

NEWSLETTER

Supporting the Derbyshire Health Community

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PACEF update

The current Traffic Lights list can be accessed via the PACEF intranet site
www.nodyis.nhs.uk/guidelines/pacef%20web.htm.

RED drugs are those where prescribing responsibility would normally lie with a hospital consultant or a specialist. AMBER drugs are those that although usually initiated within a hospital setting, could appropriately become the responsibility of the GP. This would normally be under a shared care agreement. GREEN drugs are regarded as routine for primary care prescribing. BROWN drugs are those that PACEF does not recommend for use (or only in restricted circumstances) due to lack of data on safety, effectiveness, or cost-effectiveness.

<u>Drug</u>	<u>Date considered</u>	<u>Decision</u>
Erdosteine	February 2007	BROWN
Lidocaine 5% medicated plaster	February 2007	BROWN
Armour thyroid	January 2007	BROWN
Melatonin	January 2007	AMBER (moved from RED)
Dexibuprofen	November 2006	BROWN
Valganciclovir	November 2006	RED
Efalizumab	September 2006	RED
Rituximab	September 2006	RED
Clenil Modulite (beclometasone cfc-free MDI)	August 2006	GREEN Prescribe by brand name
Celluvisc eye drops	August 2006	GREEN
Natalizumab	August 2006	RED
Rimonabant	August 2006	BROWN

Simvastatin 40mg LES proposal

Recent figures released from the NHS institute put the old North Eastern Derbyshire PCT first and the old Chesterfield PCT fifth nationally for the percentage of low-cost statins prescribed. This is at least partly due to the statin policy and its effective implementation. To maximise the use of simvastatin 40mg and avoid unnecessary cholesterol monitoring, NED PCT developed a local arrangement in 2005, which was then taken up by Chesterfield PCT.

We are now part of Derbyshire County PCT and do not want to lose the benefit from this good work. A proposal to spread this as a locally enhanced service (LES) across Derbyshire County PCT has been discussed at key groups across the county. The aim is to enable practices to continue to maximise the use of

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simvastatin 40mg as per the statin policy without being financially disadvantaged under the QoF and avoid unnecessary cholesterol monitoring, which has the potential to drive inappropriate prescribing of lipid-lowering drugs. The proposal has received strong support from PACEF in the north and PAG in the south of the county, the countywide CHD LIT, locality prescribing sub-groups, and clinical governance and GP prescribing leads. Ask your locality prescribing adviser for details.

The proposal also has the support of Dr Alan Meakin, the Medical Director, and as PEC chair he will be aiming to ensure that this LES is in place for the financial year 2007/08. **The important message is that if you are currently prescribing simvastatin 40mg and not monitoring lipid levels, there is no need to change your practice at this time.**

Use of Oxybutynin

Further to the article in the December issue of this newsletter discussing the management of urinary incontinence in women, I have been asked to remind readers that when immediate-release oxybutynin is used, the dose needs to be built up slowly. Start with 2.5mg twice daily initially and increase by 2.5mg increments at 4-6 week intervals, as necessary.

NICE guidance on inhaled insulin

NICE has finally issued Technology Appraisal Guidance No. 113 on the use of inhaled insulin for type 1 and type 2 diabetes. This is the summary:

- Inhaled insulin is not recommended for the routine treatment of people with type 1 or type 2 diabetes mellitus.
- Inhaled insulin may be used as a treatment option for people with type 1 or type 2 diabetes mellitus who show evidence of poor glycaemic control despite other therapeutic interventions (including, where appropriate, diet, oral hypoglycaemic agents and subcutaneous insulin) and adequate educational support, **and** who are unable to initiate or intensify preprandial subcutaneous insulin therapy because of either:
 - a marked and persistent fear of injections that meets DSM-IV criteria for specific phobia 'blood injection injury type' diagnosed by a diabetes specialist or mental health professional or
 - severe and persistent problems with injection sites (for example, as a consequence of lipohypertrophy) despite support with injection site rotation.
- In patients receiving inhaled insulin under the circumstances set out above, treatment should only be continued beyond 6 months, and in the longer term, if there is evidence of a sustained improvement in glycated haemoglobin (HbA1c) that is judged to be clinically relevant to the individual patient's overall risk of developing long-term complications of diabetes.
- Initiation of inhaled insulin treatment and monitoring of response should be carried out at a specialist diabetes centre. The responsible clinician should discuss the risks and benefits of inhaled insulin with the patient so that an informed choice can be made regarding appropriate options for diabetes management, including psychological support and therapy for needle phobia if necessary.

