MANAGEMENT OF ANGINA DUE TO CORONARY ARTERY DISEASE

North of Tyne, Gateshead and North Cumbria

The recommendations are presented in summary form as a quick reference guide on the first page. There are also supporting notes for additional information.

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INDEX

Contents	Page
Summary	3-4
Introduction	5
Supporting notes	6
Aims of management	6
Assessment of patients with angina	5
Symptomatic treatment	7
Risk factor management / prevention	8

Management of Angina due to CAD (2021)

It is assumed that patients with contraindications to drugs will be identified and excluded (please refer to the BNF). It is advisable to use this summary with the supporting notes.

Aims of management

- Ensure correct diagnosis (refer to specialist services if any doubt regarding the diagnosis)
- Control of symptoms with medication in the first instance
- Refer for assessment for revascularisation if optimal medical therapy fails to control symptoms
- Risk factor management
- Identify markers of adverse outcomes and prognosis
- Patient education regarding lifestyle and risk modification
- Regular review in primary and/or secondary care to optimise management of symptoms and risk factors.

Assessment of patients with angina

- Review of symptoms and initiate baseline investigations - *nature of discomfort/frequency/duration/exacerbating and relieving factors/impact on personal and professional life.*
- Consider co morbidities and quality of life – *check BP/HR/BMI/screen for diabetes if appropriate*
- Resting ECG, biochemistry, CXR and echocardiography (in selected patients) – *FBC/U+E/eGFR/LFT/lipid profile/HbA1$_c$/TFT. Secondary cause: HF, Valvular HD, other non-coronary disease.*
- Assess pre-test probability and clinical likelihood of CAD. – *risk stratification scoring system/referral for non-invasive testing if appropriate*
- Other if appropriate *e.g., spirometry for COPD.*

Symptomatic Treatment

Sublingual GTN for all with advice regarding use. Targeted HR 50-60 as tolerated.

Step 1	BB or CCB
Step 2	BB+ CCB (Add in the agent not taken in step 1)
Step 3	Add second line anti anginal (LAN, Ranolozine, Ivabradine)
Step 4	Consider referral if anginal symptoms not controlled despite used of 3 anti anginals or if medical therapy not tolerated.

Risk Factor Management/Prevention

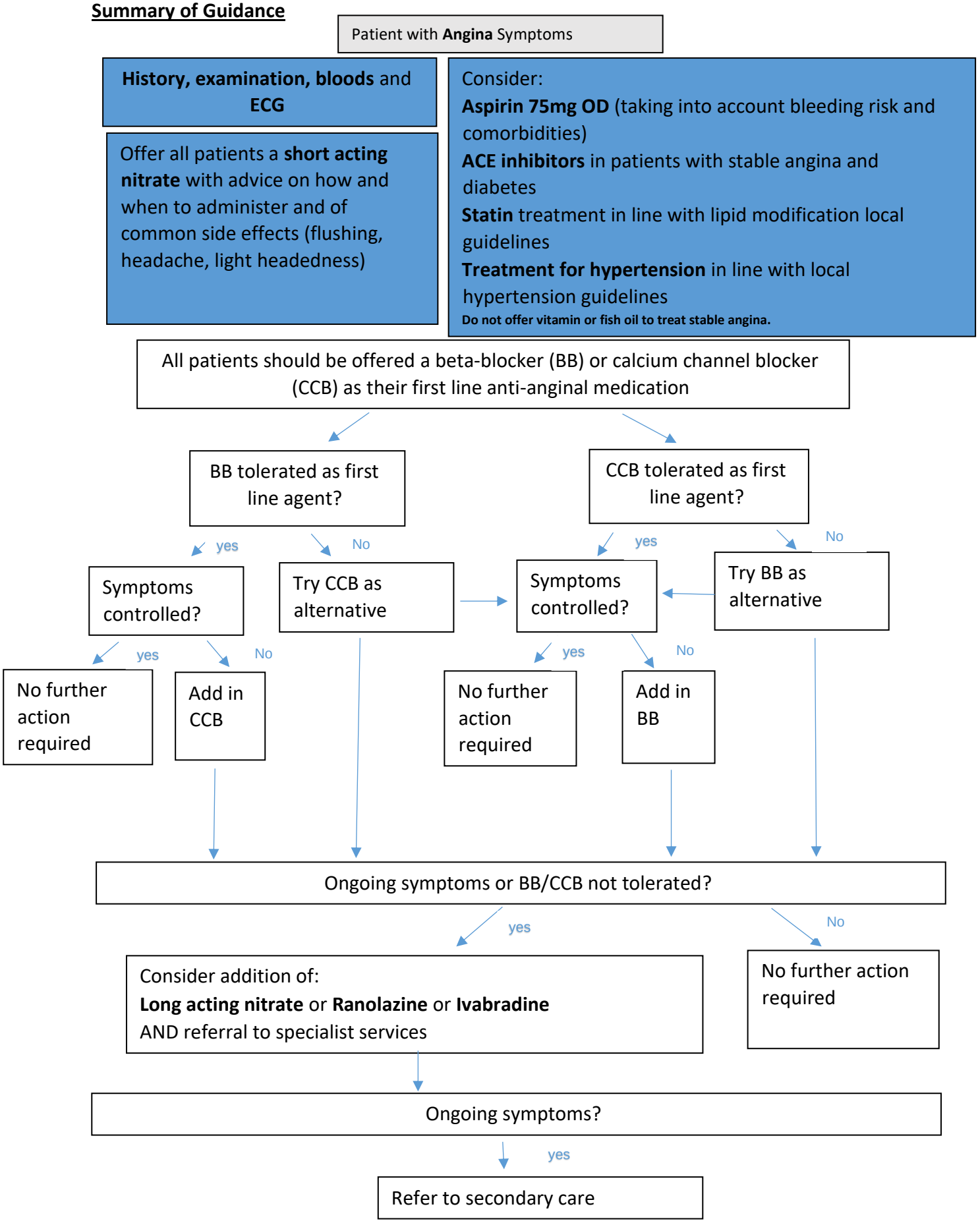
- Lifestyle changes- smoking cessation, healthy diet, physical activity, weight reduction
- Anti-platelet agents - refer to local anti-platelet guidelines
- Lipid management - refer to current NEATS and associated guidance from FH
- Hypertension- refer to local hypertension guidelines
- Diabetes -refer to local diabetes guidelines

