

New from NICE: Important changes in the use of clopidogrel and MR dipyridamole

Clopidogrel* alone is now recommended by NICE with no limits on duration of treatment in people who have had an ischaemic stroke. Modified-release (MR) dipyridamole plus aspirin is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated. This and other changes in NICE guidance on clopidogrel and MR dipyridamole for the prevention of occlusive vascular events have been introduced in technology appraisal guidance 210,¹ which replaces the NICE guidance issued in 2005.

*Treatment with clopidogrel should be started with the least costly licensed preparation.¹ In current practice, this means generic clopidogrel.

What are the implications of the new guidance?

Health professionals should follow this guidance¹ for people who have had an occlusive vascular event or who have established peripheral arterial disease. Here is **our summary of the practical implications of these changes**:

After an ischaemic stroke:

- Clopidogrel alone is now recommended, with no specified limit on duration of treatment
- MR dipyridamole plus aspirin is now recommended after an ischaemic stroke **only** if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to two years
- MR dipyridamole alone is recommended after an ischaemic stroke **only** if aspirin or clopidogrel cannot be used as above because they are contraindicated or not tolerated, again with no limit on duration of treatment.

After a transient ischaemic attack (TIA):

- Treatment with MR dipyridamole plus aspirin is still recommended for people who have had a TIA, but now there is no recommended limit on the duration of treatment
- MR dipyridamole monotherapy is recommended after TIA **only** if aspirin is contraindicated or not tolerated, again with no limit on duration of treatment
- No recommendations are made about the use of clopidogrel after a TIA because it is not licensed for this indication.

After a myocardial infarction (MI):

- Recommendations about aspirin as the treatment of choice post MI² is not affected by this new guidance
- Clopidogrel is recommended for people who have had an MI, only if aspirin is contraindicated or not

tolerated. This guidance¹ should be considered alongside existing NICE guidance, which gives details on the use of clopidogrel in combination with aspirin in people who have had an MI (see CG48³), and in people with unstable angina or non-ST-segment-elevation MI (NSTEMI, see CG94³).

Peripheral arterial disease (PAD) or multivascular disease:

- Clopidogrel alone is now recommended for patients with PAD or multivascular disease.

Treatment with clopidogrel should be started with the **least costly licensed preparation**.¹ **In current practice, this means generic clopidogrel.** Although not discussed in the guidance, aspirin monotherapy would seem to be the logical choice if both clopidogrel and MR dipyridamole were contraindicated or not tolerated.

People currently receiving clopidogrel or MR dipyridamole, either with or without aspirin, outside the revised recommendations should have the option to continue treatment until they and their clinicians consider it appropriate to stop.¹

This guidance does not apply to people with atrial fibrillation (AF). NICE guidance on prophylaxis of stroke in people with AF is given in CG36.⁴ More information on managing AF can be found in the NPC e-learning materials on atrial fibrillation. It also does not apply to those who need treatment to prevent occlusive events after coronary revascularisation or carotid artery procedures.

See MeReC Rapid Review No. 2353 for further details, particularly the background to these changes. More information can be found in the NPC e-learning materials on stroke, the NPC e-learning materials on post MI and the NPC e-learning materials on antiplatelets.

Treatment with clopidogrel should be started with the least costly licensed preparation. In current practice, this means generic clopidogrel.

All information was correct at the time of publication (May 2011)

References

1. NICE. Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events (review of NICE technology appraisal guidance 90). Technology appraisal guidance 210. December 2010
2. NICE. Secondary prevention in primary and secondary care for patients following a myocardial infarction. Clinical guideline 48. May 2007
3. NICE. Unstable angina and NSTEMI: the early management of unstable angina and non-ST-segment-elevation myocardial infarction. Clinical guideline 94. March 2010
4. NICE. The management of atrial fibrillation. Clinical guideline 36. June 2006

Observational study suggests candesartan may be preferable to losartan ▼* in heart failure

A Swedish observational study¹ (n=5,139) has suggested that patients with heart failure (HF) have improved survival when they are treated with candesartan compared with losartan ▼*. This study has limitations (e.g. there was no control arm) but it highlights the possibility that there may be some differences between individual angiotensin-2 receptor antagonists when they are used in people with HF.

* The black triangle has been reinstated for Cozaar ▼ (losartan) specifically for the new indication of heart failure.

Action

Clinicians should continue to follow NICE recommendations² that an ACE inhibitor is the first choice renin-angiotensin system (RAS) drug in HF. An angiotensin-2 receptor antagonist (A2RA) licensed for HF can be considered if the patient has an intolerable cough with an ACE inhibitor. An A2RA can also be used in combination with an ACE inhibitor and a beta-blocker in certain patients on specialist advice, if the patient remains symptomatic despite optimal therapy with an ACE inhibitor and beta-blocker. Despite this study's limitations, any change from candesartan to losartan in patients with HF, requires caution.

Further details

This study has a number of limitations as discussed in MeReC Rapid Review No. 2396. It is an observational study and, therefore, may be subject to a number of biases. Also, as it was conducted in people with heart failure, it provides no information about the comparative effects of losartan or candesartan in hypertension or other indications. However, it is worth remembering that A2RAs are **not** recommended by NICE as first choice RAS drugs for any indication; ACE inhibitors have a larger and more robust evidence base than A2RAs and, in some conditions, there is better evidence of efficacy for ACE inhibitors.

What's new from the National Prescribing Centre?

The NPC have combined the publications, information and resources on our npc.co.uk site with the e-learning resources on NPCi to create one new, streamlined and user friendly website.

The new website has been designed to enable the user to identify and utilise all NPC resources quickly and effectively. The modern design is clean and fresh, and importantly offers much improved search and navigation functions.

To access existing resources from our key work streams on the new website please follow the links below:

e-Learning: www.npc.nhs.uk/elearning.php

Our e-Learning homepage will direct you to the therapeutics and medicines management e-learning resources formerly available on NPCi.

MeReC: www.npc.nhs.uk/merec

Rapid Reviews (formerly called 'blogs'):
<http://www.npc.nhs.uk/rapidreview/>

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Controlled drugs:
www.npc.nhs.uk/controlled_drugs

Local decision-making:
www.npc.nhs.uk/local_decision_making

Non-medical prescribing:
www.npc.nhs.uk/non_medical

Events: www.npc.nhs.uk/events

Electronic Current Awareness (eCAB) bulletins: www.npc.nhs.uk/ecab.php

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Prescribing managers should review local prescribing trends for RAS drugs as suggested in the document 'Key therapeutic topics 2010/11 – Medicines management options for local implementation'³ produced by the NPC as part of the NHS 'Quality, Innovation, Productivity and Prevention (QIPP)' programme. This document highlights the productivity and quality opportunities in using ACE inhibitors in preference to A2RAs and for careful consideration of switching from A2RAs to ACE inhibitors in some selected patients. However, this study reminds us that caution is required when considering whether to change from candesartan to losartan in patients with HF, even after a careful medication review.

This study is discussed in more detail in MeReC Rapid Review No. 2396.

References

1. Eklind-Cervenka M, et al. Association of candesartan vs losartan with all-cause mortality in patients with heart failure. *JAMA* 2011;305:175–82
2. NICE. Chronic heart failure: management of chronic heart failure in adults in primary and secondary care. Clinical guideline 108. August 2010
3. NPC. Key therapeutic topics 2010/11 – Medicines management options for local implementation. First update February 2011

The National Prescribing Centre (NPC) is responsible for helping the NHS to optimise its use of medicines. NPC is part of the National Institute for Health and Clinical Excellence (NICE), an independent organisation providing national guidance on promoting good health and preventing and treating ill health.