PACEF has designated inhaled insulin (Exubera) as a RED drug.

NICE guideline on obesity

NICE has issued its guideline on the prevention, identification, assessment and management of overweight and obesity in adults and children. The key priorities for implementation are as follows:

Public Health

- Managers and health professionals in all primary care settings should ensure that preventing and managing obesity is a priority, at both strategic and delivery levels. Dedicated resources should be allocated for action.
- Primary care organisations and local authorities should recommend to patients, or consider endorsing, self-help, commercial and community weight management programmes only if they follow best practice.

Clinical care

- Multicomponent interventions are the treatment of choice. Weight management programmes should include behaviour change strategies to increase people's physical activity levels or decrease inactivity, improve eating behaviour and the quality of the person's diet and reduce energy intake.

Children

- Interventions for childhood overweight and obesity should address lifestyle within the family and in social settings.
- Body mass index (BMI) (adjusted for age and gender) is recommended as a practical estimate of overweight in children and young people, but needs to be interpreted with caution because it is not a direct measure of adiposity.
- Referral to an appropriate specialist should be considered for children who are overweight or obese and have significant comorbidity or complex needs (for example, learning or educational difficulties).

Adults

- The decision to start drug treatment, and the choice of drug, should be made after discussing with the patient the potential benefits and limitations, including the mode of action, adverse effects and monitoring requirements and their potential impact on the patient's motivation. When drug treatment is prescribed, arrangements should be made for appropriate health professionals to offer information, support and counselling on additional diet, physical activity and behavioural strategies. Information about patient support programmes should also be provided.
- Bariatric surgery is recommended as a treatment option for adults with obesity if all of the following criteria are fulfilled.
 - They have a BMI of 40 kg/m² or more, or between 35 and 40 kg/m² and other significant disease (for example, type 2 diabetes or high blood pressure) that could be improved if they lost weight.
 - All appropriate non-surgical measures have been tried but have failed to achieve or maintain adequate, clinically beneficial weight loss for at least 6 months.
 - The person has been receiving or will receive intensive management in a specialist obesity service, is generally fit for anaesthesia and surgery, and commits to the need for long-term follow-up.
- Bariatric surgery is also recommended as a first-line option (instead of lifestyle interventions or drug treatment) for adults with a BMI of more than 50 kg/m² in whom surgical intervention is considered appropriate.

This is what the guideline has to say about drug treatments.

Adults

When to consider drug treatment

- Consider only after dietary, exercise and behavioural approaches have been started and evaluated.
- Consider for patients who have not reached their target weight loss or have reached a plateau on dietary, activity and behavioural changes alone.
- Before deciding to start treatment, and choosing the drug, discuss with the patient the potential benefits and limitations, including the mode of action, adverse effects and monitoring requirements, and their potential impact on the patient's motivation.
- When prescribing, make arrangements for appropriate healthcare professionals to offer information, support and counselling on additional diet, physical activity and behavioural strategies.
- Give information on patient support programmes.
- Follow the drug's summary of product characteristics.

Continued prescribing and withdrawal

- Review regularly, to monitor the effect of drug treatment, and to reinforce lifestyle advice and need for adherence.
- Drug treatment may be used to help people to maintain weight loss, as well as to continue to lose weight.
- Consider withdrawing drug treatment if the person does not lose enough weight.
- Consider less strict goals for people with type 2 diabetes, because they may lose weight more slowly. Agree goals with the person and review regularly.
- If concerned about micronutrient intake, consider giving a supplement providing the reference nutrient intake for all vitamins and trace elements, particularly for vulnerable groups such as older people, who may be at risk of malnutrition.
- If withdrawing a person's drug treatment, offer support to help maintain weight loss because their self-confidence and belief in their ability to make changes may be low.

Specific advice on drugs

ORLISTAT

- Prescribe only as part of an overall plan for managing obesity in adults who have:
 - a BMI of 28.0 kg/m² or more with associated risk factors, or
 - a BMI of 30.0 kg/m² or more.
- Continue treatment for longer than 3 months only if the person has lost at least 5% of their initial body weight since starting drug treatment (less strict goals may be appropriate for people with type 2 diabetes).
- Continue for longer than 12 months (usually for weight maintenance) only after discussing potential benefits and limitations with the patient.
- Co-prescribing with other drugs for weight reduction is not recommended.

