

Inpatient Treatment of Acute Coronary Syndromes: Pharmacologic Implications

Introduction

The term acute coronary syndromes (ACS) refers to a range of acute myocardial ischemic states that vary in severity and extent of thrombosis. It encompasses unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI).¹ Patients with persistent ST-segment elevation are candidates for either pharmacologic or catheter-based reperfusion to restore flow. Those without ST-segment elevation are not candidates for pharmacologic reperfusion (e.g., thrombolytic therapy) but should receive anti-ischemic therapy followed by percutaneous coronary intervention (PCI). All patients with ACS should receive antiplatelet therapy.^{2,3}

Acute Coronary Syndromes

Coronary artery disease underlies most ACS; specifically, disruption of atherosclerotic plaque causes most ACS events. When plaque is disrupted, thrombogenic substances are exposed, which activate platelets, thereby leading to platelet aggregation, formation of a platelet plug, and, ultimately, creation of a thrombus within a coronary artery (FIGURE).^{2,4-6}

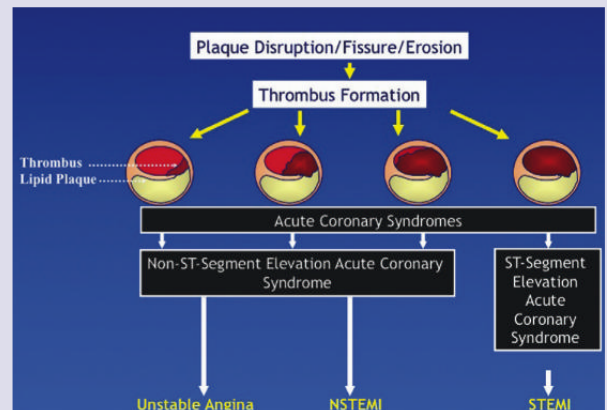
UA is the least severe form of ACS. It is characterized by increasing chest pain, which may occur during exercise or at rest, but does not cause myocardial necrosis.³

NSTEMI is caused by reduced myocardial perfusion due to narrowing of a coronary artery by a thrombus that develops on a disrupted atherosclerotic plaque. Without complete blockage, no necrosis occurs, which is why the ST segment is not elevated.¹

Together UA and NSTEMI are also called non-ST-segment elevation acute coronary syndrome (NSTEMI ACS). They are associated with an increased risk of subsequent myocardial infarction (MI) and cardiac death.¹

STEMI occurs with the abrupt rupture, erosion, or fissuring of a previously minimally obstructive plaque leading to total and persistent thrombotic occlusion. Myocardium supplied by that artery becomes ischemic, causing chest pain. Electrocardiographic evidence of full-thickness ischemia is seen as ST-segment elevation in the leads for that region of the heart.⁷

Figure. Thrombus Formation and Acute Coronary Syndrome



NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction.

Source: Reference 4. Reprinted with permission from Robert Lee Page II, *PharmD*.

Impact of ACS

Estimates of the incidence of ACS in the United States are 1.3 to 1.4 million per year.^{2,8} The American Heart Association 2009 statistical update cites a "conservative estimate" of 733,333 hospital discharges for ACS in 2006.³ When secondary discharge diagnoses are included, the number rises to 1,365,000. Of the total, 810,000 were for MI alone and 537,000 were for UA alone; 18,000 hospitalized patients received both diagnoses.³ While the inpatient mortality rate for acute MI has declined from 127.7 deaths per 1,000 admissions in 1994 to 77.5 deaths per 1,000 admissions in 2005, heart disease remains the leading cause of death in the United States, with 652,091 deaths in 2005.⁹

The total cost of cardiovascular (CV) disease in the United States was estimated to be \$448.5 billion in 2008, with direct medical costs estimated to be \$296.4 billion.⁹ Separate costs

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Activity Preview

The use of percutaneous coronary interventions (PCI) for treatment of acute coronary syndromes has improved mortality and morbidity significantly for the majority of patients undergoing these procedures. Primary PCI consists of balloon angioplasty (with or without stenting)—without the previous administration of fibrinolytic therapy or glycoprotein IIb/IIIa inhibitors—to open the infarct-related artery. However, the increasing use of PCI has raised questions about antiplatelet and anticoagulant therapy for these patients, most of whom also receive a stent. While new regimens and new pharmacologic agents have been developed as an adjunct to mechanical revascularization, published guidelines have been unable to keep current with the pace of these advancements and the latest clinical research reports. This monograph, which focuses on antiplatelet therapy used in conjunction with PCI, will help health-system pharmacists keep up to date with the latest developments on this important pharmacologic strategy.

