



# Therapeutic brief

# 24



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## Looking Ahead: Use of recommended medicines after acute coronary syndromes

Increasing age is associated with an increase in relative contraindications to recommended drugs for acute coronary syndromes (ACS), however the rates of serious adverse events remains low when evidence-based treatment is provided.<sup>1</sup>

Studies have demonstrated that even after controlling for contraindications and co-morbidities the use of effective, recommended therapies is still lower among older patients and this is evident in the veteran population.<sup>2,3,4</sup> This evidence-practice gap exists in both primary and secondary prevention of cardiovascular disease.

Older patients admitted to hospital with ACS are more likely to have co-morbidities – particularly renal impairment, hypertension and previous stroke – and their stay is more likely to be complicated by heart failure.<sup>2,5</sup> Although older patients are typically under-represented in randomised controlled trials of ACS management, when older subgroups are examined the interventions appear to achieve similar or greater absolute risk reductions than in younger patients.

This Veterans' MATES module aims to assist GPs in caring for their veteran patients by clarifying current long-term treatment guidelines for those who have had a diagnosis of ACS.

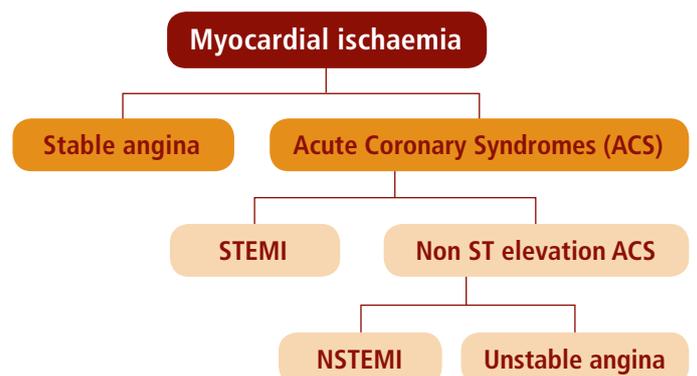
### Key points

- Review your ACS patients soon after hospital discharge to ensure they:
  - are taking aspirin and clopidogrel (unless low risk ACS), beta blocker, ACE inhibitor, statin (unless any of these medicines are contraindicated)
  - have a written chest pain action plan and a short-acting nitrate.
- Use additional strategies to optimise long-term health outcomes: educate veterans about the need for medicines and lifestyle changes, assist them to stop smoking, monitor for symptoms of depression and refer veterans to a cardiac rehabilitation program if available.
- Consider a Home Medicines Review by an accredited pharmacist, particularly for ACS patients recently discharged from hospital.

## Definitions

The terminology used to describe patterns of myocardial ischaemia has evolved over recent years potentially causing confusion amongst health care providers. Patients with symptoms of myocardial ischaemia are classified as having stable angina or acute coronary syndromes (see Figure 1). Stable angina represents coronary artery obstruction arising from a stable atherosclerotic plaque. A diagnosis of ACS signifies an accelerated pattern of symptoms where plaque rupture is then complicated by thrombus formation and vasospasm, which may ultimately lead to myocardial infarction. Acute coronary syndromes are further classified depending on the presence of ST elevation on the initial ECG – ST elevation myocardial infarction (STEMI), non ST elevation myocardial infarction (NSTEMI) and unstable angina (UA).

**Figure 1.** Terminology used to describe patterns of myocardial ischaemia (adapted from Cardiovascular Therapeutic Guidelines)<sup>6</sup>



## ② Recommended discharge medicines after acute coronary syndromes<sup>6,7</sup>

Acute coronary syndromes are associated with a high risk of early recurrent ischaemic events. This risk is reduced by the use of recommended medicines. It is important to determine whether your veteran patients discharged from hospital after ACS are currently taking each of the

recommended medicines. If a recommended medicine has not been prescribed and no reason documented, follow up is required. For recommended starting and target doses see the Australian Medicines Handbook.<sup>8</sup>

