Coronary Artery Disease
ST Elevation Myocardial Infarction
(2009)
Philippine Heart Association, Inc.

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ALGORITHM

* Initial management of AMI should be instituted: supplemental oxygen during the first 6 hours; aspirin 160-325mg tablet to be chewed; nitrates sublingual or IV; morphine 2-4mg IV for chest pain relief; anti-platelets and anticoagulants; beta-blockers if no contraindication; ACE-I
SUMMARY OF STATEMENTS

Statement 1: Pre hospital recognition
It IS RECOMMENDED that patients with symptoms of chest discomfort, shortness of breath, diaphoresis, nausea, weakness should be immediately brought to the nearest emergency room of a hospital.

Statement 2: Initial evaluation at the Emergency Room (ER)
It IS STRONGLY RECOMMENDED that a detailed history taking, physical examination and a 12-lead ECG be taken within 10 minutes of arrival at the ER.

Statement 3: ECG evaluation
It IS RECOMMENDED that patients presenting with chest discomfort and ECG finding of at least 0.1 mV ST segment elevation in two contiguous leads and without any contraindications should receive reperfusion therapy either primary PCI (in hospitals with PCI capability) or with thrombolytics (in hospitals without PCI capability).

Statement 4: Initial Treatment at the Emergency Room
It IS RECOMMENDED that the following routine treatment measures should be administered to STEMI patients upon arrival at the ER (unless with contraindication)
- Supplemental oxygen during the first 6 hours
- Aspirin 160 – 325 mg tablet (non enteric coated, chewed)
- Nitrates, sublingual or IV (contraindicated in patients with hypotension or those who took sildenafil within 24 hrs)
- Morphine 2-4 mg IV for relief of chest pain

Statement 5: Thrombolysis or fibrinolytic therapy
STEMI patients presenting to a hospital without facilities for primary percutaneous coronary intervention (PCI) IS RECOMMENDED to undergo immediate thrombolysis unless contraindicated with a door to needle time < 30 minutes as goal.

Statement 6: Catheter-based therapy
It IS RECOMMENDED that STEMI patients presenting to a PCI capable hospital and with a skilled operator available should be treated with primary PCI within 90 minutes of first medical contact.

Statement 7: Immediate Surgical Reperfusion
Emergency or urgent CABG IS RECOMMENDED in patients with STEMI in the following circumstances: failed PCI with persistent pain or hemodynamic instability, persistent and recurrent ischemia refractory to medical therapy in patients who are not candidates for PCI or fibrinolytic therapy, cardiogenic shock with left main or severe multivessel disease, and at the time of surgical repair of post-infarct ventricular septal rupture or mitral valve insufficiency.

Statement 8: Hospital management of STEMI
General recommendations for patient with STEMI in Coronary Care Unit
1. STEMI patients should be immediately admitted to a quiet and comfortable environment with qualified personnel, on continuous ECG monitoring, pulse oximetry and has ready access to facilities for hemodynamic monitoring and defibrillation
2. Administer aspirin and betablockers in adequate dose to control heart rate and assess the need for intravenous nitroglycerin for control of angina, hypertension, and heart failure
3. When stable for 6 hours, the patient should be reassessed for oxygen need (i.e., saturation of less than 90%) and discontinuation of supplemental oxygen should be considered
4. Nursing care should be provided by individuals knowledgeable in critical care

Statement 9: Risk Stratification of STEMI patients
It IS RECOMMENDED that STEMI patients should be stratified into high-risk patients and low-risk patients.

Statement 10: Hemodynamic Assessment
It IS RECOMMENDED that high–risk patients with mechanical complications of STEMI and/or progressive hypotension should have pulmonary artery catheter and intra-arterial pressure monitoring. Intra-aortic balloon counter-pulsation and early revascularization should be considered.

Statement 11: Management of Arrhythmias after STEMI
The following statements are the general recommendations of Management of Arrhythmias after STEMI:
1. Ventricular Fibrillation (VF) or pulseless VT: Immediate cardioversion with 120 J to 200 J using a manual...
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biphasic defibrillator. Give a single 360 J using a monophasic defibrillator.

2. Ventricular Tachycardia (VT): Sustained (>30 sec or causing hemodynamic collapse) polymorphic VT: Unsynchronized electric shock initially at 200 J; if unsuccessful, a 2nd shock of 200-300 J.

3. Sustained monomorphic VT associated with angina, pulmonary edema, or hypotension: synchronized electric shock of 100 J and increasing the energies if initially unsuccessful

4. Sustained monomorphic VT not associated with angina, pulmonary edema, or hypotension: Amiodarone, 150 mg for 10 min; repeat 150 mg 10-15 minutes as needed. Alternative infusion: 360 mg over 6 hours, then 540 mg over the next 18 hours and synchronized electrical cardioversion starting at 50 J.

5. Treatment of isolated ventricular premature beats, couplets, and nonsustained VT with no hemodynamic compromise is not recommended.

6. Sustained atrial fibrillation (AF) and atrial flutter with hemodynamic compromise or ongoing ischemia: Synchronized cardioversion with an initial 200 J for AF and 50 J for flutter. If unresponsive or recurrent: intravenous amiodarone and intravenous digoxin may be used to slow the ventricular response.

7. Sustained AF and atrial flutter with ongoing ischemia but without hemodynamic compromise should be treated with one or more of the following: Beta-adrenergic blockade (preferred), intravenous diltiazem or verapamil, synchronized cardioversion.

8. Reentrant paroxysmal SVT should be treated with the following in sequence: carotid sinus massage, IV adenosine, IV metoprolol or atenolol, IV diltiazem, IV digoxin.

9. Ventricular asystole. Prompt resuscitative measures, including chest compressions, atropine, vasopressin, epinephrine, and temporary pacing, should be administered to treat ventricular asystole.

Statement 12: Statement on Permanent Ventricular Pacing

It IS RECOMMENDED that Permanent Ventricular Pacing be placed in the following conditions:

1. Persistent second-degree AV block in the His-Purkinje system with bilateral bundle-branch block or third-degree AV block within or below the His-Purkinje system after STEMI.

2. Transient advanced second- or third-degree infra-nodal AV block and associated bundle branch block.

3. Persistent and symptomatic second- or third-degree AV block

Statement 13: Statement on Implantable Cardioverter Defibrillator

It IS RECOMMENDED that Implantable Cardioverter Defibrillator be placed in the following conditions:

1. Patients with VF or hemodynamically sustained VT more than 2 days after STEMI (provided that VF or VT is not judged to be due to transient or reversible ischemia or reinfarction)

2. Patients with VF or sustained VT more than 48 hours after STEMI whose STEMI occurred at least 1 month previously, with an LVEF between 0.31 and 0.40, and have inducible VF or VT on electrophysiologic testing.