Learning Objectives

At the completion of this activity, the pharmacist will be able to:

- Differentiate among the range of conditions that constitute acute coronary syndromes (ACS).
- Outline current evidence-based guidelines for inpatient treatment of ACS.
- Describe pharmacologic strategies for ACS patients undergoing percutaneous coronary interventions (PCI).
- Summarize new clinical research surrounding antiplatelet therapies.
- Identify ways the health-system pharmacist can impact quality and outcomes for ACS patients undergoing PCI.

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for ACS are not broken out on a national basis. However, a 2005 analysis of costs during the first year after diagnosis of ACS in 13,731 managed care patients quantified the costs at \$2,312 per patient month of follow-up, with 72% of the costs for hospitalizations and 7% for pharmacy.¹⁰

Inpatient Treatment of Patients With ACS

The primary goal of acute treatment for ACS is to restore or improve blood flow to ensure adequate perfusion. The methods vary according to the severity of the patient's condition, the timing of his or her encounter with medical personnel, and the availability of PCI at the hospital where the patient presents.

UA/NSTEMI

There are two treatment pathways for patients with UA/NSTEMI¹:

- Early invasive strategy—coronary angiography within 4 to 24 hours of admission (nonurgently in most, but urgently if there are ongoing ischemic symptoms of hemodynamic or rhythm instability).
- Initial conservative strategy—medical therapy (e.g., aggressive anticoagulation and antiplatelet treatment) with invasive evaluation if the initial therapy fails to relieve symptoms.

STEMI

All patients with STEMI should undergo reperfusion via fibrinolysis with a thrombolytic agent or PCI. In general, fibrinolysis is recommended if (1) symptoms occurred 3 hours or less before medical contact, (2) an invasive strategy is not an option, or (3) there will be a delay of more than 90 minutes from door-to-balloon time and the patient does not have an absolute contraindication to thrombolytic therapy. Fibrinolytic therapy is most effective within 2 hours—especially in the first hour, when it can abort MI and dramatically reduce mortality.¹¹

Primary PCI is recommended if any of the following conditions are met¹¹:

- The door-to-balloon time goal of 90 minutes or less can be achieved.
- Symptom onset was more than 3 hours previously.
- Fibrinolysis is contraindicated (e.g., because of increased risk of bleeding or intracranial hemorrhage).

If the patient presents to a hospital without PCI capability and transfer to a PCI center and administration of PCI within 90 minutes cannot be achieved, then the patient should receive

fibrinolytic therapy (unless contraindicated) within 30 minutes of hospital presentation.¹²

When considering the two modalities, primary PCI has been shown angiographically to restore normal flow in the previously occluded artery in more than 90% of patients, whereas fibrinolytic therapy does so in only 50% to 60% of such patients.⁷

PCI and Antiplatelet Strategies

Debate regarding the timing of primary PCI relative to symptom onset and hospital presentation is ongoing. Clinical investigations and the availability of new agents, dosing regimens, devices, adjunctive treatments, and combinations generate a dynamic process. Thus, the selection of reperfusion strategy remains controversial.¹³

Most PCI candidates today receive a stent to maintain patency of the artery. The increased use of stents has created new challenges. Bare-metal stents (BMS) are associated with restenosis, while drug-eluting stents (DES) are complicated by thrombosis.¹⁴ The two types of drugs implanted on a DES are paclitaxel or sirolimus, which are cell-cycle specific agents inhibiting inflammation and cell proliferation. A DES is generally preferred, provided that the patient's ability to adhere to the recommended duration of dual antiplatelet therapy is confirmed prior to implantation. If a patient is unable to adhere to this therapy, a BMS should be used.¹⁴

To maintain patency of the infarcted artery (i.e., decreasing thrombus buildup and preventing reocclusion) and to potentially minimize microvascular damage, adjunctive antiplatelet and antithrombotic treatments should be included in the management of patients with acute STEMI, regardless of the reperfusion strategy initially employed.¹³ Dual antiplatelet therapy is recommended for UA/NSTEMI patients, regardless of PCI, ideally for a duration of 12 months.¹⁴

This SPECIAL REPORT will focus on the use of antiplatelet agents following PCI, an area where new developments are occurring rapidly and for which the health-system pharmacist can have significant influence.

