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NICE CLINICAL GUIDELINE 127: *HYPERTENSION – CLINICAL MANAGEMENT OF PRIMARY HYPERTENSION IN ADULTS* (AUGUST 2011)

What's new in hypertension?

- **NICE has issued an updated Clinical Guideline on the treatment of hypertension in adults.**
- **Ambulatory BP monitoring and home BP monitoring are both given more prominent roles to address the issue of 'white coat' hypertension and to reduce the risk of misdiagnosis and inappropriate treatment.**
- **For non-black people under 55 years, either an Angiotensin Converting Enzyme Inhibitor (ACEI) or a *low cost* Angiotensin Receptor Blocker (ARB) (if an ACEI is not tolerated) is advocated at step 1. The only low cost ARB at present is generic losartan, although patent expiries in 2012 are likely to increase the range of low cost ARBs to include: candesartan, eprosartan, irbesartan and valsartan. Practices who have not already undertaken extensive product switching away from the high-cost long patent life ARBs, telmisartan and olmesartan, are encouraged to do so in 2012.**
- **For people over 55 years and black people of African or Caribbean family origin of any age, a calcium channel blocker (CCB) is advocated at step 1. The first line CCB of choice is generic amlodipine tablets.**
- **If a CCB is not suitable, due to oedema or intolerance, or if there is evidence of heart failure or high risk of heart failure, a thiazide-like diuretic is advocated. NICE prefer the thiazide-like diuretics (indapamide and chlortalidone) to the thiazides (bendroflumethiazide and hydrochlorothiazide) because the outcomes data is stronger for low dose thiazide-like products than for low-dose thiazides. Where a thiazide-like diuretic is indicated, generic indapamide 2.5mg daily in the morning should be prescribed. Indapamide 1.5mg modified release (Natrilix SR) offers no advantage over standard release indapamide and is over three times the cost.**
- **If the person's BP is stable and well controlled on bendroflumethiazide or hydrochlorothiazide, there is no need to consider switching to indapamide or chlortalidone.**
- **For people of any age, if BP is not controlled at step 1, offer step 2 treatment with a CCB in combination with either an ACEI or a low cost ARB. In black people of African or Caribbean family origin, ACEIs are associated with an increased risk of angioedema, which can be life-threatening. Although the risk of angioedema with ACEIs in this patient group is low and ARBs are not devoid of this problem, NICE consider low cost ARBs to be lower risk within this context.**

Introduction

NICE have updated their Clinical Guideline on the treatment of hypertension. It is the purpose of this special edition of the *PACE Bulletin* to summarize the key recommendations and to provide practical guidance on implementation. A treatment algorithm is included, based on the associated NICE care pathway, as an aid to decision making.

Key recommendations are as follows:

Diagnosing hypertension

- If the clinic blood pressure (BP) is 140/90 mmHg or higher, offer ambulatory BP monitoring (ABPM) to confirm the diagnosis of hypertension. NICE give further guidance on the use of ABPM.

PACEF Comment: *Ambulatory BP monitoring*
NICE have stated that 'ambulatory monitoring as a diagnostic strategy for hypertension after an initial raised reading in the clinic would reduce misdiagnosis and save costs. Additional costs from ambulatory monitoring are counterbalanced by cost-savings from better targeted treatment'.

- If a person is unable to tolerate ambulatory BP monitoring, home BP monitoring is an alternative. NICE give further guidance on home BP monitoring.

Initiating antihypertensive drug treatment

- Offer antihypertensive treatment to people aged under 80 years with stage 1 hypertension (see below) who have one or more of the following:
    - target organ damage
    - established cardiovascular disease
    - renal disease
    - diabetes
    - a 10-year cardiovascular risk equivalent to 20% or greater.

PACEF Comment: *Stage 1 Hypertension*
NICE define stage 1 hypertension as: 'Clinic BP is 140/90 mmHg or higher and subsequent ABPM daytime average or HBPM average BP is 135/85 mmHg or higher'.

- For people over 80 years, offer the same drug treatment as for 55-80 years, taking into account any co-morbidities.
- For people under 40 years with stage 1 hypertension and no evidence of target organ damage, cardiovascular disease, renal disease or diabetes, consider seeking specialist evaluation. This is because CV risk assessments can underestimate the risk of CV events in this patient group.
- Offer antihypertensive drug treatment to people of any age with stage 2 hypertension.

PACEF Comment: *Stage 2 Hypertension*
NICE define stage 2 hypertension as: 'Clinic BP is 160/100 mmHg or higher and subsequent ABPM daytime average or HBPM average BP is 150/95 mmHg or higher'.

Monitoring treatment

- For people identified as having a 'white-coat effect', consider ABPM or HBPM as an adjunct to clinic BP measurements to monitor the response to antihypertensive treatment with lifestyle modification or drugs.