Statement 14: Anticoagulant Therapy

It IS RECOMMENDED that patients undergoing reperfusion therapy with fibrinolytics receive anticoagulant therapy for a minimum of 48 hours and preferably for the duration of the index hospitalization, preferably up to 8 days.

Statement 15: Antiplatelet therapy

It IS RECOMMENDED that Clopidogrel 75 mg per day orally be added to aspirin in patients with STEMI and maintained for at least 14 days.

PHARMACOLOGIC THERAPY

Statement 16: Beta Blocker therapy

It IS STRONGLY RECOMMENDED that beta blocker therapy be started within 24 hours of STEMI in the absence of contraindication (frank heart failure, hypotension, heart block, active asthma or reactive airway disease, increased risk of cardiogenic shock i.e age more than 70, SBP less than 120 mmHg, heart rate greater than 110, Killips greater than class 1 and in the presence of concomitant hypertension or uncontrolled blood pressure).

Statement 17: Anti-cholesterol Agents: Statins

High dose statins MAY BE RECOMMENDED within 1st 24 hours of admission in the absence of contraindication (such as known allergy, active liver disease).

Statement 18: Angiotensin Converting Enzyme inhibitors (ACE-I)

It IS STRONGLY RECOMMENDED that ACE-I be started within 24 hours in patients with anterior infarction, pulmonary congestion or left ventricular ejection fraction (LVEF) of <= to 40% and continued indefinitely among patients with LVEF <= to 40%, hypertension, diabetes or chronic kidney disease (CKD).

ACE-I MAY BE RECOMMENDED among lower risk patients (S/P revascularization procedures, controlled cardiovascular risk factors, normal ejection fraction recovering from STEMI).
I. RECOMMENDATIONS ON INITIAL PATIENT EVALUATION

Statement 1: Pre hospital recognition

It is RECOMMENDED that patients with symptoms of chest discomfort, shortness of breath, diaphoresis, nausea, weakness be immediately brought to the nearest emergency room of a hospital.

Morbidity and mortality from ST elevation myocardial infarction (STEMI) can be reduced by early recognition of symptoms and timely medical consultation and institution of treatment. Patients and their relatives should be given information on how to recognize signs and symptoms of STEMI and should be informed of the urgency of seeking medical attention.

If the patient has been previously prescribed nitroglycerin, it is recommended that the patient be advised to take ONE nitroglycerin dose sublingually for chest discomfort. If the symptoms are unimproved or is worsening after five minutes, it is recommended that the patient seek medical consult without further delay. Taking additional doses of nitroglycerin or other medications is no longer recommended as to avoid further delay in seeking medical attention.

Statement 2: Initial evaluation at the Emergency Room (ER)

It is STRONGLY RECOMMENDED that a detailed history taking, physical examination and a 12 lead ECG be taken within 10 minutes of arrival at the ER.

The objective of initial evaluation is for the physician to rapidly and reliably diagnose STEMI and to determine the patient’s eligibility for reperfusion therapy. The patient should be placed on a cardiac monitor immediately, with emergency resuscitation equipment including a defibrillator, nearby.

The targeted history taken in the ER should be detailed enough to establish the probability of STEMI but should be obtained rapidly so as not to delay reperfusion therapy. The history should focus on the chest discomfort and associated symptoms, considering age and sex related differences in presentation. The chest discomfort is often described as constricting or like a sensation of something heavy on the chest. The location is usually substernal but may originate or radiate to areas such as the neck, jaw, interscapular area, upper extremities and epigastrium. The discomfort may wax and wane and typically last longer than 30 minutes. Associated symptoms of diaphoresis, nausea and vomiting, light headedness as well as weakness and fatigue may occur. Women generally present at an older age than men. Elderly patients are less likely to complain of chest discomfort and more often present with shortness of breath, nausea or syncope.

Prior episodes of myocardial ischemia, infarction, percutaneous coronary intervention (PCI) or bypass surgery, as well as co morbid illnesses including hypertension, diabetes mellitus, possibility of aortic dissection, risk of bleeding and clinical cerebrovascular disease should be sought. Severe tearing pain radiating to the back...
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associated with dyspnea or syncope without ECG changes indicative of myocardial ischemia or infarction should raise the possibility of aortic dissection (see Table 1 for differential diagnosis for Acute Myocardial Infarction [AMI]). However, previous bleeding problems, history of ulcer disease, cerebral vascular accidents, and unexplained anemia should be sought since they can be exacerbated with the use of fibrinolytics, anti-platelets and antithrombins in the treatment of STEMI.

A brief physical examination should be performed to aid in the diagnosis and assessment of the extent, location and presence of complications of STEMI. A limited neurologic examination to look for evidence of prior stroke or cognitive deficits should be performed before administration of fibrinolytic therapy.

<table>
<thead>
<tr>
<th>Table 1. Differential Diagnosis for AMI</th>
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<tr>
<td><strong>Life Threatening</strong></td>
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<td>Aortic Dissection</td>
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<td>Pulmonary embolus</td>
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<td>Perforating Ulcer</td>
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<td>Boerhave Syndrome (Esophageal rupture with mediastinitis)</td>
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<td>Pericarditis</td>
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<td>Atypical Angina</td>
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<td>Early repolarization</td>
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<td>Wolff-Parkinson-White Syndrome</td>
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<td>Deeply Inverted T waves suggestive of central nervous system lesion or apical hypertrophy</td>
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<td>LV hypertrophy with strain</td>
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<td>Brugada Syndrome</td>
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<td>Hyperkalemia</td>
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<td>Bundle Branch Block</td>
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<td>Vasospastic Angina</td>
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<tr>
<td>Hypertrophic Cardiomyopathy</td>
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<td><strong>Other Non Cardiac</strong></td>
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<td>Gastroesophageal reflux (GERD) and spasm</td>
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<td>Chest wall pain (Pleurisy)</td>
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<td>Peptic Ulcer disease</td>
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<td>Biliary or pancreatic pain</td>
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<td>Cervical disc or neuropathic pain</td>
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<td>Somatization and psychogenic pain disorder</td>
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An ECG should be taken and shown to an experienced physician within 10 minutes of arrival in the ER. If STEMI is present, a decision whether the patient will be treated with fibrinolytic therapy or PCI should be made within 10 minutes. If the initial ECG is not diagnostic and the patient remains symptomatic, and there is a high clinical suspicion for STEMI, serial ECG’s at 5-10 minute interval or continuous ST segment monitoring should be done.