Antiplatelet Therapy

Dual antiplatelet therapy is the standard of care for patients with ACS undergoing PCI. Using aspirin and a thienopyridine such as clopidogrel provides the benefits of two different classes of medication that target different platelet receptors.² Although aspirin inhibits cyclooxygenase, platelet activation may continue to occur. The thienopyridine drugs inhibit the adenosine diphosphate (ADP) P2Y₁₂ receptors to further help prevent activation and aggregation of platelets.^{15,16} The two agents together inhibit platelet aggregation to a greater extent than either agent alone.²

The original ADP receptor antagonist, ticlopidine, is not a preferred agent because of its potential to cause severe, intolerable side effects such as neutropenia, thrombocytopenia, and diarrhea. Because the glycoprotein IIb/IIIa receptor is the final common pathway to platelet aggregation, inhibiting this complex provides potent antiplatelet activity, more than aspirin with or without clopidogrel. Glycoprotein inhibitors such as abciximab, eptifibatid, and tirofiban are commonly administered intravenously during PCI; they are not used as long-term therapy.¹⁷

Aspirin is the most widely used antiplatelet agent and the first-line defense against recurrent ischemia. Aspirin inhibits cyclooxygenase and thromboxane A₂ and it has been shown to

The ACS Lexicon

- **UA** refers to chest pain or discomfort that is accelerating in frequency or severity.
- **NSTEMI** is a myocardial infarct without complete blockage of the artery.
- **STEMI** is typically caused by the sudden occlusion of a coronary artery that previously was not severely narrowed.
- **NSTE ACS** is a term used to describe UA and NSTEMI, the two less severe forms of ACS.

reduce ischemic events in UA by 50% to 70% compared with placebo.⁵ It is usually administered in a 325-mg dose acutely and then 75 to 162 mg/day for chronic therapy in patients with ACS.^{5,17}

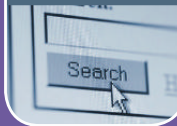
Clopidogrel is a second-generation thienopyridine derivative that inhibits one of the ADP receptors, P2Y₁₂, which provides sustained platelet aggregation. When combined with aspirin, clopidogrel has been shown to be effective and safe in reducing ischemic CV events in patients with UA, NSTEMI, and STEMI.^{2,13,17}

Clopidogrel and aspirin are recommended as dual therapy in current evidence-based guidelines.^{1,2,11,12} However, third-generation thienopyridine P2Y₁₂ receptor antagonists are in clinical development. One, prasugrel, was approved by the U.S. Food and Drug Administration (FDA) in July 2009 for the reduction of atherothrombotic CV events (including stent thrombosis) in patients with ACS who are managed with PCI.¹⁸

The use and dosages of antiplatelet agents vary according to the patient's risk of thrombosis and bleeding. When a stent is implanted, recommendations on the duration of dual antiplatelet therapy are based on the type of stent.¹⁴ Evidence-based guidelines from the American Heart Association (AHA), American College of Cardiology (ACC), and the Society for Cardiovascular Angiography and Interventions (SCAI) for the use of antiplatelet therapy following PCI are summarized in TABLE 1.^{1,11,12,19}

The goal of antiplatelet therapy in post-PCI patients is to maintain a balance between efficacy and bleeding outcomes.²³ The risk of bleeding is increased with dual antiplatelet therapy; a meta-analysis showed an 80% increased relative risk of major bleeding

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How Can You Determine the Risk of Bleeding?

Go to www.crusadebleedingscore.org to use a Bleeding Score Calculator.

Antiplatelet therapy should be given for up to 12 months after DES implantation in patients who are not at high risk of bleeding.^{1,12,17}

This Bleeding Score Calculator helps clinicians estimate a patient's baseline risk of in-hospital bleeding during NSTEMI. It was developed using data from the CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines) Quality Improvement Initiative.