Consider ACEI's if evidence of LV dysfunction, recent MI OR high risk e.g., diabetic and hypertensive patients.

Indications for referral to secondary care

- Patients with a working diagnosis of angina with ongoing symptoms despite optimal medical therapy
- Patients with worsening or unstable symptoms not controlled by anti-anginal therapy.

Summary of Guidance



INTRODUCTION

This guidance is intended to guide the management of patients diagnosed with stable angina. It has been developed following a review of the existing North of Tyne guidelines (2014), considering the NICE stable angina guideline 126 (2016)[1], the ESC guidelines on the management of stable angina[2], and consensus agreed between local primary care and secondary care clinicians.

This is intended as a practical guideline, which can be used in everyday practice. Additional background information can be obtained from the NICE and ESC guidelines above, and from other key publications referred to in the notes.

This guideline does not include recommendations for making a diagnosis of angina for which the NICE clinical guideline, "Chest pain of recent onset: Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin" should be referred to.

This guideline is intended for all clinicians in the Newcastle, North of Tyne, Gateshead and North Cumbria areas involved in managing patients with angina. However, it does not include detailed recommendations for the management of patients seen in hospital cardiology clinics.

How to use the guideline

The guideline has two parts, the *summary* and *supporting notes*.

The *summary* at the beginning is a quick reference guide, which can be easily folded over and laminated into a double-sided A5 sheet and kept readily available.

The *supporting notes* contain the recommendations in the *summary* highlighted in bold in text boxes with additional background information where this is appropriate. In some cases, the recommendations are expanded with more detailed guidance.

The *summary* is intended to be used as a quick reference guide and an everyday reminder. The *notes* contain additional supporting information and clinicians are encouraged to be familiar with these and use them to refer to for further clarification of management in individual patients as needed. It is recommended that the BNF be referred to, as necessary and clinicians should use the guideline taking into account individual patients' preferences and any contra-indications.

SUPPORTING NOTES

Aims of Management

- Ensure correct diagnosis (refer if any doubt)
- Control of symptoms with drugs and/or revascularisation
- Risk factor management / prevention
- Identify markers associated with an adverse prognosis
- Patient education and information, including for self-management
- Ensure integration between primary and secondary care, and regular review

Assessment of patients with angina

- Ensure diagnosis is correct and included on the primary care register (EMIS code G33, SYSTMONE G33)
- Review symptoms: Frequency, duration of episodes, recent change Impact on employment, leisure, everyday activities Consider recording grade of angina
- Understand: Patients expectations for symptom control
- Ensure: Symptoms are not unstable (see notes)
- Other symptoms: e.g., heart failure, valve disease (particularly aortic stenosis), other non coronary vascular disease

Physical exam: Blood pressure, pulse (rate and rhythm), BMI Look for signs of secondary causes, heart failure, valve disease, non coronary vascular disease, including AAA.