Statement 3: ECG

It is RECOMMENDED that patients presenting with chest discomfort and ECG finding of at least 0.1 mV ST segment elevation in two contiguous leads and without any contraindications receive reperfusion therapy either primary PCI (in hospitals with PCI capability) or with thrombolytics (in hospitals without PCI capability).

The presence of at least 0.1 mV ST segment elevation in two contiguous ECG leads identifies patients who benefit from reperfusion therapy. Fibrinolytic therapy has no evidence of benefit for patients with normal ECG or non specific changes and with some evidence of harm for patients with ST segment depression only. Patients presenting with marked ST segment depression in leads V1 to V4 accompanied by tall R waves in the right precordial leads and upright T waves may have true posterior infarction and may also benefit from fibrinolytic therapy. Patients with new or presumably new LBBB are at high risk when presenting with presumed MI. It has been suggested that these patients be approached with a plan to rule in MI using 1 of 3 ECG criteria that provide independent diagnostic value. These are: 1) ST elevation greater than or equal to 0.1 mV in leads with positive QRS, 2)ST depression greater than or equal to 0.1 mV in leads V1- V3 and 3) ST elevation greater than or equal to 0.5 mV in leads with negative QRS.

Statement 4: Initial Treatment at the ER

It is RECOMMENDED that the following routine treatment measures be administered to STEMI patients upon arrival at the ER (unless with contraindication)

1. Supplemental oxygen during the first 6 hours
2. Aspirin 160 - 325 mg tablet (non enteric coated, chewed)
3. Nitrates, sublingual or IV (contraindicated in patients with hypotension or those who took sildenafil within 24 hrs)
4. Morphine 2-4 mg IV for relief of chest pain

Supplemental oxygen should be administered to patients suspected of STEMI particularly for those with oxygen saturation of less than 90% on pulse oximetry. The rationale for the use of oxygen is based on the observation that even with uncomplicated AMI; some patients are modestly hypoxemic initially, presumably because of ventilation perfusion mismatch and excessive lung water.

Patients with ongoing ischemic discomfort should receive sublingual nitroglycerin (0.4 mg) every 5 minutes for a total of 3 doses, after which an assessment should be made about the need for intravenous nitroglycerin. Intravenous nitroglycerin is indicated for the relief of ongoing ischemic chest discomfort, control of hypertension, or management of pulmonary congestion. Nitrites should be avoided in patients with initial systolic blood pressures of less than 90 mmHg or greater than or equal to 30 mmHg below baseline, marked bradycardia, or known or suspected RV infarction. Nitrites should not be administered to patients who received phosphodiesterase inhibitors.
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(e.g. sildenafil) within 24 hours because of the danger of profound hypotension from the potentiation of the hypotensive effect of the nitrates.

Morphine sulfate (2-4 mg IV with increments of 2-8 mg IV repeated at 5-15 minute intervals) is the analgesic of choice for management of pain associated with STEMI.

Pain relief is an important element in the management of patients with STEMI and should be directed toward acute relief of symptoms of myocardial ischemia and the relief of anxiety and apprehension. Anxiety reduction secondary to morphine reduces the patient’s restlessness and adrenergic stimulation with resulting reduction in cardiac metabolic demand. Morphine is also beneficial in patients with heart failure and pulmonary edema.

Aspirin at a dose of 160 to 325 mg should be chewed by the patient who has not yet taken aspirin before presentation with STEMI. More rapid buccal absorption occurs with non-enteric-coated aspirin formulations. The Second International Study of Infarct Survival (ISIS 2)\(^1\) have shown conclusively the efficacy of aspirin alone (ARR 2.4%, RRR 23% in 35 day mortality) and combined with streptokinase (ARR 5.2%, RRR 42%) in the treatment of evolving acute MI. Aspirin should not be given in those with hypersensitivity to salicylates, instead clopidogrel or ticlopidine should be given.

**II. RECOMMENDATIONS ON HOSPITAL CARE**

**Statement 5: Thrombolysis or fibrinolytic Therapy**

STEMI patients presenting to a hospital without facilities for primary percutaneous coronary intervention (PCI) IS RECOMMENDED to undergo immediate thrombolysis unless contraindicated with a door to needle time < 30 minutes as goal.

The cardinal goal of treatment for all STEMI patients is to consider reperfusion therapy and to initiate such therapy as quickly as possible in patients presenting at the emergency room < 12 hours from onset of chest pain. The choice of reperfusion therapy will depend on the clinical presentation of the patient, the availability of resources and expertise, cost consideration and the patient’s preference. Thrombolysis is recommended if the clinical presentation is < 3 hours from onset of chest pain, there is lack of access to a skilled PCI laboratory, or a delay is expected of invasive strategy (prolonged transport time or catheterization laboratory occupied).

The clinician should assess the adequacy of reperfusion by monitoring the pattern of ST elevation (reduction of at least 50% of the initial ST-segment elevation injury pattern), cardiac rhythm and clinical symptoms over 90 minutes after initiation of thrombolytic therapy.\(^2\)

**Contraindications and cautions for fibrinolysis in STEMI**

(Viewed as advisory for clinical decision making and may not be all-inclusive or definitive)

**Absolute Contraindications:**
- Any prior intracranial hemorrhage

**Relative Contraindications:**
- History of chronic, severe, poorly controlled hypertension
- Severe uncontrolled hypertension on presentation (SBP greater than 180 mmHg or DBP greater than 110 mmHg)*
- History of prior ischemic stroke greater 3 months, dementia, or known intracranial pathology not covered in contraindications
- Traumatic or prolonged (greater than 10 minutes) CPR or major surgery (less than 3 weeks)
- Recent (within 2-4 weeks) internal bleeding
- Non compressible vascular punctures
- For streptokinase/anistreplase: prior exposure (more than 5 days ago) or prior allergic reaction to these agents
- Pregnancy
- Active peptic ulcer disease
- Current use of anticoagulants: the higher the INR, the higher the risk of bleeding

* Could be an absolute contraindications in low-risk patients with MI

**Statement 6: Catheter-based therapy**

It IS RECOMMENDED that STEMI patients presenting to a PCI capable hospital and with an available skilled operator be treated with primary PCI within 90 minutes of first medical contact.

