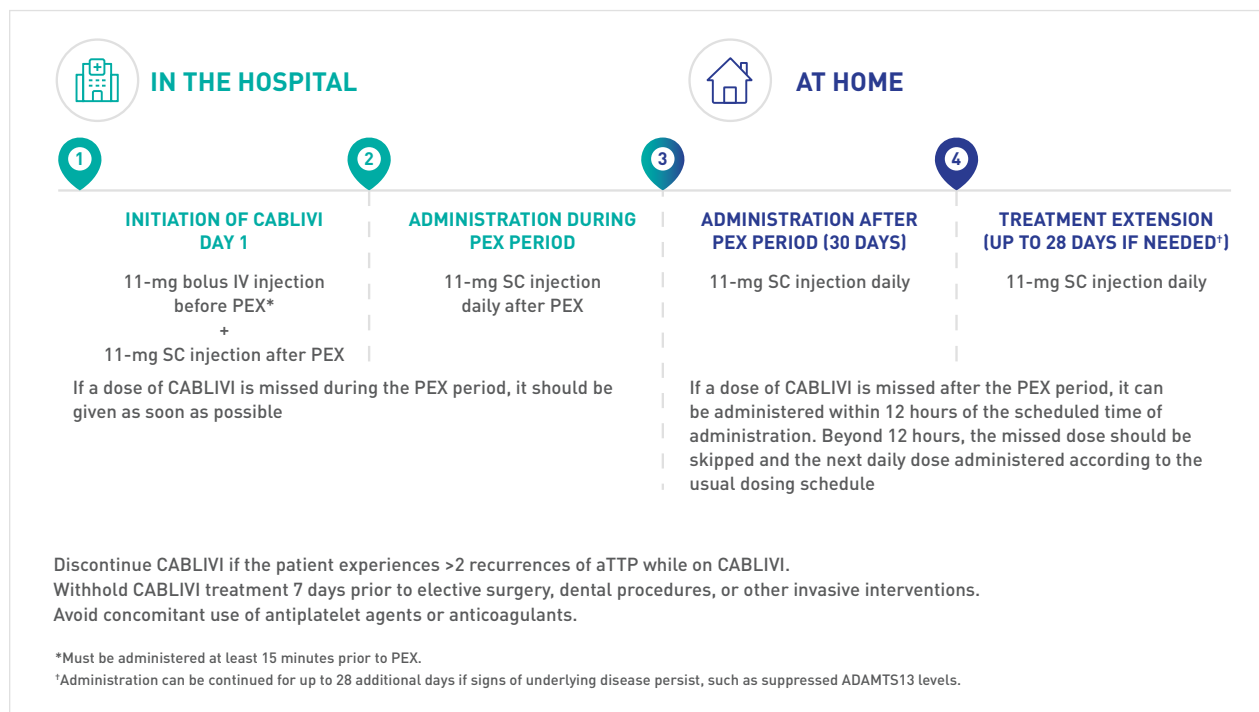
Hypothetical example of a BPA.

Using Order Sets to Help Provide Appropriate aTTP/iTTP Care

Inpatient and discharge Order Sets can be configured to include all appropriate treatments and help ensure necessary orders are placed. In the case of suspected aTTP/iTTP, these may include bloodwork for ADAMTS13 testing and/or medication orders to include CABLIVI in addition to PEX and immunosuppressive therapy.

The CABLIVI dosing regimen shows the specific information to include when adding CABLIVI to an existing inpatient hospital Order Set for PEX and immunosuppressive therapy or when creating a new Order Set for discharge.

Hospital aTTP/iTTP Order Sets for PEX and immunosuppressive therapy may need to be updated to include CABLIVI 11-mg bolus IV injection, and new Order Sets may be needed for aTTP/iTTP discharge including CABLIVI 11-mg subcutaneous injection.



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS: (cont'd)

Hemorrhage: (cont'd)

- In the postmarketing setting cases of life-threatening and fatal bleeding were reported in patients receiving CABLIVI.

Please see additional [Important Safety Information](#) throughout and accompanying full [Prescribing Information](#).