Drug	Recommendation	Benefits	Considerations
<b>Aspirin</b>	Commence following ACS and continued long term*.	Confers a 22% risk reduction of further non-fatal MIs. <sup>9</sup>	Contraindications include known allergy, active peptic ulcer, retinal bleeding and severe untreated hypertension.
<b>Clopidogrel</b>	Consider commencing in combination with aspirin** after: <ul style="list-style-type: none"> <li>• stent insertion</li> <li>• STEMI/NSTEMI</li> <li>• high risk unstable angina</li> </ul> Avoid combination in low risk ACS patients.*** Clopidogrel can be used as a single agent when aspirin is contraindicated.	Additional 20% relative risk reduction for non-fatal MI at 1 yr in CURE trial which looked at a high risk ACS population. Greatest benefit of dual antiplatelet therapy in preventing ischaemic events occurs soon after ACS and in those at greatest risk. <sup>9,11</sup>	The CHARISMA trial noted an increased risk of moderate bleeds. <sup>10</sup> In the CURE trial, bleeding complications were significantly more common with aspirin plus clopidogrel than with aspirin alone (8.5% vs. 5%). <sup>11</sup> <b>Continued surveillance of bleeding risk/benefits of dual antiplatelet therapy is warranted in older patients.</b>
<b>Beta blocker</b>	Should be prescribed for patients early after ACS and continued long term.	Beta blockers have been shown in many trials to reduce morbidity and mortality across all age groups after STEMI and NSTEMI. <sup>12</sup>	Major contraindications include reactive airways disease, severe bradycardia, pulmonary oedema and hypotension. Calcium channel blockers may be used as an alternative where angina is ongoing and beta blockers are contraindicated.
<b>ACE inhibitor</b>	Should be started early after ACS and continued long term, especially in those with a low ejection fraction and anterior MI.	ACE inhibitors reduce ventricular remodeling days to weeks after MI.	Contraindications include allergy, renal failure and hypotension. Check renal function before starting and again after 1-2 weeks. <b>Impaired renal function is not an absolute contraindication.</b> Mild non-progressive increase in creatinine after starting an ACE inhibitor is acceptable. Angiotensin receptor blockers can be used as an alternative where ACE inhibitors are not tolerated.
<b>Statin</b>	Should be initiated for all patients regardless of serum cholesterol level.	Short-term statin therapy is associated with improved coronary endothelial function and reversal of prothrombotic states. Statin therapy has been shown to reduce early recurrent ischaemic events after ACS. <sup>13</sup>	Monitor liver function and for symptoms suggestive of myopathy. Consider an alternative statin or dose reduction if not tolerated.
<b>Nitrate</b>	All patients should be prescribed a short-acting nitrate and taught how and when to use it.	Nitrates have not been shown to improve mortality outcomes after MI but short acting nitrates are an integral part of the management of acute myocardial ischaemia. <sup>14</sup>	Advise patients to administer when sitting or lying down. Sublingual glyceryl trinitrate spray has a longer shelf life than tablets. For tablets, spit out remainder of tablet when angina is relieved to avoid headache.

\*For those ACS patients who need to be on warfarin, Australian guidelines state aspirin may sometimes be added but “patients should be observed closely for signs of bleeding”.<sup>7</sup> Aspirin and/or clopidogrel in addition to warfarin are particularly high risk combinations in the elderly.

\*\*There is currently a lack of data to guide the use of clopidogrel beyond 12 months in non ST elevation MI and unstable angina; decisions are made on an individual basis. The duration of clopidogrel use after stent insertion depends on the type of stent used and expert opinion should be sought.

\*\*\*Low-risk ACS includes those patients with unstable angina aged <65 years with no diabetes or renal disease where the onset of anginal symptoms has occurred within the last month or the angina has worsened in severity/frequency or the anginal threshold has been lowered.<sup>7</sup>



Numerous studies have identified a failure to start secondary prevention medicine after a diagnosis of ACS both within the hospital setting or immediately after discharge, particularly for older patients.<sup>2,3,5</sup> Results from the GRACE study indicate statins are used less frequently in older patients and warfarin more frequently (probably reflecting the higher prevalence of atrial fibrillation).<sup>5</sup> The likelihood of clopidogrel being initiated in hospital following NSTEMI has also been shown to decrease with advancing age.<sup>15</sup>

Patients with myocardial infarction (MI) are more likely to receive therapy in line with treatment guidelines than those with unstable angina.<sup>16</sup> Analysis of the DVA claims database indicates that a higher percentage of veterans hospitalised with MI received clopidogrel and beta blockers than those with angina and more veterans with angina received statins and nitrates than those with MI.<sup>4</sup>



## Clopidogrel and proton pump inhibitors

Proton pump inhibitors (PPIs) may decrease the formation of the active metabolite of clopidogrel and interfere with the inhibition of platelet aggregation. Retrospective studies involving small cohorts suggest that concomitant use of a PPI and clopidogrel is associated with an increased risk of cardiovascular events but results have been inconsistent.<sup>17,18</sup> Differences in the pharmacokinetic

properties of the different PPIs used in the studies may partially explain differences in findings. The tendency for higher risk patients to be co-prescribed PPIs also confounds the results. Quantification of the effects of PPIs on reduced gastrointestinal bleeding and possible increased risk of cardiovascular events is still to be determined.