Generally preferred also in the following conditions:
1. PCI capable laboratory available with surgical back-up
2. High risk patient (cardiogenic shock, pulmonary edema)
3. Contraindication to thrombolysis
4. Late presentation (>3 hours from onset of chest pain)

Interhospital transfer to PCI capable hospital is recommended for patients presenting with cardiogenic shock, hemodynamic instability and patients with failed thrombolysis for rescue PCI purposes.

**Statement 7: General recommendations on hospital management of STEMI**

**General recommendations for patient with STEMI in Coronary Care Unit**

1. STEMI patients are recommended to be immediately admitted to a quiet and comfortable environment with qualified personnel, on continuous ECG monitoring,
pulsed oximetry and has ready access to facilities for hemodynamic monitoring and defibrillation.

2. It is recommended to administer aspirin and beta-blockers in adequate dose and assess the need for intravenous nitroglycerin for control of angina, hypertension, and heart failure.

3. It is recommended that patient be reassessed for oxygen need (i.e., saturation of less than 90%) if stable for 6 hours, and discontinuation of supplemental oxygen should be considered.

4. Nursing care should be provided by individuals knowledgeable in critical care.

**Statement 8: Risk Stratification**

It IS RECOMMENDED that STEMI patients be stratified into high-risk patients and low-risk patients:

High-risk patients are those with recurrent ischemia, reinfarction, life-threatening arrhythmias (sustained ventricular tachycardia or fibrillation, high-degree atrioventricular block, or major supraventricular arrhythmias), or clinical evidence of pump dysfunction (rales or hypotension); those with mechanical complications of infarction (cardiogenic shock, ventricular septal defect, acute mitral regurgitation, and free-wall rupture).

Low-risk patients: absence of recurrent ischemia, heart failure, or hemodynamically compromising arrhythmias. Low-risk patients who have undergone successful PCI should be admitted directly to telemetry or regular room in close supervision for post PCI care rather than in CCU. Further, low risk STEMI patients who demonstrate 12-24 hours of clinical stability should be transferred out of CCU.

**Statement 9: Hemodynamic Assessment**

It IS RECOMMENDED that high-risk patients with mechanical complications of STEMI and/or progressive hypotension have pulmonary artery catheter and intraarterial pressure monitoring. Intra-aortic balloon counter-pulsation and early revascularization should be considered.

**Statement 10: Management of Arrhythmias after STEMI**

The following statements are the general recommendations of Management of Arrhythmias after STEMI:

1. Ventricular Fibrillation (VF) or pulseless VT: Unsynchronized electric shock with initial shock energy of 200 J; if unsuccessful, a second shock of 200-300 J should be given, and if necessary, a third shock of 360 J.

2. Ventricular Tachycardia (VT): Sustained (>30 sec or causing hemodynamic collapse) polymorphic VT: Unsynchronized electric shock initially at 200 J; if unsuccessful, a 2nd shock of 200-300 J.

3. Sustained monomorphic VT associated with angina, pulmonary edema, or hypotension: synchronized electric shock of 100 J and increasing the energies if initially unsuccessful.

4. Sustained monomorphic VT not associated with angina, pulmonary edema, or hypotension: Amiodarone, 150 mg for 10 min; repeat 150 mg 10-15 minutes as needed. Alternative infusion: 360 mg over 6 hours, then 540 mg over the next 18 hours and synchronized electrical cardioversion starting at 50 J.

5. Treatment of isolated ventricular premature beats, couplets, and nonsustained VT with no hemodynamic compromise is not recommended.

6. Sustained atrial fibrillation (AF) and atrial flutter with hemodynamic compromise or ongoing ischemia: Synchronized cardioversion with an initial 200 J for AF and 50 J for flutter. If unresponsive or recurrent: intravenous amiodarone and intravenous digoxin may be used to slow the ventricular response.

7. Sustained AF and atrial flutter with ongoing ischemia but without hemodynamic compromise should be treated with one or more of the following: Beta-adrenergic blockade (preferred), intravenous diltiazem (not locally available) or verapamil, synchronized cardioversion.

8. Reentrant paroxysmal SVT should be treated with the following in sequence: carotid sinus massage, IV adenosine, IV metoprolol or atenolol, IV diltiazem (not locally available), IV digoxin.

9. Ventricular asystole: Prompt resuscitative measures, including chest compressions, atropine, vasopressin (not locally available), epinephrine, and temporary pacing, should be administered to treat ventricular asystole.

**Statement 11: Permanent Ventricular Pacing**

It IS RECOMMENDED that Permanent Ventricular Pacing be placed in the following conditions:

1. Persistent second-degree AV block in the His-Purkinje system with bilateral bundle-branch block or third-degree AV block within or below the His-Purkinje system after STEMI.

2. Transient advanced second- or third-degree infra-nodal AV block and associated bundle branch block.

3. Persistent and symptomatic second- or third-degree AV block.

**Statement 12: Statement on Implantable Cardioverter Defibrillator**

It IS RECOMMENDED that Implantable Cardioverter Defibrillator be placed in the following conditions:

1. Patients with VF or hemodynamically sustained VT more than 2 days after STEMI (provided that VF or VT is not judged to be due to transient or reversible ischemia or reinfarction).

2. Patients with VF or sustained VT more than 48 hours
that beta blocker

that beta blocker use, careful dose titration among selected patients

that beta blocker use, careful dose titration among selected patients

Anticoagulant therapy is beneficial in patients with STEMI, and there is benefit in more prolonged anticoagulant therapy. The mechanism of benefit may be multifactorial and may be due to prevention of rethrombosis of the infarct artery and prevention of rebound increase in events after abrupt discontinuation of unfractionated heparin (UFH).

The following anticoagulant regimens have established efficacy:

a. UFH (initial intravenous bolus 60 U per kg [maximum 4000 U] followed by an intravenous infusion of 12 U per kg per hour [maximum 1000 U per hour] initially, adjusted to maintain the activated partial thromboplastin time (PTT) at 1.5 to 2.0 times control (approximately 50 to 70 seconds).

b. On low molecular weight heparin:

a. Enoxaparin can be given provided the serum creatinine is less than 2.5 mg per dL in men and 2.0 mg per dL in women.

For patients <75 years of age, an initial 30 mg intravenous bolus is given, followed 15 minutes later by subcutaneous injections of 1.0 mg per kg every 12 hours.

For patients at least 75 years of age, the initial intravenous bolus is eliminated and the subcutaneous dose is reduced to 0.75 mg per kg every 12 hours.

Regardless of age, if the creatinine clearance (using the Cockroft-Gault formula) during the course of treatment is estimated to be less than 30 mL per minute, the subcutaneous regimen is 1.0 mg per kg every 24 hours.