SC=subcutaneous

Inpatient Order Sets



In the Hospital

Requesting and Implementing Inpatient Order Set Changes

A physician or other authorized person for hospital EHR changes may provide specific information needed for modifying an EHR inpatient Order Set for aTTP/iTTP. Necessary criteria include the categories listed below.

Requesting Changes to an Existing Inpatient Order Set

The request to update an Order Set typically requires:

- The types of Order Set(s) affected by the change. For example, “acquired thrombotic thrombocytopenic purpura - IP IV”
- The specific medication to be added. For example, “CABLIVI 11-mg bolus IV injection kit, and immunosuppressive therapy”
- Whether the order for a drug should be defaulted as “selected” or “unselected”
- Patient education information to be included, if applicable
- Patient follow-up to be included, if applicable

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS: (cont'd)

Hemorrhage: (cont'd)

- The risk of bleeding is increased in patients with underlying coagulopathies (e.g. hemophilia, other coagulation factor deficiencies). It is also increased with concomitant use of CABLIVI with drugs affecting hemostasis and coagulation.

Please see additional [Important Safety Information](#) throughout and accompanying full [Prescribing Information](#).

Order Set Clear All Orders

! acquired Thrombotic Thrombocytopenic Purpura - IP IV Remove Order Sets

- ▼ Blood Bank
 - Plasma Exchange
- ▼ Consults
 - Specialty Consults
 - Consult to case manager for patient enrollment
- ▶ Fluid and Electrolytes
- ▶ Imaging
- ▶ Nursing
- ▼ Labs
 - ADAMTS13 test
 - CBC
 - Haptoglobin
 - LDH
 - Schistocytes in peripheral blood smear
- ▼ Medications
 - CABLIVI 11 MG INJECTION KIT
 - CABLIVI 11 MG SOLUTION FOR INJECTION
 - [immunosuppressive therapy]
- ▶ Other Orders
- ▶ PRN Medications
- ▼ Patient Education
 - CABLIVI Patient Solutions Enrollment Form
 - CABLIVI Patient Brochure

Hypothetical example of an inpatient Order Set with CABLIVI IV treatment added.

Discharge Order Sets



At Home

Requesting and Implementing a New Discharge Order Set

A physician or other authorized person for hospital EHR changes provides specific information for creating a new discharge order set for aTTP/iTTP. Necessary criteria include the categories listed below.

Requesting a New Discharge Order Set

The request to create an Order Set typically includes:

- The name for the Order Set(s).
For example, acquired thrombotic thrombocytopenic purpura - Outpatient SC
- The categories of orders to be added.
For example, Blood Bank, Nursing, Labs, Medications, Other Tests

*If after initial treatment course, sign(s) of persistent underlying disease such as suppressed ADAMTS13 activity levels remain present, treatment may be extended for a maximum of 28 days.

- The specific clinical items to be added.
For example, CABLIVI (medication) 11-mg subcutaneous, 30 days post discontinuation of PEX, and (immunosuppressive therapy)
- Follow-up visit to evaluate ADAMTS13 for therapy extension evaluation*
- Whether each order should be defaulted as “selected” or “unselected”

Patients who are prescribed CABLIVI can enroll in the patient assistance program to receive additional training, specialty pharmacy services, and financial assistance for patients who qualify.

Find more information and download the enrollment form at <https://www.cablivi.com/attp/cablivi-patient-solutions>

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS: (cont'd)

Hemorrhage: (cont'd)

- Avoid concomitant use of CABLIVI with antiplatelet agents or anticoagulants. If clinically significant bleeding occurs, interrupt use of CABLIVI. Von Willebrand factor concentrate may be administered to rapidly correct hemostasis. If CABLIVI is restarted, monitor closely for signs of bleeding.

Please see additional [Important Safety Information](#) throughout and accompanying full [Prescribing Information](#).

Hypothetical example of a discharge Order Set with CABLIVI subcutaneous treatment added.