## Long term considerations after acute coronary syndromes<sup>7</sup>

### Chest pain action plan

Following admission for ACS, all patients need to be provided with a written chest pain action plan which advocates:

- rest and self-administration of short-acting nitrates
- self-administration of aspirin unless contraindicated (most patients would already be taking aspirin)
- calling an ambulance if chest pain not resolved within 10 minutes.

### Cardiac rehabilitation program

Ideally all patients with cardiovascular disease should be able to access, and be referred to, a cardiac rehabilitation program. It has been shown to enhance quality of life and functional status, and reduce hospitalisation, recurrent MI and long-term mortality.<sup>19</sup> In rural areas where this is not possible, GPs can initiate their own program using a recommended framework available from the National Heart Foundation website (see further information).

### Lifestyle advice

Patients should be advised to make lifestyle changes to reduce their risk of further cardiac events including attaining a weight in the healthy range, regular physical activity, moderate alcohol intake and good nutrition

– a diet high in omega-3 fatty acids is recommended. Smoking cessation is essential and pharmacological interventions should be considered for these patients in addition to counseling.

A wide range of evidence indicates depression is an independent risk factor for cardiovascular disease, both in otherwise healthy subjects and in those with known cardiovascular disease.<sup>20</sup> All patients with ACS need to be assessed for co-morbid depression and social isolation.

### Adherence to medical treatment

Non-adherence to medicine is a common problem. Studies have shown discontinuation of medicines after MI tends to occur early after discharge and results in significantly higher mortality rates at one year.<sup>21</sup> High drop-off rates one year after discharge have also been noted for key medicines, particularly beta blockers and antiplatelet agents.<sup>22</sup>

**The transition from hospital discharge to the community setting appears to be a critical period.** It is important to assess medicine use early after hospital discharge and as part of the ongoing care of patients who have had a diagnosis of acute coronary syndrome.



## 4 Home Medicines Review

Veterans with ACS are likely to be on complex medicine regimes. Consider the use of a Home Medicines Review (HMR) by an accredited pharmacist to help:

- reinforce patients' understanding of the diagnosis and need for each medicine, particularly those initiated recently
- identify issues affecting adherence to prescribed medicine
- identify potential interactions with other prescribed or over-the-counter medicines
- ensure patients are reminded of special considerations for each medicine
- ensure patients understand their written chest pain action plan, and check that the patient understands that nitrate products must be in-date and readily accessible
- assist in promoting lifestyle changes to reduce the risk of further cardiac events
- identify those who would benefit from a dose administration aid.

Home Medicines Reviews are of greatest benefit when the purpose of the HMR and required information are clearly specified. It is helpful to provide the accredited pharmacist with the patient's medical history, current medicines list and relevant pathology results.

## Further information

Framework for Cardiac Rehabilitation Programs:

<http://heartfoundation.org.au/images/uploads/publications/Recommended-framework.pdf>

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# Home Medicines Review for veterans with acute coronary syndromes

Over the next few months, accredited pharmacists may receive Home Medicines Review (HMR) referrals for veterans with acute coronary syndromes (ACS)\* as a result of the latest Veterans' MATES initiative. This therapeutic brief aims to reinforce long-term treatment guidelines for veterans who have a diagnosis of ACS. We have asked the veteran's GP to consider an HMR for these patients.

When you do receive such a referral, consider the following points as part as your review process. The veteran's GP will value concise feedback that includes the education you gave to the patient. If no problems are identified from the HMR, this positive result is just as important to feed back to the GP.

## GPs have been encouraged to consider the use of a Home Medicines Review, to help:

- reinforce patients' understanding of the diagnosis and need for each medicine, particularly those initiated recently, which may include aspirin, clopidogrel, beta blocker, ACE inhibitor, statin and short-acting nitrate (see table page 2)
- identify issues affecting adherence
- identify potential interactions with other prescribed or over-the-counter medicines
- remind patients of special considerations for each medicine
- ensure patients understand their written chest pain action plan and that nitrate products must be in-date and readily accessible
- promote lifestyle changes to reduce the risk of further cardiac events, including attaining a healthy weight, regular physical activity, moderate alcohol intake, good nutrition and stopping smoking
- identify those who would benefit from a dose administration aid.

The veteran will have received a veterans' brochure, encouraging them to learn about their heart medicines and ask their doctor for a HMR, particularly if they have recently started these medicines.