Maintenance dosing with enoxaparin should be continued for the duration of the index hospitalization or up to 8 days.

b. Fondaparinux can also be given provided the serum creatinine is less than 3.0 mg per dL.

Dose: initial dose is 2.5 mg intravenously then subcutaneous injections of 2.5 mg once daily. Maintenance dosing with fondaparinux should be continued for the duration of the index hospitalization, up to 8 days.

Statement 14: Antiplatelet therapy

It IS RECOMMENDED that Clopidogrel 75 mg per day orally should be added to aspirin in patients with STEMI and maintained for at least 14 days.

The COMMIT-CCS-2 randomized 45,852 patients within 24 hours of suspected AMI to 75 mg clopidogrel daily for up to 4 weeks versus placebo in addition to 162 mg of aspirin daily. The composite primary endpoint of death, reinfarction, or stroke was reduced from 10.1% in the placebo to 9.2% in the clopidogrel group (OR 0.91 [95% CI 0.86 to 0.97]).

The CLARITY-TIMI 28 (Clopidogrel as Adjunctive Reperfusion TherapyThrombolysis in Myocardial Infarction 28) study randomized 3491 patients receiving fibrinolytic therapy within 12 hours of STEMI to clopidogrel (300 oral loading dose followed by 75 mg oral daily dose) or placebo. There was a reduction in the primary composite endpoint of an occluded infarct artery or recurrent MI before angiography from 21% in the placebo to 15% in the clopidogrel group. (OR0.64 [95% CI 0.53 to 0.76]; p less than 0.001. This benefit has been thought to be primarily due to prevention of infarct related artery reocclusion. The rate of TIMI major bleeding was 1.7% in the placebo and 1.9% in the clopidogrel group (p=0.80).

There is no available data on long term therapy with clopidogrel in STEMI but extrapolating from experience with UA/NSTEMI suggests that it can be useful.

It is reasonable to administer an oral loading dose of 300 mg of clopidogrel in patients less than 75 years old.

Statement 15: Beta Blocker therapy

It IS STRONGLY RECOMMENDED that beta blocker therapy be started within 24 hours of STEMI in the absence of contraindication (frank heart failure, hypotension, heart block, active asthma or reactive airway disease, increased risk of cardiogenic shock i.e age more than 70, SBP less than 120 mmHg, heart rate greater than 110, Killips greater than class I and in the presence of concomitant hypertension or uncontrolled blood pressure).

Use of beta blocker should also be considered and carefully titrated during the latter phase of STEMI among patients who initially presented contraindications to its use within the 24 hours.

The use of beta blocker in patients after myocardial infarction has been proven to increase survival, decrease magnitude of extension and associated complication even when used early in the fibrinolytic era (ISIS-I, MIAMI, TIMI II). These findings were later refuted by GUSTO I which revealed no benefit in survival among patients given early IV atenolol.

The COMMIT/CCS-2 trial using intravenous and high dose oral metoprolol (200 mg/day) given at day 0-1 of myocardial infarction has shown lesser episodes of reinfarction and ventricular fibrillation but with significantly higher episodes of cardiogenic shock. Because of these findings and lack of benefit of early (day 0-1) oral beta blocker use, careful dose titration among selected patients should be exercised when giving beta blocker early in the course of myocardial infarction.

Use of beta blocker in the latter course (from day 2) among patients with no contraindication has been proven to increase survival and major adverse cardiac events (MACE).
Locally, we have no available IV metoprolol in the market hence, oral route sufficed in our administration of beta blockers.

Statement 16: Anti-cholesterol agent: Statins

High dose statins MAY BE RECOMMENDED within 1st 24 hours of admission in the absence of contraindication (such as known allergy, active liver disease).

The use of statins as secondary prevention in patients who survived a myocardial infarction is no longer of question. Its use in the early phase of acute coronary syndrome has also proven to confer some benefit as seen in the study Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (MIRACL).10 Atorvastatin 80 mg vs placebo was started within 24 to 96 hours in patients with unstable angina and acute myocardial infarction in this trial. Though there was no mortality benefit in the atorvastatin arm, there is a significant reduction in recurrent ischemic events in the first 16 weeks post AMI.

In a prospective cohort study using data from the Swedish Registry of Cardiac Intensive care on patients admitted to the coronary care units of 58 Swedish hospitals, it was shown that early use of statin improved 1 year mortality (relative risk, 0.75; 95% confidence interval 0.63 to 0.89, P=0.001) in 5528 vs 14071 who did not receive statins before discharge for their first recorded AMI.11

Statement 17: Angiotensin Converting Enzyme inhibitors (ACE-I)

It IS STRONGLY RECOMMENDED that ACE-I be started within 24 hours in patients with anterior infarction, pulmonary congestion or left ventricular ejection fraction (LVEF) of <= to 40% and continued indefinitely among patients with LVEF <= to 40%, hypertension, diabetes or chronic kidney disease (CKD).

ACE-I MAY BE RECOMMENDED among lower risk patients (S/Prevascularization procedures, controlled cardiovascular risk factors, normal ejection fraction recovering from STEMI).

Several studies have shown benefit in starting ACE inhibition in acute STEMI within the 1st 24 hours of the event. In ISIS-4 study, it resulted to a 7% relative risk reduction in the 5-week mortality of AMI patients who were given captopril vs placebo, the benefit was mostly noted in those patients having anterior infarction.12 In GISSI-3 trial, administration of lisinopril to patients with STEMI or NSTEMI resulted to a decreased mortality in 6 weeks when compared to active control.13 In both studies the survival benefit was significant during the 1st week of the AMI hence the emphasis on early treatment. Further, in the report submitted by Chinese Cardiac Study group which enrolled more than 16, 000 patients also showed survival benefit in the early use of captopril in AMI patients.14 A meta-analysis on early ACE inhibition conducted in both major and smaller trials also resulted to 6.5% odds reduction in mortality.15-18 However, one trial that did not show any improvement in survival is the CONSENSUS II study which randomized AMI patients to IV enalapril or placebo. IV enalapril resulted to hypotension especially among the elderly which led to premature discontinuation of the study due to safety issues.17

In summary, there is enough evidence to support initiating ACE-I in AMI in the absence of contraindications (hypotension, bilateral renal artery stenoses, significant renal failure and known allergy). Patients should be started on small doses and titrated to optimal levels (captopril 50 mg BID in ISIS-4 and lisinopril 10 md OD in GISSI-3) in the absence of adverse reactions. The subsets of patients in whom ACE-inhibitors are most beneficial are those with heart failure, anterior infarction and low LVEF. The data is equivocal among lower risk patients although no harm has been documented.