At baseline: FBC, U&E, eGFR, LFT, TFT, HbA1c, lipid profile, ECG (e.g., rhythm, previous MI, repolarisation changes)

If worsening symptoms:

- FBC, U&E, eGFR, TFT, ECG
- Chest X-ray: If any suspected complications e.g., heart failure, or other pathology e.g., COPD, lung tumour
- Echocardiogram: If ECG abnormal and no previous assessment and or suspected heart failure/ LVSD (e.g., LBBB, previous MI). Suspected valve disease/ other non-vascular causes of angina
- Other: As indicated e.g., spirometry if COPD

This summarises the clinical assessment of a patient with angina. It incorporates recommendations for the clinical assessment of symptoms, the examination and initial investigations prior to referral at the time of diagnosis. The majority of patients have angina due to coronary artery disease, but other causes such as aortic stenosis and hypertrophic cardiomyopathy should be excluded during initial examination. At baseline and again if symptoms worsen, secondary causes (e.g., anaemia) should be excluded. Patients with worsening angina should have a careful history taken and be considered for referral to secondary care. Patients with unstable angina and or suspected myocardial infarction should be referred as an emergency.

Symptomatic treatment

Sublingual GTN for all with advice about use.
***Anti-anginal drug flow** – treated target heart rate at rest 50-60 bpm (as tolerated)*

First step:	Beta blocker (e.g., bisoprolol) or rate limiting calcium channel blocker (e.g., diltiazem), particularly if heart rate > 60 bpm.
Second step:	Add in the agent from step one (CCB or beta blocker) that wasn't used.
Third step:	If beta blocker and or CCB not tolerated/contraindicated, or a third drug is being considered: add isosorbide mononitrate, ranolazine (see notes for considerations with different agents) or ivabradine (not with rate limiting CCB or in AF). Nicorandil can be considered if intolerant of others, but patients need to be made aware of MHRA safety alert.[3]
AND Consider referral / revascularisation if:	3 anti-anginal drugs prescribed, patient preference, drug side effects, poor symptom control.

The recommended drug flow in patients for symptomatic management of angina is summarised above and is consistent with the recommendations in the NICE guideline for management of stable angina. Treatment should be individualised for each patient, and the NICE guideline recommends that anti-anginal drugs other than beta blockers and calcium channel blockers are not offered routinely as first line agents. This guideline further recommends that if both beta blockers and calcium channel blockers are not tolerated or are contraindicated, monotherapy with isosorbide mononitrate, nicorandil, ivabradine or ranolazine be considered, considering comorbidities, contraindications, the persons preferences and costs. These agents can also be combined with beta blockers or calcium channel blockers considering individual drug interactions etc.

The local guideline group recognised that there was less familiarity in primary care with some agents and an exhaustive summary is beyond the scope of this guideline. However, the following felt should be pointed out. Serious adverse events have been reported with nicorandil, i.e., gastro-intestinal ulceration: oral ulcers, colitis and perianal ulceration. These may be severe and, in a few patients, have led to perforation. In some patients pre-existing conditions such as colitis may be exacerbated. Time to onset varies and the symptoms are often refractory to treatment and usually require withdrawal of nicorandil. A MHRA alert about this was published in June 2008[3]. Ivabradine cannot be combined with diltiazem or verapamil and is ineffective in atrial fibrillation / atrial flutter / atrial tachycardia. If treatment with a beta blocker has been optimised and additional rate limiting action is required, ivabradine can be combined with a beta blocker. There are several drug interactions with ranolazine, which has

also been reported to prolong the QT interval. Drug costs vary and a summary is included in the appendix.

Referral for possible coronary revascularisation should be considered if symptoms are not well controlled, and patients should be asked in detail how any remaining symptoms affect them in their day-to-day life. Some patients may prefer to consider coronary revascularisation rather than additional drug therapy, and patients who experience drug side effects should generally be referred. Revascularisation is often possible with percutaneous coronary intervention (PCI), although some may require coronary artery bypass graft surgery (CABG).

