Ticagrelor (BRILINTA)
Criteria for Use
October 2025

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

Exclusion Criteria

If the answer to ANY item below is met, then the patient should NOT receive ticagrelor.

- ☐ Active pathological bleeding
- ☐ Clinically important anemia or thrombocytopenia
- ☐ History of intracranial hemorrhage (ICH)
- ☐ Severe hepatic impairment
- ☐ Increased risk for symptomatic bradycardia events (e.g., sick sinus syndrome, 2nd or 3rd degree atrioventricular block, bradycardia-related syncope not protected by a pacemaker)
- ☐ Concomitant simvastatin or lovastatin in doses greater than 40 mg daily
- ☐ Concomitant use of strong CYP3A4 inhibitors (e.g., atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole)
- ☐ Concomitant use of strong CYP3A4 inducers (e.g., rifampin, phenytoin, carbamazepine, and phenobarbital)
- ☐ Concomitant oral anticoagulant therapy (clopidogrel is preferred $P2Y_{12}$ inhibitor for use in combination with an oral anticoagulant)[1]
- ☐ Anticipated urgent coronary artery bypass graft (CABG) surgery (i.e., within 5 days)
- ☐ Receiving concomitant aspirin at a dose of greater than 100 mg daily

Inclusion Criteria

The answer to one of the following must be fulfilled in order to meet criteria.

- ☐ ST-elevation myocardial infarction acute coronary syndrome (STEMI-ACS) undergoing percutaneous coronary intervention (PCI)[2] or receiving no reperfusion
- ☐ Non-ST elevation acute coronary syndrome (NSTE-ACS) with at least 2 of the following: ST-segment changes on electrocardiogram indicating ischemia, positive cardiac biomarkers, and/or other high risk feature[2,3]
- ☐ Definite or probable acute stent thrombosis (Academic Research Consortium definition) in patients compliant with aspirin and clopidogrel
- ☐ Extended duration dual antiplatelet therapy (DAPT=aspirin plus $P2Y_{12}$ inhibitor) beyond 12 months following an ACS event as per Cardiology re-evaluation; reduce dose to 60 mg twice daily
- ☐ Reduced clopidogrel response (e.g., any documented CYP2C19 intermediate or poor metabolizer phenotypes or high on-treatment platelet reactivity by $P2Y_{12}$ reaction units [PRU] testing) and continued indication for $P2Y_{12}$ inhibitor therapy[4]
- ☐ Confirmed CAD and type 2 diabetes without prior MI, at particularly high ischemic risk AND low bleed risk given neutral net clinical benefit – restricted to Cardiology
- ☐ Non-cardioembolic acute ischemic stroke (NIH Stroke Scale score ≤5) or high-risk transient ischemic attack when no other recommended antiplatelet agents are appropriate for use – restricted to Neurology[5]
- ☐ Undergoing PCI with or without ACS in patients with clopidogrel or true aspirin allergy

[1]Ticagrelor may be an alternative in patients with high thrombotic/acceptable bleed risk.

[2]Consider prasugrel rather than ticagrelor in STEMI or NSTE-ACS patients who are undergoing PCI based on improved ischemic outcomes without increased bleeding found with prasugrel vs. ticagrelor in the ISAR-REACT 5 trial.

[3]Other high risk features: age 60 yrs or older, prior MI or CABG, CAD with stenosis of 50% or more in 2 or more vessels, prior stroke, transient ischemic attack, carotid stenosis of 50% or more, cerebral revascularization, diabetes mellitus, peripheral arterial disease, or chronic renal dysfunction (i.e., creatinine clearance less than 60 ml/min)

[4]If prior pharmacogenomic test results are available, the results should be reviewed and added to the decision-making process

[5]Alternatives include aspirin or clopidogrel monotherapy, clopidogrel with aspirin, and aspirin-extended release dipyridamole. Use ticagrelor with aspirin, initiate within 24 hours of symptom onset and for a duration of 30 days.

Supplemental Information

- **Extended durations of therapy:** DAPT for at least 12 months is guideline recommended therapy after ACS; longer or shorter durations may be considered with the understanding that DAPT reduces ischemic risk but increases bleeding risk. The optimal $P2Y_{12}$ antagonist for extended treatment is unclear due to lack of head-to-head data. In ACS populations, the risk of bleeding with clopidogrel is typically lower than prasugrel or ticagrelor. If continued beyond 12 months, consider a reduced dose of ticagrelor 60 twice daily.
- **Reduced clopidogrel response:** In total, evidence suggests that patients with known CYP2C19 intermediate or poor metabolizer phenotypes or high on-treatment platelet activity testing on clopidogrel are at increased risk of subsequent cardiovascular events. However, routine pharmacogenomic or platelet function screening is not currently guideline recommended, and the ultimate clinical benefit of a guided-use strategy is unknown. A genotype-guided strategy may be considered based on clinical judgment of a patient's risk profile and testing availability.
- **Established CAD with no prior MI:** In patients with type 2 diabetes, confirmed CAD (prior PCI, CABG or 50% angiographic stenosis in at least 1 coronary artery) but no prior MI, ticagrelor (plus aspirin) reduced first MI and stroke and increased major and intracranial bleeding without an apparent net clinical benefit in the THEMIS trial. Ticagrelor use should be reserved for patients who closely match those studied and may be more likely to have some benefit (e.g., confirmed CAD, type 2 diabetes, and prior PCI, particularly those with a stent).
- **Acute ischemic stroke or high risk transient ischemic attack:** In patients with a mild-moderate stroke (NIH Stroke Scale score of ≤5) or high-risk transient ischemic attack (ABCD2 score ≥6 or ipsilateral atherosclerotic stenosis ≥50% in the internal carotid or an intracranial artery) who did not undergo thrombolysis or thrombectomy, the THALES trial evaluated ticagrelor in conjunction with aspirin, started within 24 hours of symptom onset, versus aspirin alone for 30 days. Ticagrelor with aspirin was associated with reduced incidence of recurrent stroke but increased ICH or fatal bleeding versus aspirin alone. As monotherapy, ticagrelor was not shown to be superior to aspirin in secondary stroke/TIA prevention, and there is no available data comparing ticagrelor with clopidogrel or aspirin-extended release dipyridamole for secondary prevention of stroke and TIA.

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