Statement 18: Angiotensin receptor blockers (ARB)

ARB IS RECOMMENDED in patients who are intolerant to ACE-I inhibitors and have clinical or radiological sign of heart failure or EF less than 40%.

ARB IS ALSO RECOMMENDED in patients who are intolerant to ACE inhibitors and have hypertension.

ARB in combination with ACE inhibitors may also be recommended in those patients with systolic dysfunction and heart failure. Compared to ACE inhibitors, ARB’s role in acute MI is not well established hence in these guidelines, the use of ARB’s is only recommended among patients who are intolerant to the former.

Statement 19: Renin-Angiotensin-Aldosterone System Blockers: Aldosterone Blockade

It IS RECOMMENDED to use aldosterone blockade (spironolactone ) in post STEMI patients without significant renal dysfunction or hyperkalemia who are already receiving therapeutic doses of beta clocker and ACE inhibitor who have LVEF<= 40% and have either diabetes or heart failure.

Statement 20: Glucose control therapy

It IS RECOMMENDED that insulin IV, ideally via infusion pump should be used to achieve optimum sugar level among patients with STEMI particularly with complicated hospital course.

It is prudent to administer IV insulin among patients with STEMI during the first 24 to 48 hours to achieve optimum blood sugar level even among patients with uncomplicated course. The surge of catecholamines in acute STEMI increases glucagon and cortisol which in turn decreases insulin sensitivity contributing to impaired glucose utilization and increased fatty oxidation. Free fatty acid concentration and their metabolite increase potentiating ischemic injury through myocardial toxicity, increased oxygen demand and direct inhibition of glucose utilization. Insulin promotes glucose oxidation, decreases free fatty acids increased energy levels (ATP) and promotes fibrinolytic property in STEMI.

Statement 21: Metabolic Modulators (trimetazidine, nicorandil)

It IS NOT RECOMMENDED to give Trimetazidine among patients with STEMI undergoing thrombolysis.
Rest, Exercise and Exercise Training

Rest
Physical rest or bed rest is necessary in patients with heart failure. Passive mobilization exercises are carried out to prevent untoward effects resulting from prolonged bed rest and to decrease the risk of venous thrombosis.

Exercise
In order to prevent muscle de-conditioning, a stable patient should be advised on how to carry out daily physical activities that do not induce symptoms. Strenuous or isometric exercises, competitive and tiring sport should be discouraged. If the patient is employed, their work tasks must be assessed and advised on whether they can be continued.

Exercise Training
Exercise training programs are encouraged in stable patients. Some randomized trials have shown that regular exercise can safely increase physical capacity by 15-25%, improve symptoms and perception of quality of life in patients with stable class II and III heart failure. All CHD patients should have a planned preventive measure as part of the usual care. The following are guidelines for long term management:

1. Smoking cessation
2. To maintain/achieve the ideal body weight
3. To educate patient on a diet low in saturated fat and cholesterol. A patient with a low density lipoprotein cholesterol greater than 100 mg/dl despite diet should be given drug therapy with the goal of reducing LDL to less than <70 mg/dL
4. Blood pressure control
5. Sugar control
6. Stress management
7. Exercise prescription to help increase exercise tolerance

Statement 23: Hospital discharge and post STEMI risk stratification: Timing of Hospital Discharge

If patient have undergone reperfusion therapy with no significant arrhythmias, recurrent ischemia or congestive heart failure, patient can be safely discharged in less than 5 days.

Statement 24: Exercise Testing

Exercise testing IS RECOMMENDED either before discharge (submaximal), early after discharge (2-3 wks) or late after discharge (3-6wks) for prognostic, activity prescription, evaluation of medical therapy.

Sub-maximal protocol requires that patient exercise until symptoms of angina appear, ECG changes of ischemia is seen or 5mets is reached.

Exercise testing is not indicated in the following conditions:
1. Patients with severe co-morbidity likely to limit life expectancy and/or candidacy for revascularization.
2. Patients in heart failure, cardiac arrhythmia or non-cardiac condition that limit their ability to exercise

V. REFERENCES

5. First International Study of Infarct Survival Collaborative Group. Randomized Trial of Intravenous Asenapine among 16,027 Cases of Suspected Acute Myocardial Infarction:
 Coronary Artery Disease


CPM Editor’s Notes (Not part of the Guidelines):


b. The PHA guidelines on CAD (2009) contains two other topics. See (c) and (d) below.

c. PHA Clinical Practice Guidelines for the Management of Patients with Chronic Stable Angina Pectoris (CSAP) (2009) summary:

