



# STROKE

## Top tips for MURs

- Check that patient has had their blood pressure (BP) measured regularly and treatment is increased as is necessary or as indicated to consistently achieve a clinic systolic BP of <130mmHg (except for people with severe bilateral carotid stenosis - target 140-150mmHg)
- Check that patient has had renal and liver function tests every twelve months (monitor more frequently in high risk patients) and regular INR tests (if taking warfarin)
- Counsel patient on purpose of each medication, how long their treatment should continue and INR target range (if taking warfarin)
- Check patient does not have any complications of stroke - swallowing difficulties, dry mouth, excessive saliva or spasticity, dexterity problems that may limit medication use or cognitive disabilities (see dealing with physical complications post stroke)
- Check patient understands the purpose of warfarin or the non-vitamin K antagonist oral anticoagulants (NOACs) (see separate MUR quick practise guide for Warfarin and NOACs)
- Counsel patient on signs / symptoms of complications that need referral (see red flags below) and common side effects (see side effects overleaf)
- Advise patient to take medication with or after food (aspirin & dipyridamole) or at night (simvastatin) and to avoid cranberry juice (warfarin) and grapefruit juice (simvastatin)
- Advise patient to discard dipyridamole modified release capsules 6 weeks after opening
- Explain to the patient that a stroke can result from a leakage of blood, or from a clot travelling to the brain. Clots form from a number of things, including cholesterol or fat, or from the heart if it is beating irregularly and blood cells are sticky. Re-inforce the importance of taking medications regularly to prevent this from happening.
- Check that patient has had an annual influenza vaccination
- Report any relevant adverse drug reactions to the Yellow Card Scheme

## Pathophysiology of Stroke

- Stroke is an acute loss of brain function for greater than 24 hours due to a disturbance of blood flow to the brain. This can be due to a lack of blood flow (ischaemia) caused by a blockage or by a leakage of blood (haemorrhage). Stroke symptoms include numbness, weakness or paralysis, slurred speech, blurred vision, confusion and severe headache<sup>1</sup>.
- Transient Ischaemic Attack (TIA) is defined as an episode of neurologic dysfunction caused by focal brain, spinal cord, or retinal ischaemia without acute infarction, which lasts for a short time (symptoms usually resolve within 24 hours)<sup>2</sup>.

## Lifestyle issues

- Counsel patient on reducing alcohol intake to within safe limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days)
- Counsel patient on healthy eating, gentle exercise & weight loss (if BMI > 25kg/m<sup>2</sup>) - reduce saturated fat and salt intake, avoid salt substitutes, increase oily fish intake, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Advise patient who smokes of the benefits of stopping smoking and how to access enhanced smoking cessation services in community pharmacy and GP practices

## Physical complications of stroke

Complication	Recommendation
Swallowing difficulties	Follow speech and language therapist or GP recommendations for individual patients. Some patients may require liquids or dispersible tablets. Some patients on thickened fluids may require tablets to be crushed and added to thickened fluid/food or enteral tube.
Dry mouth	Frequent sips of cool drinks or sucking sugar free fruit pastilles and ensure good oral hygiene to prevent infection. Avoid glandosane or glycerine based mouthwashes as these can cause webbing in the mouth.
Excessive saliva causing drooling	Refer to GP for possible addition of antimuscarinics to inhibit salivary glands or short term hyoscine patches.
Spasticity	Refer to GP for possible addition of muscle relaxants or botulinum injections.

## Red flags that need referral

- Any heaviness in the centre of your chest, triggered by effort or emotion, any fatigue, water retention or hypotension
- Signs of thrombosis - symptoms of DVT i.e. redness, tenderness, swelling or chest pain / shortness of breath
- Chronic gastrointestinal bleeding, persistent vomiting or iron deficiency anaemia
- Any signs of bleeding, purpura, purple toes or skin necrosis
- Severe itching or rash
- Diarrhoea and vomiting may lead to poor absorption so the INR should be checked
- Any symptoms of depression (low self esteem, lack of energy, weight loss, appetite loss, early morning wakening, lack of concentration)
- Seizures
- Pregnancy, as risk of teratogenity and risk of haemorrhage (warfarin)
- Breastfeeding as present in milk and a risk of toxicity in the infant
- Any new signs of stroke or TIA as these are an alarm to a possible major stroke

