**What are the potential advantages of warfarin over dabigatran and rivaroxaban?**
- Warfarin has been prescribed for more than 50 years so there is plenty of experience of its clinical use.
- There are no long-term safety data for dabigatran or rivaroxaban (both launched 2011) and their safety profiles are still not fully understood. Also there is limited knowledge about their use in certain patient groups (recent strokes, high bleeding risk, liver disease, prosthetic heart valves or severe renal impairment (CrCl <30ml/min)). As black triangle drugs, dabigatran and rivaroxaban are under intensive surveillance – all adverse effects need to be reported via the yellow card scheme.
- Reversal of warfarin can be achieved with vitamins K and prothrombin complex concentrate. There is no proven antidote available for dabigatran or rivaroxaban and the clinical application of emerging strategies for managing bleeding associated with their use is uncertain.
- In the RE-LY clinical trial, rates of major GI bleeding (D150 only) and dyspepsia (both doses) were greater with dabigatran than warfarin. Use of antiplatelets/NSAIDs, or GI irritation increase the risk of GI bleeding.
- In the ROCKET-AF clinical trial, rivaroxaban was associated with a greater risk of major GI bleeding than warfarin.
- In RE-LY, dabigatran (both doses) was associated with an increased risk of MI compared to warfarin, although this trend did not reach statistical significance.
- The anticoagulant effect of warfarin is easier to measure (INR monitoring). This enables assessment of compliance with warfarin. Prescribers will not receive any confirmation that dabigatran or rivaroxaban are being taken since they do not require any monitoring.
- Patients with poor concordance may be at greater risk of thromboembolic complications with dabigatran or rivaroxaban, as their shorter half-lives will potentially result in more time without any degree of anticoagulation.
- In clinical trials, more patients stopped taking dabigatran or rivaroxaban than warfarin due to adverse events.

**What are the potential advantages of dabigatran and rivaroxaban over warfarin?**
- In RE-LY, D150 reduced the rate of stroke or systemic embolism (SEE) compared to warfarin with a similar rate of major bleeding. D110 was associated with a rate of stroke or SEE comparable to warfarin, but a lower rate of major bleeding.
- In ROCKET-AF, rivaroxaban was non-inferior to warfarin in reducing the rate of stroke or SEE, with a comparable rate of major bleeding.
- However, the above clinical benefits of dabigatran and rivaroxaban compared to warfarin diminish with improving INR control. In patients where warfarin treatment is well controlled (TTR≥65%) the use of dabigatran or rivaroxaban may be less favourable. NICE emphasise the need to take the level of INR control into consideration when assessing the benefits of a change to dabigatran or rivaroxaban.
- There is no need for routine anticoagulant monitoring. However, anticoagulant testing can guide management in severe bleeding; seek specialist advice. Note that INR is not valid to measure the anticoagulant activity of dabigatran or rivaroxaban and should not be used.
- The dosing regimens are uncomplicated and a more stable level of anticoagulation is achieved with full concordance.
- There are fewer potential interactions with other medications, alcohol and diet. However, drug-specific dose adjustments are required in some situations (check SPC for drugs that will interact).

**What are the relative advantages of dabigatran and rivaroxaban?**
- No clinical trial has directly assessed dabigatran and rivaroxaban in a head-to-head comparison. Consequently there is insufficient evidence to draw conclusions regarding their relative safety and efficacy.
- When dabigatran, rivaroxaban and warfarin were compared indirectly across trials:
  - D150 had the highest probability of being best at reducing stroke or SEE.
  - D110 had the highest probability of being best at reducing major bleeding.
  - Rivaroxaban was associated with the most favourable results regarding MI.
- Dabigatran (dyspepsia) and rivaroxaban (epistaxis, haematuria) have different side effects profiles.
- Dabigatran and rivaroxaban interact with different medicinal products.
- Dabigatran is predominantly renally excreted, although both agents require drug-specific dose adjustments in renal impairment and are contra-indicated where there is severe impairment. Renal function should be assessed before initiating dabigatran, and at least once a year during treatment or more frequently as needed in clinical situations when it is suspected that the renal function could decline or deteriorate.
- Dabigatran requires a dose adjustment in older patients due to an increased bleeding risk.
- There is limited direct trial evidence assessing rivaroxaban among people with a baseline CHADS2 score of <2.
- Rivaroxaban is administered once daily; dabigatran twice daily.
- Dabigatran capsules are not recommended for compliance aids, because they are moisture sensitive and must not be removed from their packaging before administration. They must be swallowed whole and not opened.
Glossary

References

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