**Statement 1:** Detailed history. **Statement 2:** Detailed PE. **Statement 3:** Recommended: Resting 12-lead ECG. **Statement 4:** Recommended: Laboratory tests (fasting lipid profile [including total cholesterol, HDL chol., LDL chol., and triglycerides], FBS/OGTT/2-hr postprandial glucose, CBC, creatinine, biomarkers of cardiac injury [if clinical evaluation suggests ACS]. **Statement 5:** Recommended: Chest x-ray (PA & lateral) for patients w/ CHF, VHD, aortic dissection/aneurysm, pericardial disease, pulmonary disease. **Statement 6:** Recommended: Echocardiography for clinical murmurs; history & ECG changes of prior MI; signs/symptoms of heart failure. **Statement 7:** Recommended: Treadmill exercise test (TET) for patients with an intermediate pretest probability of CAD who have normal resting ECG and are able to exercise. **Statement 8:** Recommended: Stress imaging studies for patients with abnormal resting ECG; who cannot exercise; with previous revascularization (PCI or CABG). **Statement 9:** May be recommended: Computed tomographic (CT) coronary angiography to diagnose/rule out CAD in patients w/ low intermediate pretest probability of CAD or those with equivocal/non-conclusive treadmill exercise or stress imaging test. **Statement 10:** Recommended: Invasive coronary angiography for patients (1) known or suspected surgical anatomy; (2) patients who survived a sudden cardiac arrest or with serious ventricular arrhythmias; (2) with severe stable angina with a high pretest probability of left main or 3- vessel CAD; (3) early recurrence of angina in post-revascularization patients; (4) high risk criteria on noninvasive testing regardless of angina severity; (5) with occupational requirement for a definitive diagnosis; (6) with inconsiderable diagnosis or inadequate prognostic information after noninvasive testing with intermediate to high risk of CAD; (7) who cannot undergo noninvasive testing due to disability, illness or morbid obesity; (8) Patients who were being considered for major noncardiac surgery, especially vascular surgery, with high risk features on noninvasive testing. **Statement 11:** Recommended: Lifestyle Modification and Treatment of Coronary Disease Risk Factors. **Statement 12:** Strongly recommended: Pharmacologic Therapy to Improve Prognosis (aspirin, statins, ACE-I/ARB, beta-blockers [post-MI]). **Statement 13:** Pharmacologic therapy to reduce angina (recommended: if w/o contraindication, as initial therapy: beta-blocker; anti-anginals that may be substituted or added in descending order of preference include: calcium channel blockers, long-acting nitrates, ivabradine, trimetazadine). **Statement 14:** Recommended: Revascularization is recommended in (1) high-risk patients known to benefit from revascularization (eg, significant left main disease, severe 3 vessel disease, left ventricular dysfunction, high risk features on non-invasive imaging); (2) Patients with technically suitable coronary anatomy who do not respond adequately to optimal medical therapy and who wish to remain physically active. **Statement 15:** Recommended: Revascularization with Percutaneous Coronary Intervention (PCI) for relief of angina symptoms in patients without high-risk coronary anatomy and in whom procedure risks do not outweigh potential benefits. **Statement 16:** Recommended: Revascularization with CABG for patients (based on evidence of prognostic benefit) with (1) significant left main coronary disease; (2) high risk coronary anatomy not suitable for PCI; (3) stenosis of 3 major coronary arteries and severe stenosis of 2 major coronary arteries, including high-grade stenosis of the proximal left anterior descending artery in patients with high SYNTAX scores. **Statement 17:** Not-conventional treatment. NOT recommended: chelation therapy - may be harmful to patients with CAD. **Statement 18:** Recommended: Follow-up tests for patients with worsening angina or development of co-morbid conditions despite optimal medical therapy and/or revascularization.
Statement 1: Diagnosis and risk assessment. Requires immediate assessment for initiation of ACS protocol: (1) Chest pain/severe epigastic pain, non-traumatic, with component typical of myocardial ischemia or MI: Central/substernal compression or crushing chest pain pressure, tightness, heaviness, crawling, burning, aching sensation; (2) unexplained indigestion, belching, epigastric pain; (3) radiating pain in neck, jaw, shoulders, back, or 1 or both arms; (4) associated dyspnea; (5) associated nausea and/or vomiting; (6) associated diaphoresis.

Statement 2: Strongly recommended: 12-lead ECG within 10 minutes of ER presentation in patients with chest discomfort. Recommended: Treating pain with nitroglycerin (NTG) or when acute pulmonary congestion and/or severe agitation persists with pharmacotherapy by statins, or combination with other lipid-lowering agents to reduce LDL-C <100 mg/dL, and ideally reduced to 70 mg/dL or less. Hemodynamic instability; (f) Sustained ventricular tachycardia; (g) PCI within 6 months; (h) Prior CABG; (i) High-risk score (e.g., TIMI, GRACE); (j) Reduced LV systolic function (LVEF less than 40%). Statement 20: Not recommended: Coronary angiography before significant left anterior descending CAD but with a large area of viable myocardium and high risk criteria on non invasive testing. Statement 21: Recommended: Early invasive PCI strategy for patients with UA/NSTEMI who have no serious comorbidity and who have coronary lesions amenable to PCI and any of the high risk features.PCI (or CABS) is also recommended for UA/NSTEMI patients with TVs with similar risk of death and AMI as patients without TVs when the risks of revascularization are not likely to outweigh the benefits or in patients with acute chest pain and a low likelihood of ACS or in patients who will not consent to revascularization regarding the risks of the procedure. Statement 21: Recommended: Early invasive PCI strategy for patients with UA/NSTEMI who have no serious comorbidity and who have coronary lesions amenable to PCI and any of the high risk features. Statement 22: Recommended: CABG for patients with significant left main disease and the preferred revascularization strategy for patients with significant left main CAD who have left ventricular dysfunction (LVEF less than 40%). Statement 23: Recommended: CABG for patients with significant left main disease and the preferred revascularization strategy for patients with significant left main CAD who have left ventricular dysfunction (LVEF less than 40%). Statement 24: Recommended: Start clopidogrel for patients (1) in whom an early noninterventional approach is planned in addition to ASA as soon as possible on admission and administered to patients with continuing ischemia, (2) with a minimum of 1 month and ideally up to 12 months (unless the patient is at high risk of bleeding, aspirin 160-325 mg daily should be given for at least 1 month after BMS implantation, 3 months after sirolimus-eluting stent implantation, and 6 months after paclitaxel-eluting stent implantation), (3) who are not at high risk of bleeding, (4) who have asymptomatic LV systolic dysfunction or congestive heart failure (CHF), high risk chronic CAD, in post ACS (with or without diabetes mellitus) or CKD patients, (5) with a history of recurrent ischemia or associated symptoms. Statement 25: Recommended: Beta blockers by oral/IV route if there is ongoing chest pain in the absence of contraindications. Statement 25: Recommended: Beta blockers by oral/IV route if there is ongoing chest pain in the absence of contraindications. Statement 26: Recommended: Morphine Sulfate - given IV when symptoms are not immediately relieved with NTG or when acute pulmonary congestion and/or severe agitation are present. Statement 13: Strongly recommended: Aspirin at initial dose of 160-325 mg non-enteric formulation, followed by 80-160 mg daily) be administered as soon as possible after presentation and continued indefinitely. Statement 14: Strongly recommended: Start copidogrel for patients (1) in whom an early noninterventional approach is planned in addition to ASA as soon as possible on admission and administered to patients with continuing ischemia, (2) who are unable to take ASA because of hypersensitivity or major gastrointestinal intolerance; (3) in whom a PCI is planned and should be continued for at least 12 months in patients who are not at high risk for bleeding. Statement 15: Strongly recommended: Antiagulation with subcutaneous enoxaparine or intravenous unfractionated heparin (UFH) should be added to antiplatelet therapy with ASA and/or clopidogrel. Statement 16: Recommended: Use glycoprotein IIb/IIIa inhibitors (tirofiban) in addition to aspirin and unfractionated heparin (UFH), to patients with elevated troponin, or with other high risk features in whom an invasive management strategy is not planned; or inpatients undergoing PCI with or without clopidogrel administration. Statement 17: Recommended: Use fondaparinux, in lieu of enoxaparine, to SC once daily in patients undergoing PCI with or without antiplatelet therapy. Statement 18: NOT recommended: IV fibrinolytic therapy in patients with UA or in patients without acute ST-segment elevation, a true posterior MI, or a presumed new left bundle-branch block (LBBB). Statement 19: Early Conservative versus Invasive Strategies. Recommended: Early invasive strategy (as early as possible up to 72 hours) followed by revascularization (PCI or CABS) with any of the ff. high-risk indicators: (a) Recurrent angina/ischemia at rest or with low-level activities despite improvement in symptoms. (b) Elevated cardiac biomarkers (TnT or Tnl); (c) New/previously normal ST-segment depression; (d) Intensive lipid-lowering therapy is strongly recommended by combining dietary interventions with pharmacotherapy by statins, or combination with other lipid-lowering agents to reduce LDL-C <100 mg/dL, and ideally reduced to 70 mg/dL; (e) Hemodynamic instability; (f) Sustained ventricular tachycardia; (g) PCI within 6 months; (h) Prior CABG; (i) High-risk score (e.g., TIMI, GRACE); (j) Reduced LV systolic function (LVEF less than 40%). Statement 20: Not recommended: Coronary angiography in patients with diabetes co-morbidities (e.g., liver or pulmonary failure, cancer), in whom the risks of revascularization are not likely to outweigh the benefits or in patients with acute chest pain and a low likelihood of ACS or in patients who will not consent to revascularization regarding the risks of the procedure. Statement 21: Recommended: Early invasive PCI strategy for patients with UA/NSTEMI who have no serious comorbidity and who have coronary lesions amenable to PCI and any of the high risk features. Statement 22: Recommended: CABG for patients with significant left main disease and the preferred revascularization strategy for patients with significant left main CAD who have left ventricular dysfunction (LVEF <50%), and diabetes. 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## Index of Drugs Mentioned in the Guideline