Blood pressure targets

	Under 80 years	Over 80 years
Clinic BP	<140/90 mmHg	<150/90 mmHg
Ambulatory or Home BP Monitoring	<135/85 mmHg	<145/85 mmHg

Antihypertensive Drug Treatment

- Prescribe medicines to be taken once daily if possible.
- Prescribe generic drugs if possible to minimise cost.

Step 1

ACEIs and Low Cost ARBs

- For non-black people under 55 years, offer an ACEI or a *low cost* ARB (if an ACEI is not tolerated).
- Do not use a combination of an angiotensin converting enzyme inhibitor (ACEI) or an angiotensin II receptor blocker (ARB) to treat hypertension.

PACEF Comment: *ACEIs and Low Cost ARBs*
In accordance with previously issued PACEF advice (see *PACE Bulletin* Vol 4, No 10 (July 2010)), ACEIs remain the renin-angiotensin system (RAS) drugs of choice; low cost ARBs should be reserved for those patients who cannot tolerate ACEIs. An updated cost comparison of the ACEIs and ARBs appears at the end of this *Bulletin.* Ramipril capsules, lisinopril tablets and perindopril erbumine tablets are all suitable low cost generic ACEI options; perindopril arginine (Coversyl Arginine) is a premium priced branded ACEI and should not be used.
Losartan tablets represent the first (and currently the only) *low cost* generic ARB and should be used preferentially where an ARB is indicated for hypertension in accordance with NICE guidance. However, this situation looks set to change in 2012. Valsartan is already available generically with falling generic reimbursement prices expected soon. Other ARBs that will become available generically in 2012 include: candesartan, eprosartan and irbesartan. Prescribers are advised not to initiate new patients on the high-cost, branded, long patent-life ARBs, telmisartan (Micardis) and olmesartan (Olmetec). Many practices have been switching existing patients away from these two ARBs in 2011; further therapeutic switches in practices yet to undertake this work will be encouraged and supported in 2012/13

Calcium Channel Blockers

- For people over 55 years and black people of African or Caribbean family origin of any age, offer a calcium channel blocker (CCB). If a CCB is not suitable, due to oedema or intolerance, or if there is evidence of heart failure or high risk of heart failure, offer a thiazide-like diuretic.

PACEF Comment: *Calcium Channel Blockers*
Prescribers are reminded that generic amlodipine tablets are the preferred once daily dihydropyridine CCB of choice.

Thiazide-like diuretics

- If treatment with a diuretic is being initiated or changed, offer a *thiazide-like* diuretic (e.g. chlortalidone (12.5-25mg once daily) or indapamide (1.5mg M/R once daily or 2.5mg once daily) in preference to bendroflumethiazide or hydrochlorothiazide). If the person's BP is stable and well controlled on bendroflumethiazide or hydrochlorothiazide, there is no need to consider switching to indapamide or chlortalidone.

PACEF Comment: *Thiazides and Thiazide-Like Diuretics*
There are currently two broad groups of thiazide diuretics in use in the UK. These are: (1) classical thiazide diuretics (e.g. bendroflumethiazide and hydrochlorothiazide); and (2) thiazide-like diuretics (e.g. chlortalidone and indapamide). NICE had reservations about the outcomes data relating to bendroflumethiazide and hydrochlorothiazide. The data demonstrating the benefits of bendroflumethiazide in preventing clinical outcomes derives from older studies which utilised doses as high as 10mg; evidence confirming that these benefits can also be attributed to the lower 2.5mg dose is limited. There is a similar lack of evidence supporting low doses of hydrochlorothiazide within this context. This does not mean that either of these agents is ineffective, but it does make it difficult to assess whether they are as effective as chlortalidone and indapamide, two agents for which there is evidence of benefit on a range of different clinical outcomes when used at low doses. Chlortalidone is only available in the UK as a 50mg tablet; this creates significant practical difficulties within the NICE recommended dose range. As a result, where a thiazide-like diuretic needs to be initiated, indapamide (generic) 2.5mg once daily is advocated; indapamide 1.5mg sustained release (SR) tablets (Natrilix SR) present a possible alternative, but are over three times the price of the 2.5mg generic and *should not be used preferentially* (see cost comparison). Generic indapamide 2.5mg is more expensive than generic bendroflumethiazide 2.5mg, but not substantially so. Prescribers are reminded of the extent to which hydrochlorothiazide appears in combination products. While NICE would not advocate routine switching away from these combinations where the patient's BP is well-controlled and stable, prescribers will need to consider alternatives for new initiations.