Risk factors for major bleeding:

- Female sex
- Older age
- Renal insufficiency
- Low body weight
- Tachycardia
- High or low systolic arterial pressure
- Low hematocrit
- History of diabetes mellitus

with clopidogrel plus aspirin versus aspirin alone, or an absolute risk of 1.5%.¹⁶ However, the benefit-risk profile still favors the use of dual therapy, with many more patients gaining a benefit from reduced risk of recurrent ischemic events than patients at risk of a major bleeding event.^{16,24}

Clopidogrel

Landmark studies have shown dramatic reductions in acute and subacute stent thrombosis when clopidogrel is used with aspirin.² However, a number of concerns exist about clopidogrel, including its delayed onset of action, moderate antiplatelet effect, high variability in response among patients, and potential drug-drug interactions. Evidence from clinical trials suggests that a lower response rate in patients receiving clopidogrel can lead to increased risks of MI and stent thrombosis.^{23,25}

Variability in response to antiplatelet drugs is well known; clopidogrel nonresponsiveness occurs in up to 30% of patients.² It has been suggested that this variability may be due to pharmacogenomic differences in the way an individual metabolizes clopidogrel or caused by other drugs that may interfere with how the body metabolizes clopidogrel.²⁶

Because clopidogrel is metabolized by cytochrome P450 2C19, there is concern about potential interaction with proton pump inhibitors (PPIs). PPIs are often coadministered with antiplatelet agents to reduce the potential for gastrointestinal bleeding, however there is no clear evidence that doing so reduces the incidence of bleeding. Current guidelines recommend decreasing the aspirin dosage in patients with a history of gastrointestinal bleeding rather than administering a PPI.¹⁷

These concerns have led to an Ongoing Safety Review of clopidogrel by the FDA. Additional studies are under way to investigate the effects of genetic factors and other drugs on the effectiveness of clopidogrel. Until those results are known, FDA recommends that health care providers should continue to prescribe clopidogrel and should reevaluate the need for starting or continuing treatment with a PPI. Patients taking clopidogrel should check with their health care provider if they are taking or considering taking a PPI, including over-the-counter products.²⁶

Other studies are investigating the duration of therapy

Table 1. ACC/AHA/SCAI Guidelines for Antiplatelet Therapy Following Percutaneous Coronary Interventions

Aspirin	Clopidogrel
<p>Patients without aspirin allergy and not at increased risk of bleeding:</p> <ul style="list-style-type: none"> • 162–325 mg/day for a minimum of: <ul style="list-style-type: none"> – 1 month after implantation of BMS – 3 months after implantation of DES containing sirolimus – 6 months after implantation of DES containing paclitaxel • 75–162 mg/day subsequently, indefinitely^{a,b} 	<p>Patients not at an increased risk of bleeding:</p> <ul style="list-style-type: none"> • 75 mg/day for a minimum of: <ul style="list-style-type: none"> – 1 month after implantation of BMS – 3 months after implantation of DES containing sirolimus – 6 months after implantation of DES containing paclitaxel • Ideally up to 12 months
<p>Patients at increased risk of bleeding:</p> <ul style="list-style-type: none"> • 75–162 mg/day during initial period after stent implantation 	<p>Patients at increased risk of bleeding:</p> <ul style="list-style-type: none"> • 75 mg/day for minimum of 2 weeks

^a Available dose in the United States is 81 mg.

^b Guidelines from the American College of Chest Physicians recommend that the aspirin dose for all patients with acute coronary syndrome be reduced to 75–100 mg/day when given with another antiplatelet agent to minimize hemorrhagic risk.

ACC = American College of Cardiology; AHA = American Heart Association; BMS = bare-metal stent; DES = drug-eluting stent; SCAI = Society for Cardiovascular Angiography and Interventions.

Source: References 12, 14, and 19–22.

after stent implantation, pharmacologic interactions between clopidogrel and statins, and the value of triple antiplatelet therapies.^{17,27}

Prasugrel

More potent platelet aggregation inhibitors are being developed for use in patients with ACS. The newest P2Y₁₂ receptor antagonist is prasugrel, a novel oral thienopyridine with a more rapid onset of action than clopidogrel.^{2,28}

In laboratory tests, prasugrel was more potent than clopidogrel, and its slightly different kinetics provided faster, higher, and more consistent inhibition of platelet aggregation than clopidogrel.⁵ Prasugrel also showed less inter-individual response variability compared with clopidogrel. Clinical investigators have suggested that high-risk ACS patients may achieve better outcomes with prasugrel than clopidogrel.^{25,27,29,30}