IMPORTANT SAFETY INFORMATION AND INDICATIONS

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- In the postmarketing setting cases of life-threatening and fatal bleeding were reported in patients receiving CABLIVI.
- The risk of bleeding is increased in patients with underlying coagulopathies (e.g. hemophilia, other coagulation factor deficiencies). It is also increased with concomitant use of CABLIVI with drugs affecting hemostasis and coagulation.
- Avoid concomitant use of CABLIVI with antiplatelet agents or anticoagulants. If clinically significant bleeding occurs, interrupt use of CABLIVI. Von Willebrand factor concentrate may be administered to rapidly correct hemostasis. If CABLIVI is restarted, monitor closely for signs of bleeding.
- Withhold CABLIVI for 7 days prior to elective surgery, dental procedures or other invasive interventions. If emergency surgery is needed, the use of von Willebrand factor concentrate may be considered to correct hemostasis. After the risk of surgical bleeding has resolved, and CABLIVI is resumed, monitor closely for signs of bleeding.

Visit www.cablivi.com/hcp for more information.

References: **1.** Grall M, Azoulay E, Galicier L, et al. Thrombotic thrombocytopenic purpura misdiagnosed as autoimmune cytopenia: causes of diagnostic errors and consequence on outcome. Experience of the French thrombotic microangiopathies reference centre. *Am J Hematol.* 2017;92(4):381-387. **2.** Scully M, Hunt BJ, Benjamin S, et al. On behalf of British Committee for Standards in Haematology. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *Br J Haematol.* 2012;158(3):323-335. **3.** Goel R, King KE, Takemoto CM, Ness PM, Tobian AAR. Prognostic risk-stratified score for predicting mortality in hospitalized patients with thrombotic thrombocytopenic purpura: national representative data from 2007 to 2012. *Transfusion.* 2016;56(6):1451-1458. **4.** Peyvandi F, Scully M, Kremer Hovinga JA, et al. Caplacizumab reduces the frequency of major thromboembolic events, exacerbations and death in patients with acquired thrombotic thrombocytopenic purpura. *J Thromb Haemost.* 2017;15(7):1448-1452. **5.** Zheng XL, Vesely SK, Cataland SR, et al. ISTH guidelines for the diagnosis of thrombotic thrombocytopenic purpura. *J Thromb Haemost.* 2020;18(10):2486-2495. doi:10.1111/jth.15006. **6.** Dean L. Blood Groups and Red Cell Antigens [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2005. Chapter 1, Blood and the cells it contains. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK2263/>. **7.** MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2020 Jun 24]. Haptoglobin blood test; [updated 2022 Jan 25; cited 2022 Sep 15]. Available from: <https://medlineplus.gov/ency/article/003634.htm>. **8.** MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2020 Jun 24]. Lactate dehydrogenase test; [Updated 2022 Jan 25; cited 2022 Sep 15]. Available from: <https://medlineplus.gov/ency/article/003471.htm>. **9.** Saha M, McDaniel JK, Zheng XL. Thrombotic thrombocytopenic purpura: pathogenesis, diagnosis and potential novel therapeutics. *J Thromb Haemost.* 2017;15:1889-1900.

ADVERSE REACTIONS:

The most common adverse reactions (>15% of patients) were epistaxis (29%), headache (21%) and gingival bleeding (16%).

CONCOMITANT USE OF ANTICOAGULANTS OR ANTIPLATELET AGENTS:

Concomitant use of CABLIVI with any anticoagulant or antiplatelet agent may increase the risk of bleeding. Avoid concomitant use when possible. Assess and monitor closely for bleeding with concomitant use.

PREGNANCY:

There are no available data on CABLIVI use in pregnant women to inform a drug associated risk of major birth defects and miscarriage.

- **Fetal/neonatal adverse reactions:** CABLIVI may increase the risk of bleeding in the fetus and neonate. Monitor neonates for bleeding.
- **Maternal adverse reactions:** All patients receiving CABLIVI, including pregnant women, are at risk for bleeding. Pregnant women receiving CABLIVI should be carefully monitored for evidence of excessive bleeding.

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