

### Comparison of oral anticoagulants

| Property                                       | Warfarin                                                                                     | Rivaroxaban                                                                                                                                                  | Dabigatran etexilate                                                                                                                                         |
|------------------------------------------------|----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Anticoagulant action                           | Reduced synthesis of functional clotting factors II, VII, IX and X                           | Direct competitive reversible inhibition of activated factor X                                                                                               | Direct competitive reversible inhibition of thrombin                                                                                                         |
| Prodrug                                        | No                                                                                           | No                                                                                                                                                           | Yes                                                                                                                                                          |
| Bioavailability                                | Almost 100%                                                                                  | 80%                                                                                                                                                          | 6.5%                                                                                                                                                         |
| Onset of anticoagulant action                  | 36–72 hours                                                                                  | Within 30 minutes<br>$T_{max}$ 2.5–4 hours                                                                                                                   | Within 30 minutes<br>$T_{max}$ 0.5–2 hours                                                                                                                   |
| Duration of anticoagulant action               | 48–96 hours                                                                                  | 24 hours                                                                                                                                                     | 24–36 hours                                                                                                                                                  |
| Elimination half-life (anticoagulant activity) | 20–60 hours                                                                                  | 5–9 hours in young adults<br>11–13 hours in older adults                                                                                                     | 7–9 hours in young adults<br>12–14 hours in older adults                                                                                                     |
| Predictable pharmacokinetics                   | No                                                                                           | Yes                                                                                                                                                          | Yes                                                                                                                                                          |
| Interactions with diet or alcohol              | Yes, clinically significant                                                                  | Low potential                                                                                                                                                | Low potential                                                                                                                                                |
| Drug interactions                              | Numerous clinically significant interactions                                                 | Potent cytochrome P450 3A4 and P-glycoprotein inhibitors augment anticoagulant effect (e.g. ketoconazole, clarithromycin, ritonavir)                         | Proton pump inhibitors reduce absorption<br>Possible interactions with P-glycoprotein inhibitors and inducers                                                |
| Dosing and dose adjustments                    | Dose individualised for each patient, requires frequent INR monitoring and adjustment        | Fixed according to clinical indication                                                                                                                       | Fixed according to clinical indication                                                                                                                       |
| Monitoring                                     | INR every 1–2 weeks                                                                          | No routine monitoring required                                                                                                                               | No routine monitoring required                                                                                                                               |
| Use in liver failure                           | Contraindicated or caution advised                                                           | Contraindicated as hepatic metabolism                                                                                                                        | Possibly safe as no hepatic metabolism but caution advised                                                                                                   |
| Use in severe renal impairment                 | No dose adjustment required                                                                  | Increased drug exposure and elimination half-life in renal impairment<br>Safety and dosing not yet established<br>Contraindicated in severe renal impairment | Increased drug exposure and elimination half-life in renal impairment<br>Safety and dosing not yet established<br>Contraindicated in severe renal impairment |
| Use in pregnancy                               | Category D<br>Teratogenic in first trimester                                                 | Contraindicated as safety not established (excluded from clinical trials)                                                                                    | Contraindicated as safety not established (excluded from clinical trials)                                                                                    |
| Reversibility after cessation                  | Several days, requires synthesis of clotting factors                                         | 24 hours, dependent on plasma concentration and elimination half-life                                                                                        | 24–36 hours, dependent on plasma concentration and elimination half-life                                                                                     |
| Antidote                                       | Immediate reversal with plasma or factor concentrate<br>Reversal within hours with vitamin K | None available                                                                                                                                               | None available                                                                                                                                               |

INR international normalised ratio

$T_{max}$  time to maximum concentration