Risk factor management / prevention

Lifestyle changes	Smoking cessation, healthy eating/ alcohol safe limits / increase physical activity / weight management
Anti-platelet agents	Refer to local anti-platelet guidelines
Lipid management	Refer to current NEELI, and associated guidance for FH
Hypertension	Refer to local hypertension guidelines
Diabetes	Refer to local diabetes guidelines
ACE inhibitors if:	Existing indications (LVSD, post MI, CKD with proteinuria); refer to other local guidelines If high risk, for example if diabetes and or hypertension Angiotensin II receptor antagonists; only if shown to be intolerant of ACE inhibitor

This summarises risk factor management and treatment for secondary prevention, which should be optimised in all patients, with referral to other local guidelines as appropriate.

Adjunctive therapy used in smokers motivated to quit was discussed. Nicotine replacement therapy (NRT) can be used, and there is considerable clinical experience of doing so. There is less evidence for the use of varenicline and buproprion in patients with stable cardiovascular disease. There is no good evidence of a large increased risk of cardiovascular events or mortality, although the numbers in the RCTs have tended to be quite small[3 4], and a RCT of varenicline[4] in which there was a small increase in events at 52 weeks with varenicline treatment compared with placebo acknowledged that the study size was too small to detect small changes in cardiovascular outcomes. Neither could the conclusions be extended to smokers with recent or acute cardiovascular events[5]. Patients with a history of depression or psychiatric illness, or other contra-indications to treatment with varenicline were excluded from the study.

The group discussed the use of ACE inhibitors for the prevention of cardiovascular events. Existing recommendations to treat those with left ventricular systolic dysfunction, a previous MI, as well as non-cardiac indications were re-iterated. It was also recognised that there is evidence that ACE inhibitors reduce the relative risk of cardiovascular events in patients with stable cardiovascular disease / coronary disease or who are at high risk without known heart

failure and left ventricular systolic dysfunction[6,7]. There was a consensus to recommend preventative treatment with an ACE inhibitor in those with co-existing indications and in those with stable angina at highest risk, for example those with diabetes and or hypertension. This is consistent with the NICE guidelines for stable angina which recommend "Consider angiotensin-converting enzyme (ACE) inhibitors for people with stable angina and diabetes. Offer or continue ACE inhibitors for other conditions, in line with relevant NICE guidance"[8].

ARBs have been shown to be non-inferior to ACE inhibitors in patients with stable cardiovascular disease or who at high risk of cardiovascular disease without known heart failure and left ventricular systolic dysfunction[9]. An ARB with the lowest acquisition cost should be used, although not all agents are licensed for the indications and appropriate dosing should be taken into consideration. In patients with heart failure and left ventricular ejection fraction less than 40% there is evidence that losartan 150 mg od reduced the rate of death and admission with heart failure compared with losartan 50 mg od[10] for example.

Indications for referral to secondary care

Patients with a new diagnosis of angina or suspected angina
Consider if never assessed for revascularisation (symptoms/markers of an adverse prognosis)
Worsening angina symptoms, even if improve either spontaneously or with additional treatment if there are markers of an adverse prognosis
Unstable symptoms: urgent / emergency referral

In primary care, patients who have stable symptoms which are not worsening, and which are not of concern to the patient, generally do not require referral to secondary care. However, if that is not the case and or patients wish to consider additional and or alternative treatment for their angina should be considered for referral to a cardiologist.

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1 NICE stable angina guideline CG 126. http://guidance.nice.org.uk/CG126/NICEGuidance/pdf/English
2 http://eurheartj.oxfordjournals.org/content/34/38/2949.full.pdf
3 MHRA Drug Safety Update Volume 1, Issue 11, June 2008
4 Rigotti, N et al. Efficacy and Safety of Varenicline for Smoking Cessation in Patients with Cardiovascular Disease. Circulation. 2010;121:221-229.
5 Hughes JR et al. Antidepressants for smoking cessation (review). The Cochrane Collaboration. Available at http://mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD000031/pdf_fs.html. Accessed 28 January 2010.
6 The HOPE study investigators. Effects of an Angiotensin-Converting–Enzyme Inhibitor, Ramipril, on Cardiovascular Events In High-Risk Patients. New Engl J Med 2000;342:145-53.
7 The EUROPA study investigators. Efficacy of perindopril in reduction of cardiovascular events among patients with stable coronary artery disease: randomised, double-blind, placebo-controlled, multicentre trial (the EUROPA study). Lancet 2003;362:782-88.
8 NICE stable angina guidelines, CG 126 available at http://guidance.nice.org.uk/CG126/NICEGuidance/pdf/English
9 The ONTARGET Investigators. Telmisartan, Ramipril, or both in Patients at High Risk for Vascular Events. New Engl J Med 2008;358:1547-59.
10 Konstam MA et al. Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial. Lancet 2009;374:1840-8