SIBUTRAMINE

- Prescribe only as part of an overall plan for managing obesity in adults who have:
 - a BMI of 27.0 kg/m² or more and other obesity-related risk factors such as type 2 diabetes or dyslipidaemia, or
 - a BMI of 30.0 kg/m² or more
- Prescribe only if there are adequate arrangements for monitoring both weight loss and adverse effects (specifically pulse and blood pressure).
- Continue treatment for longer than 3 months only if the person has lost at least 5% of their initial body weight since starting drug treatment (less strict goals may be appropriate for people with type 2 diabetes).
- Treatment is not recommended beyond the licensed duration of 12 months.
- Co-prescribing with other drugs aimed at weight reduction is not recommended.

Surprisingly there is no mention of rimonabant in the guideline. This was discussed in the August and November 2006 PACE Newsletters and is designated by PACEF as a BROWN drug for third-line use.

Children

When to consider treatment

- Consider drug treatment only after dietary, exercise and behavioural approaches have been started and evaluated.
- For children younger than 12 years:
 - drug treatment is not generally recommended
 - prescribe only in exceptional circumstances, if there are severe life-threatening comorbidities (such as sleep apnoea or raised intracranial pressure)
 - prescribing should be started and monitored only in specialist paediatric settings.
- For children aged 12 years and older:
 - drug treatment is recommended only if there are physical comorbidities (such as orthopaedic problems or sleep apnoea) or severe psychological comorbidities
 - prescribing should be started by a specialist multidisciplinary team with experience of prescribing for this age group.
- Multidisciplinary teams prescribing orlistat or sibutramine should have expertise in:
 - drug monitoring
 - psychological support
 - behavioural interventions
 - interventions to increase physical activity
 - interventions to improve diet
- After drug treatment has been started in specialist care, it may be continued in primary care if local circumstances and/or licensing allow.

Continued prescribing and withdrawal

- Offer a 6-12 month trial of orlistat or sibutramine, with regular review of effectiveness, adverse effects and adherence.
- Drug treatment may be used to help the child or young person to maintain weight loss, as well as to continue to lose weight.
- If concerned about micronutrient intake, consider a supplement providing the reference nutrient intake for all vitamins and trace elements.

- If a child or young person's drug treatment is withdrawn because they have not reached their target weight, offer support to help maintain weight loss because their self-confidence and belief in their ability to make changes may be low.

New guidance on the prevention of malaria in travellers

The Health Protection Agency (HPA) has published new practical guidance on the prevention of malaria for UK-based visitors to malaria endemic areas, which updates and combines the 'Guidelines for malaria prevention in travellers from the United Kingdom for 2003' and 'Malaria prophylaxis for long-term travellers'.

The guidelines are intended for use by healthcare workers such as GPs, travel health nurses and pharmacists who advise travellers, but may also be of use to prospective travellers who wish to read about the options themselves on the Agency's website.

The prevention guidelines cover general issues on the 'ABCD's' of malaria prevention (awareness of risk, bite prevention, chemoprophylaxis and diagnosis and treatment) as well as providing advice for special medical needs groups; advice for different types of traveller; frequently asked questions and a listing of information resources. Tables of guidance by country and selected maps are also available. Updates include the latest advice for travellers to the Indian sub-continent and an extended section on bite prevention to emphasise its importance.

The guideline is available at www.hpa.org.uk/infections/topics_az/malaria/guidelines.htm. It is a large, comprehensive document (106 pages) with 8 chapters but each chapter can be downloaded separately. Chapter 8 is 'Frequently asked questions' and maybe particularly useful. The questions are:

- What malaria prevention should be advised for travellers going on cruises?
- What alternative antimalarial drugs can be used for India (and Sri Lanka) if chloroquine and proguanil are unsuitable for a traveller?
- Which antimalarial can I give to a traveller with a history of psoriasis?
- Which antimalarial can I give a traveller who is taking warfarin?
- How long is it safe to continue a course of antimalarial tablets?
- Which antimalarial drugs are suitable for women during pregnancy?
- Which antimalarial drugs can be taken by breastfeeding women?
- Which malaria drugs can be given to babies and young children?
- What is the easiest way to calculate the correct dose of chloroquine for babies and young children?
- Many travellers I see intend to travel through several areas where different anti-malarials are recommended as they progress through their journey. How do we advise these travellers?
- Which antimalarial drugs can I advise for a traveller who has epilepsy?
- What do I advise for the traveller with Glucose 6-phosphate dehydrogenase deficiency?
- What do I advise people working on oil rigs?
- What do I advise for the traveller on a stopover?

