

Contraindications to The Initiation of Oral Anticoagulants & Anti-platelet Agents in Patients with Atrial Fibrillation in Primary Care

As a patient's relative stroke & bleeding risk can change, it is essential that all AF patients are reviewed at **LEAST** annually for a re-assessment of their stroke versus bleeding risk & the anti-thrombotic treatment option of choice.

Contraindications listed below apply to **BOTH** anti-platelet agents (e.g. aspirin, clopidogrel, dipyridamole) & **ALL** oral anticoagulants (e.g. warfarin, phenindione, dabigatran, rivaroxaban) except where indicated.

Absolute Contraindications

- Known large oesophageal varices.
- Significant thrombocytopenia (platelet count < 50 x 10⁹/L) - *refer to haematologist.*
- Within 72 hours of major surgery with risk of severe bleeding - *defer & reassess risk postoperatively.*
- Previously documented hypersensitivity to either the drug or excipients – *consider cardiology opinion.*
- Acute clinically significant bleed - *defer & re-assess stroke versus bleeding risk within 3 months.*
- Decompensated liver disease or deranged baseline clotting screen (INR>1.5) – *refer to Gastroenterology /Hepatology. **Contraindication applies to oral anticoagulants only***
- Pregnancy or within 48 hours post partum - *seek urgent haematological advice. **Contraindication applies to oral anticoagulants only.***
- Severe renal impairment (GFR < 30 mL/min/1.73 m² or on dialysis). **Contraindication applies to dabigatran only.**

Relative Contraindications

- Previous history intracranial haemorrhage - *as some AF patients especially those considered at higher stroke risk (i.e. CHADS2 score ≥3) may benefit from anti-thrombotic therapy, seek the opinion of a stroke specialist.*
- Recent major extracranial bleed within the last 6 months where the cause has not been identified or treated – *decision for oral anti-thrombotic therapy should be deferred.*
- Recent documented peptic ulcer (PU) within last 3 months– *decision for oral anti-thrombotic therapy should be deferred until treatment for PU completed. In all cases with history PU give PPI cover whilst on anti-thrombotic.*
- Recent history recurrent iatrogenic falls in patient at higher bleeding risk.

A patient at higher bleeding risk is assessed by having 3 or more of the following risk factors:-

- age > 65 years
- previous history bleed or predisposition to bleeding (e.g. diverticulitis)
- uncontrolled hypertension
- severe renal impairment (i.e. serum creatinine > 200µmol/L, GFR < 30 mL/min/1.73 m² or on dialysis)
- acute hepatic impairment (e.g. bilirubin > 2xULN + LFTS > 3x ULN), chronic liver disease (e.g.cirrhosis)
- low platelet count < 80 x 10⁹/L or a thrombocytopenia or anaemia of undiagnosed cause
- on concomitant drugs associated with an increased bleeding risk e.g. SSRIs, oral steroids, NSAIDs, methotrexate or other immune-suppressant agents.

N.B. A risk of falls is not a contraindication to initiating oral anticoagulation. (e.g. a patient with an annual stroke risk of 5% (CHADS2 score 2-3) would need to fall 295 times for fall risk to outweigh stroke reduction benefit of warfarin).

- Dementia or marked cognitive impairment with poor medicines compliance & no access to carer support.
- Chronic alcohol abuse – especially if associated with binge drinking.

N.B. Poor compliance with any oral anticoagulant agent will reduce benefits and may increase risks associated with use.

Contraindications to the Initiation of Oral Anticoagulant & Anti-Platelet Therapy for Atrial Fibrillation in Primary Care - Supporting Information & Acknowledgements.

Summary

The aim of this document is to give GPs a pragmatic decision guide on the absolute and relative contraindications to oral anticoagulants and anti-platelet agents in AF management in primary care. The information given has been drawn from “expert clinical opinion” together with established documented clinical evidence where available.

The key message is that although aspirin or aspirin/clopidogrel combinations may be chosen in preference to oral anticoagulants to reduce stroke risk in AF, the contraindications to using anti-platelet agents almost mirror those of oral anticoagulants. In addition the reduction in stroke risk in AF conferred by antiplatelets has never been shown to be as effective as oral anticoagulants.

