Analysis of the Anticoagulant Market
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Novel Oral Agents are Expected to Increase Market Size and Heighten Competition

United States
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Executive Summary

• The U.S. anticoagulant market is on the verge of a potential major shift in clinical practice, from a market dominated by a single injectable anticoagulant to a highly competitive market dominated by first-in-class novel oral anticoagulants.

• The anticoagulant drug development space has become intensely competitive as companies race to introduce novel therapies which offer superior safety, efficacy and convenience to patients and physicians, a medical need which has gone unfulfilled for decades.

• Four new products are planned to be successively introduced to the market beginning in late 2010 and are expected to revolutionize antithrombotic therapy by providing safe, effective alternatives to the standard of care for chronic anticoagulation, warfarin: Pradaxa (dabigatran), an oral direct thrombin inhibitor (DTI); Xarelto (rivaroxaban), an oral factor Xa inhibitor; Eliquis (apixaban), an oral factor Xa inhibitor; and edoxaban, an oral factor Xa inhibitor.

• These new oral agents are expected to eventually become the standard of care for stroke prevention for atrial fibrillation patients, a population estimated to be at least x.x million in the U.S., and as high as x to x million total.

• These novel oral anticoagulants are also expected to grab substantial market share from the parenteral anticoagulants for those indications in which they have demonstrated positive data and net clinical benefit, namely prophylaxis of venous thromboembolism in orthopedic surgery.

Source: Frost & Sullivan analysis.
Executive Summary (continued)

- Parenteral anticoagulants will likely maintain their hold on hospital-based critical care applications, particularly cardiac indications, for which rapid acting, reversible agents are well suited. Agents such as Lovenox (enoxaparin sodium), Arixtra (fondaparinux sodium), Fragmin (dalteparin sodium) and Angiomax (desirudin) along with unfractionated heparin (UFH) will likely continue to dominate critical care due to their advantageous pharmacological profiles.

- However, the genericization of two key parenteral anticoagulants, Lovenox, a low-molecular-weight heparin (LMWH), and Arixtra, a synthetic pentasaccharide, are expected to partially diminish overall market growth.

- These collective changes are predicted to result in an increase in U.S. revenues from approximately $x.x billion in 2010 to approximately $xx.x billion by the year 2016.

- Substantial growth could be realized as premium priced therapies gradually replace the widely used inexpensive generic warfarin while simultaneously attracting new patients previously left untreated with no therapeutic options.

- Safety, particularly with respect to bleeding, is crucial for regulatory, patient and physician acceptance of new therapies, and it is expected that this factor will primarily drive market share for emerging products.

Source: Frost & Sullivan analysis.
Market Overview—Key Questions This Study Will Answer

Is the market growing, how long will it continue to grow and at what rate?

Are the existing competitors structured correctly to meet customer needs?

Is this an industry or a market? Will these companies/products/services continue to exist or will they get acquired by other companies?

How will the structure of the market change with time? Is it ripe for acquisitions?

Are the products/services offered today meeting customer needs or is there additional development needed?

Are the vendors in the space ready to go it alone, or do they need partnerships to take their business to the next level?

Source: Frost & Sullivan analysis.
Market Overview—Segmentation

Anticoagulant Market Segmentation, U.S., 2010

Anticoagulant Market

Oral
- VKA
- Factor Xa inhibitors
- Direct Thrombin Inhibitors

Parenteral
- Indirect Thrombin Inhibitors
- Direct Thrombin Inhibitors
- LMWH
- UFH
- Synthetic Pentasaccharides

Note: This research service is forecasted at the level of oral and parenteral anticoagulants. Drug classes are provided for informational purposes only.

Source: Frost & Sullivan analysis.
Market Overview—Segmentation (continued)

- The anticoagulant market is broadly divided into two main segments: the orals and the parenterals.

- Parenteral anticoagulants can be further segmented into the indirect thrombin inhibitors, which are those agents that require a co-factor for anticoagulant activity, and direct thrombin inhibitors, which have the ability to independently block thrombin.

  - The available classes of indirect thrombin inhibitors are unfractionated heparin (UFH), low-molecular-weight heparins (LMWH), and synthetic pentasaccharides, which is represented by a single drug, fondaparinux.

    - Unfractionated heparin is non-proprietary natural compound sourced from animal tissues. Its main attributes are its rapid onset of action and reversibility, making the anticoagulant of choice of many clinicians for critical care applications such as cardiology procedures or for elderly patients. However, its unpredictable pharmacokinetics and anticoagulant activity monitoring requirements make it difficult to manage in most settings.

    - The LMWHs (enoxaparin, dalteparin, tinzaparin) and fondaparinux have more predictable pharmacokinetics, short half-lives and do not require monitoring. They also have greater efficacy with less bleeding complication compared to heparin. Thus, these agents have largely replaced UFH for applications when immediate reversibility is not critical.

    - The parenteral direct thrombin inhibitors (argatroban, bivalirudin, desirudin, lepirudin) represent another alternative to heparin with greater efficacy and safety.

  - The parenteral anticoagulants are well suited for short-term use in the hospital setting, particularly for acute care when immediate onset of action is critical. However, chronic use is inhibited by the necessity to inject, sometimes twice daily.

Source: Frost & Sullivan analysis.
Market Overview—Segmentation (continued)

• Until recently, the only available oral anticoagulant was warfarin, a vitamin K antagonist (VKA). The oral segment now comprises VKAs along with factor Xa inhibitors and oral direct thrombin inhibitors. Patients are typically transitioned from parenteral to oral anticoagulants for chronic use.
  
  o Warfarin, which was initially discovered as a rat poison, has been approved by the Food and Drug Administration (FDA) as an anticoagulant since 1954. Warfarin is an effective anticoagulant with undisputable clinical benefits. However, it also has several drawbacks, such as necessity of titration and monitoring, and numerous drug and food interactions, making its use difficult for many patients.
  
  o The emerging novel oral anticoagulants (factor Xa inhibitors and oral DTIs) have demonstrated greater safety, efficacy and convenience compared to warfarin and are expected to eventually dominate the market, particularly for chronic applications.

Source: Frost & Sullivan analysis.
Percent Sales Breakdown
Total Anticoagulant Market
U.S., 2010

Note: All figures are rounded. The base year is 2010. Source: Frost & Sullivan analysis.