Guidance for steroids in MS

Having been asked to consider issuing some guidance for steroid use in multiple sclerosis, PACEF has discussed the advice from the Sheffield Teaching Hospitals NHS Trust. This was deemed to be appropriate and consistent with the NICE guideline and can be found hosted on the PACEF intranet site.

Primary prevention with statin therapy

The role of statins in secondary prevention of cardiovascular events and mortality is established and not controversial. However, their value for primary prevention is less clear. A recently published meta-analysis of RCTs helps to clarify the role of statins for patients without CV disease¹.

Seven trials with 42,848 patients were included in the meta-analysis and 90% of patients had no history of CV disease. Mean follow-up was 4.3 years. Statin therapy reduced the relative risk of major coronary events (by 29.2%), major cerebrovascular events (by 14.4%), and revascularisations (by 33.8%). However, the absolute risk reductions were much less impressive. For major coronary events the ARR was 1.4% and this gives an NNT of 71 over 4.3 years. For major cerebrovascular events the ARR was only 0.3% giving an NNT of 333.

This information is important for sharing with patients to enable them to make concordant decisions about treatment. Figures were not provided in the paper to be able to calculate the NNT for revascularisations. CHD mortality and overall mortality were not statistically significantly reduced.

In a recent editorial, 'Are lipid-lowering guidelines evidence based?', some other authors also consider primary prevention with statins². They also found that statins do not reduce mortality. They found a similar reduction in cardiovascular events – an ARR of 1.5% and an NNT of 67 over 5 years. They go on to say that further analysis revealed that the benefit might be limited to high-risk men aged 30-69 years. Statins did not reduce total coronary heart disease events in 10,990 women in primary prevention trials (RR 0.98, 0.85 – 1.12). Similarly, in 3239 men and women older than 69 years, statins did not reduce total cardiovascular events (RR 0.94, 0.77 – 1.15).

They conclude "our analysis suggests that lipid-lowering statins should not be prescribed for true primary prevention in women of any age or for men older than 69 years. High-risk men aged 30-69 years should be advised that about 50 patients need to be treated for 5 years to prevent one event".

1. Arch Intern Med 2006; 166:2307-13
2. Lancet 2007; 369:168-9

The ADOPT trial

In this study, 4351 patients (most of whom were white) between the ages of 30 and 75 years with newly diagnosed type 2 diabetes were randomly assigned to receive either 4mg rosiglitazone, 500mg metformin, or 2.5mg glibenclamide once a day¹. Analysis was by intention to treat and allocation to groups appears to have been properly concealed. The dose was increased as needed to achieve a fasting blood glucose level of less than 140 mg/dL (7.8 mmol/L); the maximum doses were 4mg rosiglitazone twice daily, 1g metformin twice daily, or 7.5mg glibenclamide twice daily. Patients with significant cardiovascular disease or contraindications to the study medications were excluded.

The primary outcome of this study was a disease-oriented end point: whether the patient required a second drug to control their blood sugar, with failure defined as a fasting blood sugar reading higher than 180 mg/dL (10 mmol/L). At the end of the study, 15% of patients taking rosiglitazone, 21% taking metformin, and 34% taking glibenclamide had failed monotherapy. Interestingly, the number of patients studied and the length of the study were both increased beyond 4 years because the authors were having difficulty proving that the sponsor's drug (rosiglitazone) was better than metformin on the primary outcome. The majority of patients did not reach the endpoint regardless of treatment (66% with glibenclamide, 79% with metformin and 85% with rosiglitazone).

In terms of HbA_{1c} levels, the currently accepted measure of diabetic control and a secondary outcome of the study, the differences between rosiglitazone and metformin in particular were less marked. At 4 years, 40% of the rosiglitazone group had HbA_{1c} levels below 7% compared to 36% in the metformin group (p=0.03) and 26% in the glibenclamide group (p<0.001). The data indicate that for every 25 patients treated with rosiglitazone instead of metformin for 4 years, one additional patient will have a HbA_{1c} <7%.