Copies of the therapeutic brief and veteran brochure are available on the Veterans' MATES website [www.veteransmates.net.au](http://www.veteransmates.net.au)

HMRs can improve health outcomes for veterans.<sup>1</sup> Thank you for your work with veterans and we hope this information will help you respond to a GP's HMR referral for veterans with ACS.

Veterans' MATES would like to work more closely with accredited pharmacists to help you improve health outcomes for veterans. Please complete the enclosed response form to help us better meet your needs.

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\*Diagnoses in the referral letter used to describe ACS: ST elevation myocardial infarction (STEMI), non ST elevation myocardial infarction (NSTEMI) and unstable angina (see therapeutic brief).

<sup>1</sup> Roughead EE, Barratt JD, et al. The effectiveness of collaborative medicine reviews in delaying time to next hospitalisation for heart failure patients in the practice setting: results of a cohort study. *Circulation: Heart Failure* 2009 Sep;2(5):424-8.

## Recommended discharge medicines after acute coronary syndromes<sup>6,7</sup>

Drug	Recommendation	Benefits	Considerations
<b>Aspirin</b>	Commence following ACS and continued long term*.	Confers a 22% risk reduction of further non-fatal MIs. <sup>9</sup>	Contraindications include known allergy, active peptic ulcer, retinal bleeding and severe untreated hypertension.
<b>Clopidogrel</b>	Consider commencing in combination with aspirin** after: <ul style="list-style-type: none"> <li>• stent insertion</li> <li>• STEMI/NSTEMI</li> <li>• high risk unstable angina</li> </ul> Avoid combination in low risk ACS patients.*** Clopidogrel can be used as a single agent when aspirin is contraindicated.	Additional 20% relative risk reduction for non-fatal MI at 1 yr in CURE trial which looked at a high risk ACS population. Greatest benefit of dual antiplatelet therapy in preventing ischaemic events occurs soon after ACS and in those at greatest risk. <sup>9,11</sup>	The CHARISMA trial noted an increased risk of moderate bleeds. <sup>10</sup> In the CURE trial, bleeding complications were significantly more common with aspirin plus clopidogrel than with aspirin alone (8.5% vs. 5%). <sup>11</sup> <b>Continued surveillance of bleeding risk/benefits of dual antiplatelet therapy is warranted in older patients.</b>
<b>Beta blocker</b>	Should be prescribed for patients early after ACS and continued long term.	Beta blockers have been shown in many trials to reduce morbidity and mortality across all age groups after STEMI and NSTEMI. <sup>12</sup>	Major contraindications include reactive airways disease, severe bradycardia, pulmonary oedema and hypotension. Calcium channel blockers may be used as an alternative where angina is ongoing and beta blockers are contraindicated.
<b>ACE inhibitor</b>	Should be started early after ACS and continued long term, especially in those with a low ejection fraction and anterior MI.	ACE inhibitors reduce ventricular remodeling days to weeks after MI.	Contraindications include allergy, renal failure and hypotension. Check renal function before starting and again after 1-2 weeks. <b>Impaired renal function is not an absolute contraindication.</b> Mild non-progressive increase in creatinine after starting an ACE inhibitor is acceptable. Angiotensin receptor blockers can be used as an alternative where ACE inhibitors are not tolerated.
<b>Statin</b>	Should be initiated for all patients regardless of serum cholesterol level.	Short-term statin therapy is associated with improved coronary endothelial function and reversal of prothrombotic states. Statin therapy has been shown to reduce early recurrent ischaemic events after ACS. <sup>13</sup>	Monitor liver function and for symptoms suggestive of myopathy. Consider an alternative statin or dose reduction if not tolerated.
<b>Nitrate</b>	All patients should be prescribed a short-acting nitrate and taught how and when to use it.	Nitrates have not been shown to improve mortality outcomes after MI but short acting nitrates are an integral part of the management of acute myocardial ischaemia. <sup>14</sup>	Advise patients to administer when sitting or lying down. Sublingual glyceryl trinitrate spray has a longer shelf life than tablets. For tablets, spit out remainder of tablet when angina is relieved to avoid headache.

\*For those ACS patients who need to be on warfarin, Australian guidelines state aspirin may sometimes be added but “patients should be observed closely for signs of bleeding”.<sup>7</sup> Aspirin and/or clopidogrel in addition to warfarin are particularly high risk combinations in the elderly.

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\*\*\*Low-risk ACS includes those patients with unstable angina aged <65 years with no diabetes or renal disease where the onset of anginal symptoms has occurred within the last month or the angina has worsened in severity/frequency or the anginal threshold has been lowered.<sup>7</sup>

Note: For recommended starting and target doses see the Australian Medicines Handbook.<sup>8</sup>

See therapeutic brief for references.