In a randomized clinical trial comparing prasugrel with clopidogrel (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel–Thrombolysis in Myocardial Infarction [TRITON-TIMI] 38), 13,608 moderate- to high-risk patients with ACS received a prasugrel 60-mg loading dose followed by a 10-mg daily maintenance dose or a clopidogrel 300-mg loading dose followed by a 75-mg daily maintenance dose, for up to 15 months. The prasugrel-treated patients experienced a greater reduction in the primary composite endpoint of CV death, nonfatal MI, or nonfatal stroke than clopidogrel-treated patients (12.1% vs 9.9%; $P < .001$). The rate of stent thrombosis was significantly reduced in the prasugrel group (2.4% vs 1.1%; $P < .001$). However, overall mortality did not differ significantly between the two groups.^{5,30-32}

Prasugrel's greater platelet inhibitory effect also was responsible for increased rates of major bleeding. In the trial, life-threatening bleeding was greater in the prasugrel group.^{25,31} This led the FDA to require a black box warning of bleeding risk in the prasugrel labeling. This warning states that prasugrel can cause significant, sometimes fatal, bleeding and should not be used in patients with active pathological bleeding or a history of transient ischemic attack or stroke. Prasugrel is generally not recommended in patients aged 75 years or older because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk patients (those with diabetes or prior MI) where its benefits may outweigh the risks. Prasugrel should not be administered to patients likely to undergo urgent coronary artery bypass graft (CABG) surgery and should be discontinued at least 7 days prior to any surgery. Additional risk factors for bleeding include body weight less than 60 kg (132 lb), propensity to bleed, and concomitant use of medications that increase the risk of bleeding. Clinicians are advised to suspect bleeding in any patient taking prasugrel who becomes hypotensive and has recently undergone coronary angiography, PCI, CABG, or other surgical procedures. It is also recommended that bleeding be controlled if possible without discontinuing prasugrel, because stopping prasugrel in the first few weeks after ACS increases the risk of subsequent CV events.³²

The benefit of prasugrel appears to be greatest in ACS patients with diabetes.²⁴ Patients with both ACS and diabetes are at higher risk of recurrent atherothrombotic events, attributed to increased platelet reactivity. They may also have a higher prevalence of impaired responsiveness to clopidogrel. In a subset of TRITON-TIMI 38 (3,146 diabetic patients with and without insulin therapy), prasugrel led to a greater reduction in ischemic events compared

with clopidogrel. Moreover, this reduction was achieved without an increase in major bleeding events in this group.²⁵

Other patients most likely to benefit from prasugrel are those younger than 75 years of age with no history of stroke.³³ The target population for prasugrel includes patients with diabetes and those at high risk of thrombo-occlusive events, specifically^{24,28}:

- Patients undergoing PCI and those with STEMI.
- Patients at risk of stent thrombosis and after stent thrombosis.
- Diabetic patients undergoing PCI.
- Patients with genetic variants resulting in nonresponsiveness to clopidogrel.

Additional next-generation agents are under development optimally to reduce both ischemic and hemorrhagic events. These include the reversible ADP receptor antagonists ticagrelor (AZD6140) and cangrelor.^{2,5}

Role of the Health-System Pharmacist

In the hospital, pharmacists can make sure that clinicians treating patients with ACS are following current evidence-based guidelines for the use of PCI and antiplatelet therapy.³⁴ This type of guidance can help to ensure optimal performance on The Joint Commission surveys and various performance measures increasingly used to rate hospitals. Moreover, from a clinical point of view, doing so improves patient outcomes.^{10,35,36} According to data from the Global Registry of Acute Coronary Events (GRACE) of 44,372 patients, improvements in the management of patients with ACS were associated with significant reductions in the rates of new heart failure and mortality as well as decreased rates of stroke and MI at 6 months.^{35,37}

Educating clinicians about new medications and clinical trial results, ensuring that the proper dosages of antiplatelet medications are used, and making sure patients on antiplatelet therapy are monitored for bleeding are among the contributions that pharmacists can make in optimizing therapeutic outcomes in patients with ACS.³⁸

Pharmacists should be aware of the indications for dual antiplatelet therapy and the appropriate duration of dual antiplatelet therapy in patients undergoing PCI. Patients receiving a DES must be carefully selected to ensure long-term adherence to dual antiplatelet therapy to minimize the risk of late stent thrombosis. Dual therapy should be continued for at least 1 month in patients receiving a BMS, for 3 to 6 months in patients receiving a DES, and ideally for 1 year or longer.¹⁴

Upon patients' hospital admission, pharmacists should participate in the reconciliation of current medications to check for interactions with potential ACS therapies. Furthermore, pharmacists should take an active role in ensuring proper dosage of current and new medications both in the hospital and upon discharge.