Regarding patient-oriented outcomes, there was no difference in all-cause mortality, but there were somewhat fewer cardiovascular events (largely heart failure) with glibenclamide and metformin than with rosiglitazone. Weight gain was more common with rosiglitazone, it increased LDL cholesterol, and it was associated with more edema and use of loop diuretics than metformin or glibenclamide. These effects are especially undesirable in patients with diabetes. The mean weight changes were +4.8 kg for rosiglitazone, -2.9 kg for metformin and +1.6kg for glibenclamide. More people were prescribed statins on rosiglitazone (51.5%) compared to metformin (43.5%, NNH = 12-13) and glibenclamide (40.2%, NNH = 9).

PACEF has discussed this study and concluded that the results should not change the current practice of beginning treatment with metformin whenever possible in patients with type 2 diabetes. Metformin is the only drug of the three proven to reduce the risk of CV events and improve mortality and is therefore the first-line choice. ADOPT provides inadequate evidence to change the place of glitazones in therapy beyond the licensed indications and NICE guidance. Sulphonylureas remain the second-line choice.

1. N Engl J Med 2006; 355:2427-43

Guidelines update

PACEF has recently ratified the following guidelines. These and all the other guidelines/policies/formulary are available on the PACEF intranet site.

- Erectile dysfunction – update
- Dyspepsia – update
- Gastroscopy referral – update
- Hypertension – update
- Varicose vein referral – update
- Breast cancer family history risk assessment – update
- Food supplements and nutritional management – update
- PAD management – update
- Otitis externa – new
- Melatonin shared care – new
- Insulin therapy in type 2 diabetes - new

Treatment of vasomotor symptoms of menopause

The most intensively studied treatment for vasomotor symptoms is oestrogen. Used by itself or with progestins, it is the most effective therapy for vasomotor symptoms, reducing their frequency by about 77%¹. However, there is much interest in finding safer alternatives to HRT. The recently published HALT study was a 1-year double-blind, randomised, controlled trial designed to investigate the effects of three naturopathic approaches for vasomotor symptom relief and hormone therapy compared with placebo². This is the longest and largest placebo-controlled, double-blind trial to date.

351 women aged 45-55 years with 2 or more vasomotor symptoms per day (average 6) took part; 52% were in menopausal transition and 48% were postmenopausal. They were randomised to one of 5 interventions; 1) black cohosh 160mg daily; 2) multibotanical with black cohosh 200mg daily and 9 other ingredients; 3) multibotanical plus dietary soy counselling; 4) conjugated equine oestrogen 0.625mg daily, with or without medroxyprogesterone acetate 2.5mg daily; 5) placebo.

Vasomotor symptoms per day and symptom intensity did not differ between the herbal interventions and placebo at 3, 6 or 12 months or for the average over all the follow-up time points, with one exception. At 12 months, symptom intensity was significantly worse with the multibotanical plus soy intervention than with placebo ($p=0.016$). Hormone therapy significantly reduced vasomotor symptoms by 4 per day compared with placebo for the average over all the follow-up time points ($p<0.001$). The authors concluded that black cohosh used in isolation, or as part of a multibotanical regimen, shows little potential as an important therapy for relief of vasomotor symptoms.