This index is not part of the guideline. It lists the products and/or their therapeutic classes as mentioned in the guideline. For the doctor's convenience, brands available in the PPD references are listed under each of the classes. For drug information, refer to PPD, PPD Pocket Version, PPD Text, PPD Tabs, and www.TheFilipinoDoctor.com.

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Coronary Artery Disease

**Anti-arythmics**
- Amiodarone
- Ami
- Amiron
- Anion
- Cordarone
- Rythma
- Rythma 50 mg/mL
- Winthrop Amiodarone

**Morphine Sulfate**
- Hizon Morphine Sulfate
- MST Continus

**Diyoxin**
- Lanoxin

**Insulins**
- Short-acting Insulins
  - Actrapid HM
  - Apidra Solostar
  - Humalog
  - Humulin R (Regular)
  - Insuget-R
  - Lupinsulin R
  - NovoRapid FlexPen
  - Wosulin-R
- Intermediate-acting Insulins
  - Humalog Mix 25
  - Humulin 70/30
  - Humulin N (NPH)
  - Insuget-N/Insuget 70/30
  - Insulatard HM/Insulatard HM Flexpen
  - Lupinsulin 30:70
  - Lupinsulin N
  - Mixtard 30 HM/Mixtard 30 HM Flexpen
  - NovoMix 30 FlexPen
  - Wosulin-30/70
  - Wosulin-N
- Long-acting Insulins
  - Lantus/Lantus Solostar
  - Levernir FlexPen

**Diuretics**

**Spironolactone**
- Aldactone

**Spironolactone/Butizide**
- Aldazide

**Statins**
- Atorvastatin calcium
  - Atopolar
  - Ator-10/Ator-20/

**Beta blockers**
- Atenolol
  - Cardoten
  - RiteMED Atenolol
  - Tenomin
  - Therabloc
  - Velorin
- Atenolol/Chlorthalidone
- Bisoprolol
  - Bisoprolol Sandoz
  - Concore
- Bisoprolol/Chlorothiazide
- Ziac
- Esmolol
- Metoprolol succinate
  - Betazok
  - Betazok 25 mg
  - Cardiosel-OD
- Metoprolol tartrate
  - Betaloc
  - Cardiosel
  - Cardiostat
  - Metocare
  - Neobloc
  - Pharex Metoprolol
  - RiteMED Metoprolol
- Valvexin
- Metoprolol/Hydrochlorothiazide
- Pindolol
  - Pyndale
  - Visken
- Pindolol/Clopamide
- Viskalix
- Propranolol
  - Inderal
- Timolol

**Organic Nitrates**
- Isosorbide dinitrate
  - Isoket
  - Isoket IV
  - Isoket Spray
  - Isordil
- Isosorbide mononitrate
  - Elantan
  - Elantan Long
  - GlaxoSmithKline ISMN 60
  - Imdur Durules
  - Isominit
  - Isonate
  - Montra
  - Solotrate SR
  - Vasotrate-20
  - Vasotrate-60 OD
- Nitroglycerin
  - Depotit NT 5/Depotit NT 10
  - Nitrostat
  - Transderm-Nitro

**Digoxin**
- Lanoxin

**Insuli**

**Antiretimumics**
- Amiodarone
- Ami
- Amiron
- Anion
- Cordarone
- Rythma
- Rythma 50 mg/mL
- Winthrop Amiodarone

**Morphine Sulfate**
- Hizon Morphine Sulfate
- MST Continus

**Diyoxin**
- Lanoxin

**Insuli**

**Beta blockers**
- Atenolol
  - Cardoten
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  - Tenomin
  - Therabloc
  - Velorin
- Atenolol/Chlorthalidone
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  - Bisoprolol Sandoz
  - Concore
- Bisoprolol/Chlorothiazide
- Ziac
- Esmolol
- Metoprolol succinate
  - Betazok
  - Betazok 25 mg
  - Cardiosel-OD
- Metoprolol tartrate
  - Betaloc
  - Cardiosel
  - Cardiostat
  - Metocare
  - Neobloc
  - Pharex Metoprolol
  - RiteMED Metoprolol
- Valvexin
- Metoprolol/Hydrochlorothiazide
- Pindolol
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  - Visken
- Pindolol/Clopamide
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- Propranolol
  - Inderal
- Timolol

**Organic Nitrates**
- Isosorbide dinitrate
  - Isoket
  - Isoket IV
  - Isoket Spray
  - Isordil
- Isosorbide mononitrate
  - Elantan
  - Elantan Long
  - GlaxoSmithKline ISMN 60
  - Imdur Durules
  - Isominit
  - Isonate
  - Montra
  - Solotrate SR
  - Vasotrate-20
  - Vasotrate-60 OD
- Nitroglycerin
  - Depotit NT 5/Depotit NT 10
  - Nitrostat
  - Transderm-Nitro

**Statins**
- Atorvastatin calcium
  - Atopolar
  - Ator-10/Ator-20/