

Annotations

- #4) Updated Annotation Title to “Pregnancy - High Risk” rather than “Contraindicated” due to new information. Advanced the discussion of pregnant patients with mechanical heart valves (Nishimura, 2008).
- #7) Updated information about patients on warfarin using self-testing and self-management (CMS Memo 2008; Finkel, 2010; Heneghan, 2006; Matchar, 2010) including the new CMS practice to reimburse for atrial fibrillation and venous thromboembolism.
- #9) Added details about oral vitamin K used to correct supratherapeutic anticoagulation by warfarin.
- #12) The United States brought the UFH and LMWH standards in line with the WHO International Standard unit dose for heparin. Addressed the FDA announcement, of October 2009, that the new USP monograph results in 10% less anticoagulant activity (Bauer, 2001), adding that due to pre-existing dosing ranges in the PTT/ACT protocols, there may be no need for policy changes.
- #13) Deleted renal failure CrCl <30mL/minute as a contraindication to heparin (UF and LMWH).
- #14) Added to the list of precautions: use of LMWH with impaired renal function (defined as CrCl <50mL/min).

Added a table to distinguish dosing differences between CrCl <30 mL/min and CrCl 30-50 mL/min for enoxaparin and dalteparin.
- #15) Updated this section with guidance from a leading author regarding off-label use of fondaparinux to treat HIT and clarification that warfarin alone is contraindicated in patients with HIT (Warkentine, 2010).
- #28) Added as precaution for fondaparinux: Renal impairment defined as CrCl 30-50 ml/min.
- #36) The DTI Introduction now includes the first ever, FDA-approved oral DTI, dabigatran, for use in patients with non-valvular atrial fibrillation.
- #37) The new section, “Oral Direct Thrombin Inhibitors: Dabigatran” has been added to the guideline. A list of key considerations gives quick overview of five caveats which apply to starting use of this new drug (Wallentin, 2010; Stangier, 2009; van Ryn, 2010).

The section also includes information about patient care of the product.

- #38) The new section, “Dosing,” gives instruction for what a patient ought to do if patient misses a dose. Explains the indication (atrial fibrillation) as studied in the RE-LY trial.
- #39) The new section, “Contraindications and Precautions,” addresses bleeding risks, side effects and drug interactions.
- #40) The new section, “Monitoring and Effect on Laboratory Tests,” states routine monitoring is not necessary and, in fact, the more widely available assays do not give accurate reading of plasma dabigatran levels, nor accurate risk of surgical hemorrhage.
- #41) The new section, “Managing Bleeding Complications,” outlines that there is no antidote and that management would consist of supportive measures. It lists measures for minor bleeding and for major bleeding (van Ryn, 2009; van Ryn, 2008; Stangier, 2010; Stangier, 2008).
- #42) The new section, “Perioperative Management of Oral Direct Thrombin Inhibitors,” outlines: pre- and post- procedure management (van Ryn, 2010; The Medical Letter, 2010); bridging of warfarin patients and cardioversion (Nagarakatani, 2011).
- #43) The section formerly titled “Direct Thrombin Inhibitors, was renamed as “Parenteral Direct Thrombin Inhibitors;” added brief context that these IV drugs are used for a patient who has had HIT (so cannot take heparin) and consultation with experts is recommended due to drug and disease complexities.
- #50) The formatting in section, “Dosing,” formerly numbered as Annotation #43, has added a table to specify dose adjustments between the three agents.
- #53) Annotation was updated for readability throughout, with more specific elucidation of the PPI/clopidogrel interaction issue and the addition of practical management for the patients affected (Holmes, 2010).

Appendices

- Revised Appendix A, Risk Factors for Bleeding During Warfarin Therapy