Beta-blockers

- Beta-blockers (BBs) are no longer a preferred initial therapy for hypertension. However, BBs may be considered for younger people particularly: if ACEIs and ARBs are unsuitable due to intolerance or contraindication; or if there is evidence of increased sympathetic drive or if treatment is required for a woman of child-bearing potential.

Step 2

- For people of any age, if BP is not controlled at step 1, offer step 2 treatment with a CCB in combination with either an ACEI or a low cost ARB.
- If a CCB is not suitable at step 2, for example because of oedema or intolerance, or if there is evidence of heart failure or high-risk of heart failure, offer a thiazide-like diuretic.
- For black people of African or Caribbean family origin, consider a low cost ARB in preference to an ACEI, in combination with a CCB.

PACEF Comment: Using a low cost ARB in preference to an ACEI (in combination with a CCB) in black people of African or Caribbean family origin
In black people of African or Caribbean family origin, ACEIs are associated with an increased risk of angioedema, which can be life-threatening. Although the risk of angioedema with ACEIs in this patient group is low and ARBs are not devoid of this problem, NICE considered a low cost ARB to be lower risk in this context. As in Step 1, the emphasis is on a *low cost* ARB (see earlier).

Step 3

- Before moving to step 3, review medication to ensure that step 2 treatment is optimal and at best tolerated doses.
- If treatment with three drugs is considered necessary, the combination of an ACEI (or low cost ARB) plus a CCB plus a thiazide-like diuretic is preferred.

Step 4

- Clinic BP that remains above 140/90 mmHg even after treatment with optimal or best tolerated doses of an ACEI (or low cost ARB) plus a CCB plus a thiazide-like diuretic should be regarded as resistant hypertension. Addition of a fourth antihypertensive agent should be considered; specialist advice may need to be sought.
- For the treatment of resistant hypertension, consider further diuretic therapy with low-dose spironolactone (25mg once daily) if the blood potassium level is 4.5mmol/l or lower. Spironolactone is not licensed for this indication and informed consent should be obtained and documented. If blood potassium is higher than 4.5mmol/l, consider higher-dose thiazide-like diuretic treatment.
- Monitor blood sodium and potassium and renal function if using further diuretic therapy.
- If further diuretic therapy for resistant hypertension at step 4 is not effective, consider an alpha- or beta-blocker.
- If BP remains uncontrolled with optimal or maximum tolerated doses of four drugs, seek expert advice if this has not yet been obtained.

Appendix 1: Cost comparisons

Costs of selected ACE inhibitors

	Dose range (hypertension)	**Cost / 28 days (*Drug Tariff* December 2011)**
Enalapril	2.5 – 40mg once daily	£0.95 – 1.90
Lisinopril	2.5 – 80mg once daily	£0.75 – 4.08
Perindopril erbumine (generic)	2 – 8mg once daily	£1.38 -1.62
Perindopril arginine	2.5 – 10mg once daily	£4.43 – 10.65
Ramipril capsules	1.25mg – 10mg once daily	£0.97 – 1.23

Costs of ARBs

	Dose	**Cost for 28 tabs / caps *Drug Tariff* December 2011**
Candesartan (Amias) tablets Patent expiry due: April 2012	2mg	£14.32
	4mg	£9.78
	8mg	£9.89
	16mg	£12.72
	32mg	£16.13
Eprosartan (Teveten) tablets Patent expiry due: April 2012	300mg	£7.31
	600mg	£14.31
	800mg	£15.77
Irbesartan (Aprovel) tablets Patent expiry due: August 2012	75mg	£9.69
	150mg	£11.84
	300mg	£15.93
Losartan (Generic) tablets	**12.5mg**	**£6.61**
	25mg	**£0.99**
	50mg	**£1.07**
	100mg	**£1.24**
Olmesartan (Olmetec) tablets Patent expiry due: February 2017	10mg	£10.95
	20mg	£12.95
	40mg	£17.50
Telmisartan (Micardis) tablets Patent expiry due: January 2017	20mg	£8.00
	40mg	£12.50
	80mg	£17.00
Valsartan (Generic) tablets/ capsules Patent expired: November 2011	40mg	£13.97
	80mg	£13.97
	160mg	£18.41
	320mg	£20.23

Cost of Indapamide Formulations

	Dose range (hypertension)	**Cost / 28 days (*Drug Tariff* December 2011)**
Bendroflumethiazide tablets 2.5mg	2.5mg daily in the morning	£0.66
Indapamide 2.5mg tablets (generic)	2.5mg daily in the morning	£0.96
Indapamide MR tablets 1.5mg (Natrilix SR)	1.5mg daily in the morning	£3.16

Stephen Gibson
Head of Prescribing and Medicines Management
NHS Lincolnshire

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ANTIHYPERTENSIVE DRUG TREATMENT