Minimizing the risk of recurrent CV events requires optimizing patient adherence to prescribed therapies and lifestyle modifications.¹ Adherence is a critical requirement for patients on antiplatelet therapy. Even with dual antiplatelet therapy, many patients continue to have recurrent atherothrombotic events (stent restenosis and thrombosis) after PCI. Approximately 10% of PCI patients will experience MI, stroke, or CV death. Factors contributing to failure with dual antiplatelet therapy include lack of prescribing and nonadherence.^{23,39}

Patients and providers must be educated about the potential

Table 2. Counseling Patients About Antiplatelet Therapy

- Advise patients against taking the medication and to notify the prescriber if they have active bleeding (e.g., abdominal bleeding [ulcer], brain hemorrhage) or a history of stroke or transient ischemic attack.
- Inquire about other medications the patient is taking, particularly other antithrombotic medications.
- Inform patients that their antiplatelet medication will prolong blood clotting. Therefore, they are at a higher risk of bleeding if they experience trauma or have severe liver disease or ulcer.
- Advise patients that, while taking an antiplatelet medication, they will bruise and bleed more easily and are more likely to have nose bleeds. It will take longer for any bleeding to stop.
- Tell patients to call their health care provider right away if they have any of these signs or symptoms of bleeding:
 - Unexpected bleeding or bleeding that lasts a long time
 - Bleeding that cannot be controlled
 - Blood in their urine (urine appears pink or brown)
 - Red or black tarry stools
 - Bruises that appear without a known cause or that get larger
 - Coughing up blood or blood clots
 - Blood in their vomit (vomit will look like coffee grounds)
- Stress the need for long-term adherence. Emphasize that the patient should not stop taking the medication without talking to the physician who prescribed it. These medications are recommended as ongoing therapy for at least 1 year, depending on tolerability. Patients who have stopped taking their medication too soon have experienced blood clots in their stents, heart attacks, and death.
- Tell patients to inform all of their health care providers, including dentists, about their use of antiplatelet medication. Patients may need to interrupt therapy for 5 to 7 days prior to surgery but should do so only on the advice of the prescribing physician.
- Explain the risks of thrombotic thrombocytopenic purpura. Alert patients of the warning signs and advise them to get medical help right away if they experience:
 - Purpura (purplish spots) on the skin or mucous membranes (e.g., in the mouth)
 - Paleness or jaundice
 - Weakness or tiredness
 - Fever
 - Fast heart rate or shortness of breath
 - Headache, speech changes, confusion, coma, stroke, or seizure
 - Low urine output
 - Abdominal pain, nausea, vomiting, or diarrhea
 - Visual changes

Source: References 32, 39, 41, and 42.

hazards associated with premature discontinuation of dual antiplatelet therapy.²⁰ The number one predictor of stent thrombosis after DES placement is premature discontinuation of thienopyridine therapy.²³ Such patients are more likely to die during the ensuing 11 months or to require rehospitalization.¹⁴ Hence, it is critical that clinicians explicitly emphasize medication adherence with dual antiplatelet therapy, especially when DES stents are used.²³

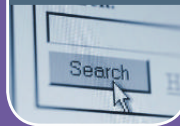
Oral anti-ischemic, antiplatelet, and other secondary preventive medications generally should be continued after discharge.¹ The pharmacist can help to optimize long-term outcomes by making sure that antiplatelet medications have been prescribed for sufficient duration. The reasons for non-use of antiplatelet therapy after NSTEMI ACS in a French survey of discharged patients were failure to prescribe at hospital discharge (22.8%) or prescription for only 1 month.⁴⁰ Other factors associated with premature discontinuation include affordability of medication, lack of referral to rehabilitation, no discharge medication instructions, inadequate patient education, and older age.^{23,39}

At discharge, all patients with ACS should receive detailed instructions including education on medications, diet, exercise, and smoking cessation (if relevant).¹ TABLE 2 presents specific advice for patients taking antiplatelet agents.