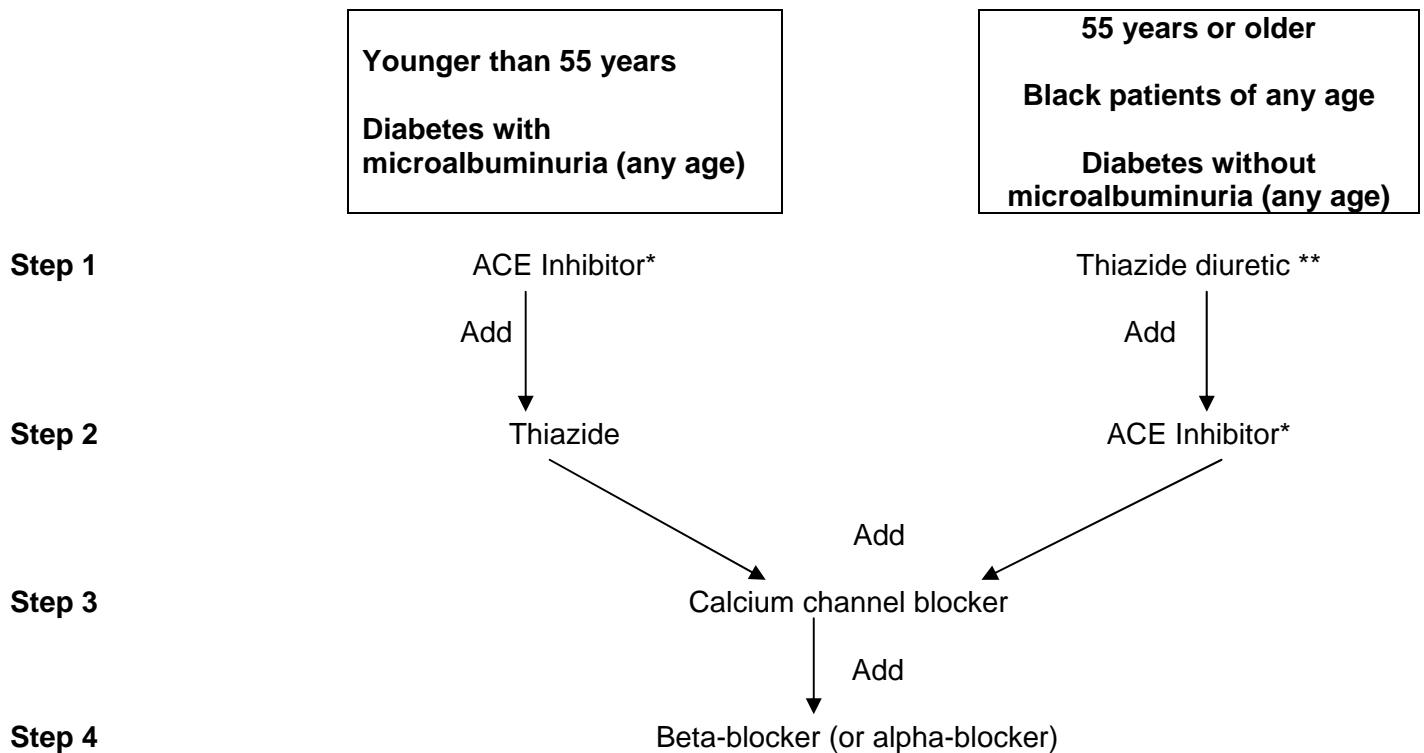
The accompanying editorial¹ comments that HALT is a well-designed, adequately powered RCT that makes an important contribution – strong evidence that black cohosh is ineffective for the treatment of vasomotor symptoms. The author considers that the negative dietary soy results are not definitive because the majority of the participants assigned to this group did not achieve the target level of soy intake (at least 2 soy-containing foods a day).

1. Ann Intern Med 2006; 145:924-5
2. Ann Intern Med 2006; 145:869-79

Updated hypertension guideline

The new PACEF guideline on the management of hypertension in adults in primary care is now available. This is a substantial update and there are sections on measuring blood pressure, ambulatory BP monitoring, lifestyle interventions, thresholds and targets, and drug treatment. The drug treatment algorithm is included overleaf.

Choosing drugs to lower blood pressure and reduce cardiovascular risk
Thiazides remain first-line in most people needing treatment for raised blood pressure



* use angiotensin–II antagonist if ACEI intolerant (as the evidence for using an ACEI first-line in those aged <55 years is not strong, a thiazide could be considered in this group of patients before changing to an A-II antagonist)

ACEIs and A-II antagonists are contraindicated in pregnancy and should be avoided in women of childbearing potential (or ensure effective contraception)

** use calcium channel blocker if thiazide contraindicated or not tolerated (except in diabetes – straight to step 2 if cannot use thiazide)

Most drugs take 6-8 weeks to attain maximum benefit. Reassess 2 months after starting treatment before modifying medication, unless urgent intervention is needed (e.g. malignant hypertension).

Beta-blockers

- are no longer preferred as a routine initial therapy for hypertension
- may be appropriate for those who have another indication for beta-blocker therapy – angina, previous MI, heart failure
- should be considered for some younger people, particularly:
 - women of childbearing potential
 - patients with evidence of increased sympathetic drive
 - patients with intolerance of or contraindications to ACE inhibitors and angiotensin-II antagonists

Target clinic BP

The aim is to reduce blood pressure to target if possible, adding drugs as needed, *taking account of tolerability and concordance for each individual patient.*

No diabetes – 140/90 mmHg or less

With type 2 diabetes – less than 140/80 mmHg

Type 2 diabetes with microalbuminuria/proteinuria (ACE inhibitor first-line [or A-II antagonist if not tolerated]) – 135/75 mmHg or less