Key Supporting References

- ✚ European Society of Cardiology (ESC) Guidelines for the management of atrial fibrillation. Eur Heart J. Aug 29 2010. <http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf>
 - *Recommendation that selection of anti-thrombotic therapy should be based upon the absolute risks of stroke/thrombo-embolism and bleeding and the relative risk and benefit for a given patient. Highlights the use of the ‘HAS-BLED’ bleeding risk score as a tool to assess bleeding risk in AF patients.*
- ✚ Keeling D, Baglin T et al; Guidelines on oral anticoagulation with warfarin – 4th Ed 2011; British Journal of Haematology 1365-2141. http://www.bcsghguidelines.com/documents/warfarin_4th_ed.pdf
 - *Latest updated BCSH guidance- includes statement re concomitant use of anticoagulants & anti-platelets*
- ✚ Mant J Hobbs FDR, et al, Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (AF),(BAFTA RCT study): Lancet 2007;370: 493-503.
 - *BAFTA study showed clear superiority of warfarin over aspirin with no increase in risk of major haemorrhage. Mean age of population was 81.5 years.*
- ✚ Bailey RD, Hart RG, Benavante O, Pearce LA. Recurrent brain haemorrhage is more frequent than ischaemic stroke after intracranial haemorrhage. Neurology 2001;56:773-7.
 - *Recurrent stroke among survivors of primary intracranial haemorrhage (ICH) occurs at a rate of about 4% per patient year and most are recurrent ICH. Survivors of ICH likely to have a higher risk of recurrent ICH than of ischaemic stroke with CHADS 2 score < 3. (Adjusted annual stroke rate risk with CHADS2 2 score 3 is 5.9%)*
- ✚ Man-Son Hing M, Nichol G, Lau A, Laupacis A. Choosing antithrombotic therapy for elderly patients with atrial fibrillation who are at risk of falls. Arch Intern Med 1999; 159: 677-85.
 - *Showed a calculated risk of a subdural haemorrhage from falling in patients with annual stroke risk 5% would require a patient to fall 295 times for falls risk to outweigh stroke reduction benefit of warfarin.*
- ✚ 2. The ACTIVE Writing Group on behalf of the ACTIVE investigators. Lancet 2006;367:1903–12
 - *Study found incidence of bleeding was significantly greater with aspirin + clopidogrel compared with warfarin (19.3% vs. 16.5%; NNH 35; RR=1.21, 95% CI 1.08–1.35, P=0.001).*
- ✚ Wehinger C, Stollberger C, Lamger T et al. Evaluation of risk factors for stroke/embolism & of complications due to anticoagulant therapy in atrial fibrillation. Stroke 2001;32(10):2246-2252
 - *Study found significant difference in bleeding complications between those patients prescribed at least three additional medicines & those prescribed less than three.*
- ✚ Shireman TI, Howard PA, Kresowik TF et al. Combined anticoagulant –antiplatelet use and major bleeding events in elderly atrial fibrillation patients. Stroke.2004;35(10)2362-2367.
 - *Found history of bleeding to be a significant independent predictor of future bleeding events.*
- ✚ PROGRESS Collaborative Group. RCT of a perindopril-based BP-lowering regimen among 6,105 individuals with previous stroke or transient ischaemic attack. Lancet. 2001 Sep 29;358(9287):1033-41
 - *study showed importance of BP control in patients with cerebrovascular disease in significantly lowering risk of first ICH.*
- ✚ Laupacis A, Boysen G, Connolly S et al. Risk factors for stroke & efficacy of antithrombotic therapy in AF: analysis of pooled data from five randomised controlled trials. Archives of Internal Medicine. 1994;154(13):1449-1457.
 - *Study found both systolic and diastolic BP to be significantly higher in those patients with bleeding complications than in those without bleeding complications.*
- ✚ Dite PD, Labrecque D et al. World Gastroenterology Organisation Practice Guideline Oesophageal Varices 2008.
 - *Oesophageal varices develop in patients with cirrhosis at an annual rate of 5–8%, but varices large enough to pose a risk of bleeding occur in only 1–2% of cases. Approx 4–30% of pts with small varices will develop large varices each year & therefore be at risk of bleeding. Mortality resulting from bleeding depends on the severity of the underlying liver disease.*
- ✚ UK Teratology Information/Toxicology database report on use of Warfarin in Pregnancy. National Poisons Information service commissioned by HPA. March 2011 <http://www.toxbase.org>
- ✚ Summary Product Characteristics for Marevan (warfarin) Pradaxa (Dabigatran); Plavix (Clopidogrel). Electronic Medicines Compendium @ <http://www.medicines.org.uk>

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