Remember FAST - Face, Arm, Speech & Time to call 999



## How do medications to treat stroke long term & as secondary prevention work?

<b>Aspirin</b>	Inhibits the enzyme cyclo-oxygenase which is needed to convert arachidonic acid to prostaglandin, which is then involved in production of thromboxane, which is needed to activate and bind platelets together to form a clot. Aspirin reduces the stickiness of the blood.
<b>Clopidogrel</b>	Inhibits the platelet cell membrane receptors responsible for aggregation of platelets by blocking the glycoprotein pathway, which prevents arterial and venous thrombosis and blocks platelet activation.
<b>Dipyridamole MR preparations</b>	Inhibits thrombus formation by acting as a thromboxane inhibitor preventing platelet aggregation and vasoconstriction. It also has an effect on phosphodiesterase enzymes preventing conversion of cyclic AMP to inactive 5 AMP, which blocks the platelet response to adenosine diphosphate.
<b>Statins</b>	Inhibits the conversion of HMG-CoA to mevalonic acid by blocking HMG-CoA reductase, an early and rate-limiting step in cholesterol biosynthesis. It reduces total cholesterol, LDL-cholesterol and triglycerides and increases HDL-cholesterol levels.
<b>Warfarin</b>	Inhibits Vitamin K dependent clotting factors by interfering with the synthesis of vitamin K dependant clotting factors <sup>3</sup> .
<b>NOACs</b>	Inhibits thrombin ( <i>dabigatran</i> ) or clotting factor Xa ( <i>apixaban</i> , <i>rivaroxaban</i> , <i>edoxaban</i> ) which prevents the conversion of fibrinogen into fibrin during the coagulation cascade, thus preventing the development of a thrombus.
<b>Antihypertensive medication</b>	One of the main treatment goals of secondary prevention is to keep the patient's blood pressure within safe limits. Antihypertensives are important because it is high blood pressure that drives fat and blood cells to stick together, so lowering the BP may still be of benefit. See 'Quick practice guide for targeted MURs for patients taking antihypertensive medication' for more detail.

## What are the common side effects to look out for?

Drug	Common side effects	Recommendation
<b>Antithrombotic agents</b>	Gastro-intestinal disturbances including discomfort, nausea, diarrhoea, occasionally bleeding & ulceration	Take medication with milk or food as may reduce symptoms. Refer to prescriber for change of formulation, medication or addition of low dose gastro-protection if persistent.
	Rashes, angioedema	Refer immediately for medical assistance as potentially life threatening.
	Bronchospasm, jaundice, abdominal pain & renal failure	Refer to prescriber – medication needs to be stopped.
	Headache, dizziness, vertigo and insomnia	Explain to patients newly started on dipyridamole MR that headaches are likely but they often resolve within a few days or weeks. Take paracetamol and refer to prescriber if still a problem.
<b>Statins</b>	Headache, nausea and gastro-intestinal disturbances	Refer to prescriber if a problem.
	Unexplained bruising, muscle aches and pains	Refer to prescriber for liver function tests.
<b>Warfarin</b>	Bleeding, rash, purpura, purple toes, skin necrosis, diarrhoea or vomiting	Refer to prescriber for INR tests and potential change of dose.
<b>NOACs</b>	Bleeding and signs of anaemia	Refer to prescriber for tests. Treatment should be stopped if severe bleeding.
	Nausea and gastro-intestinal disturbances	Refer to prescriber if a problem.

## Potential serious drug interactions?

- Antithrombotic drugs interact with many other medications which may increase risk of bleeding so may require avoidance of concomitant use, dose alteration or additional monitoring requirements such as: Aspirin, NSAIDs, antibacterials, anticoagulants, antidepressants, antiepileptics, antifungals, antivirals, methotrexate, dipyridamole, clopidogrel and ulcer healing drugs
- Statins interact with many other medications such as amiodarone, antibacterials, antifungals, antivirals, ciclosporin and other lipid lowering agents. The MHRA recommend a maximum dose of simvastatin 20mg when used in conjunction with amlodipine, verapamil, diltiazem or ranolazine<sup>5</sup>
- Anticoagulants (warfarin & NOACs) effects on the blood can be enhanced by concomitant use of clarithromycin, amiodarone, ketoconazole or reduced by concomitant use of St. John's Wort, rifampicin, so dosages must be adjusted when these drugs are started or stopped and INR must be checked regularly if taking warfarin. The risk of bleeding is increased by use of antiplatelets & NSAIDs, so it is usual to avoid concomitant use of NSAID and consider the need for ongoing anti-platelet use for example recent acute coronary syndrome

Drugs used to treat stroke interact with many other medications - **see BNF Appendix 1: interactions for more details**

## Where can you find more information?

- Cardiovascular system – BNF sub-section 2.8, 2.9 & 2.12
- NICE guidance: Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events can be found on NICE website ([www.nice.org.uk](http://www.nice.org.uk))
- Stroke Association ([www.stroke.org.uk](http://www.stroke.org.uk))
- Clinical Knowledge Summary Stroke can be found on CKS website (<http://cks.nice.org.uk>)
- Stroke guidelines can be found on (<https://www.rcplondon.ac.uk/guidelines-policy/stroke-guidelines>). (Updated version October 2016)

## References

1. National Institute for Health and Clinical Excellence. Diagnosis and initial management of acute stroke and transient ischaemic attack. July 2008
2. American Heart Association and American Stroke Association. Definition and evaluation of Transient Ischemic Attack 2009
3. Anticoagulation – managing patients, prescribing and problems, CPPE distance learning package
4. Stroke guidelines, Royal College of Physicians, 2012
5. Drug Safety Update, MHRA, August 2012. Available online at <http://www.mhra.gov.uk>