Conclusion

The classification of ACS provides a framework to guide therapeutic strategies. Along with PCI, platelet inhibition is an integral component of ACS treatment. It is of proven benefit in reducing the risk of major CV events (including death) in patients with ACS. The goal of antiplatelet therapy in post-PCI patients is to maintain a balance between efficacy and bleeding outcomes. The pharmacist can assist in achieving this goal by educating clinicians

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How Can You Improve Adherence to Antiplatelet Therapy?

The Science Advisory “Prevention of Premature Discontinuation of Dual Antiplatelet Therapy in Patients With Coronary Artery Stents” provides essential information for pharmacists and their patients receiving antiplatelet therapy.³⁹

Go to <http://content.onlinejacc.org/cgi/reprint/49/6/734.pdf> to view the advisory statement online.

on evidence-based guidelines, the latest clinical research findings, and the availability of new pharmacologic agents. Furthermore, clinical outcomes can be improved with patient counseling regarding warning signs of bleeding to report to their health care provider and education on the importance of adhering to long-term therapy with their antiplatelet medication.

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Inpatient Treatment of Acute Coronary Syndromes: Pharmacologic Implications

Instructions: The assessment questions printed below allow you to preview the online CPE exam. Please review all of your answers to be sure you have marked the proper letter on the online CPE exam. There is only one correct answer to each question.

- 1. NSTEMI is an acute coronary condition that is:**
 - a. Characterized by complete occlusion of a coronary artery.
 - b. An MI without complete blockage of a coronary artery.
 - c. Caused by increasing or accelerating chest pain.
 - d. Associated with necrosis of myocardial tissue.
- 2. In the United States, ACS affects an estimated:**
 - a. 500,000 people.
 - b. 1.3 to 1.4 million people.
 - c. 2.1 million people.
 - d. 3 million people.
- 3. Patients with STEMI should:**
 - a. Undergo fibrinolysis before an invasive intervention.
 - b. Receive pharmacologic reperfusion if their symptoms occurred 6 hours previously.
 - c. Be treated initially with aggressive warfarin and antiplatelet therapy.
 - d. Undergo primary PCI if it can be done within 90 minutes of hospital arrival.
- 4. The use of primary PCI:**
 - a. Involves implantation of a BMS in the majority of patients.
 - b. Restores normal blood flow in up to 75% of patients.
 - c. Restores normal blood flow in more than 90% of patients.
 - d. Is equally effective as fibrinolysis for reperfusion in patients with STEMI.
- 5. Antiplatelet therapy is important in ACS patients because:**
 - a. Platelets activated by rupture of arterial plaque aggregate.
 - b. Damage to a coronary artery destroys platelets.
 - c. It promotes the release of ADP.
 - d. Patients with ACS have a lack of platelets.
- 6. The most widely used antiplatelet agent in ACS is:**
 - a. Clopidogrel.
 - b. Aspirin.
 - c. Abciximab.
 - d. Ticlopidine.
- 7. The antiplatelet agent clopidogrel:**
 - a. Is the only available oral thienopyridine derivative.
 - b. Is the only antiplatelet agent recommended in evidence-based guidelines.
 - c. Inhibits the ADP P2Y₁₂ receptor.
 - d. Inhibits thromboxane A₂.
- 8. A patient with STEMI has recently undergone PCI with a DES (containing sirolimus) implanted in his right coronary artery. He is not at high risk of bleeding and is started on clopidogrel with aspirin. Ideally, how long should his clopidogrel therapy be continued?**
 - a. 1 month.
 - b. 3 months.
 - c. 6 months.
 - d. 12 months.
- 9. Nonresponsiveness to clopidogrel:**
 - a. Occurs in more than 30% of patients.
 - b. Is due to its delayed onset of action.
 - c. May be related to variations in patients' metabolism of the drug.
 - d. Is not associated with long-term risks.
- 10. Clinical studies have demonstrated that prasugrel is:**
 - a. Superior to clopidogrel in reducing stent thrombosis.
 - b. Not as potent as clopidogrel.
 - c. Similar to other thienopyridines in its onset of action.
 - d. Safe to use in patients undergoing CABG surgery.

CPE Instructions

Completing a posttest at www.pharmacist.com/education is as easy as 1-2-3...

1. Go to **Online CPE Quick List** and click on the title of this activity.
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