



Modeling Federal Cost Savings of Follow-on Biologics

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Project Purpose

- Develop a scoring framework for modeling the impact of FOB entry on overall spending for biologics in United States
 - » Determine key scoring levers, through:
 - A literature review
 - Assessment of relevant economic models
- Use key scoring levers as basis for creating a scoring model
 - » Model assumptions based on previous research
 - Tested against biologics market data
 - » Model can be modified to score legislative proposals

Key Levers Drive Assumptions in Modeling Follow-on Biologics Savings

- Biologics baseline spending estimate and projected growth rates
- Timing of legislation and implementing regulations
- FDA review timeframe and regulatory pathway requirements for follow-on biologics (FOBs)
- Patent life and trade secrets limitations
- Market size distribution for brand biologics and effect on FOB entry
- Market share attained by FOB entrants
- Pricing of FOB entrants
- Share of estimated effect that is Federal (versus other payers)

■■■ Biologics Baseline Spending Estimate and Projected Growth Rates

- Modeling budgetary effect of FOB entry is based on current law biologic spending levels
 - » Data from IMS show total 2005 biologic spending at \$31.5 billion
 - IMS data are revenues (units times prices paid by various entities)
- Baseline in budget window is calculated using historical growth rates
 - » Historical growth has averaged 20% over 2001-2005 period
- Adjust baseline to account for share of growth attributable to new product (pipeline) entry
 - » New products would have patent protection over budget window
 - » Calculate share of growth that is price inflation and increases in utilization by pegging to National Health Expenditures growth rates for pharmaceuticals (7.7% - 8.2% over 2008-2017) – rest of growth is assumed to be new product entry
- Reduce baseline by 14% to account for spending on insulin and human growth hormone
 - » Potential FDA approval pathway currently available for select class of products under FDCA

Timing of Legislation and Implementing Regulations

- Modeling budgetary effect of FOBs requires assumptions of timeframe for passage of legislation and promulgation of regulations
- Legislation may specify timeframes for regulation promulgation, clinical testing requirements, and other milestones
 - » Absent this, we use historical experience
- Model assumes passage of legislation this year (with effective date Oct. 1, 2007)
- Relevant actual timeframes for promulgation of regulations and application reviews
 - » Time between passage of Hatch-Waxman and final regulations (4 years)
 - » FDA review time at CDER (15.7 months), 75% of BLAs reviewed in 10 months
 - » EMEA review time all drugs: (15.8 months); approved biosimilars (about 2 years)
- If legislation or FDA adopt a case-by-case approach to approval, then guidance for classes of biologics may be released incrementally – thereby staging FOB entry for more complex biologics to later in the budget period

Regulatory Pathway Requirements for FOBs

- Because FOBs are more complex than small molecule generics, the abbreviated pathway in Hatch-Waxman will likely have to be modified to accommodate complexity
- Modification of FOB application requirements will affect timing of FOB market entry
 - » Requirements for proving similarity to reference product
 - » Requirements for proving safety and efficacy
 - Some form of clinical trial
 - » Requirements to prove no patent infringement
- FOB applicants will also have to meet current BLA (and FDCA) requirements for biologic manufacturers
 - » For instance, licensing and inspection of manufacturing facilities
- Assuming passage of legislation by FY 2008, this timeframe is possible:
 - » FDA promulgation of final rules by start of FY 2011 (Hatch-Waxman less 1 year)
 - » Immediate submission of FOB applications (clinical testing requirements delay entry)
 - » 2 year review of applications by FDA (EU) (assume reduced review time in out years)
 - » 1st FOB entry by beginning of FY 2013

Patent Life and Access to Patent Information

- Patent expiry dates for patent-protected biologics determine FOB entry timing
- Avalere analysis of patent expiry dates for brand biologics indicates a few biologics currently off-patent; some portion going off-patent in 10 year budget window
 - » Avalere model assumes 10% of the biologics baseline (net new biologics) goes off-patent in a year
- The mechanism by which manufacturers access patent information could affect scoring
 - » H.R. 1038 approach – patent disclosure by brands – may expedite entry
 - » FOB manufacturers would not have access to trade secrets related to process under current legislative proposals
 - Without trade secrets FOB manufacturers will have incomplete information about manufacturing process and hence will directly impact time to market entry

Market Size Distribution for Brand Biologics

- Brand biologics command different shares of the market in their class and in the total biologics market
 - » It is reasonable to assume that large revenue biologics would be more likely to have FOB competition, and more FOB entrants
 - Similar to dynamics in the small molecule generics market
 - » The cost of producing FOBs would likely inhibit FOB entry into very small markets
- Avalere model assumes:
 - » 3 FOBs per large revenue off-patent biologic (large revenue: >\$1 billion annually)
 - » 1 FOB for medium revenue (medium revenue: \$250 million - \$1 billion annually)
 - » No FOBs for small revenue biologics (small revenue: <\$250 million annually)
- Other competitive forces could affect FOB potential market share (not modeled)
 - » Innovator biologics will enter market and disrupt demand
 - » FOBs may also compete with small molecule drugs in some classes

Market Share Attained by FOB Entrants

- Market share attained by FOBs is a function of payer coverage, physician prescribing behavior, consumer demand, and pricing
- Current small molecule generic drug penetration is high (upwards of 60%)
- FOBs will have difficulty reaching similar share levels
 - » FOBs that are similar to the reference brand may be viewed as therapeutic alternatives by payers and consumers
 - Whereas generics are considered therapeutic substitutes
 - » Generic substitution is aided by state pharmaceutical interchange laws, which may not apply to FOB therapeutic alternatives
 - About 64% of biologics are used in the physician's office
 - » It may take time for prescribers and consumers, who are primarily concerned about safety, to adopt these products
 - Omnitrope's market share in Europe is less than 1%
- Unless FOB prices are significantly lower, the trade-off may not be apparent
- Avalere model assumes FOB market penetration reaches 60% over 3 year period

■ ■ ■ Pricing of FOB Entrants

- Pricing of FOB entrants will be a function of production and testing costs, number of market entrants, and overall market size
 - » Research shows that development of biologics is more expensive than development of small molecule drugs
 - » Any clinical trial requirements would augment those costs
 - » Distribution and marketing costs for FOBs will exceed generics
- In near term, FOB market entry may be immature, which affects pricing
 - » Single FOB entrant would not have incentive to price significantly lower than innovator
 - » Early EU shows price reductions of 10-25% for classes where FOBs compete
- Industry analysts do not expect savings to reach generics levels
- Avalere model assumes FOB pricing after 3 years on market to be:
 - » Large revenue FOBs priced at 70% of brand (with 3 competitors)
 - » Medium revenue FOBs priced at 90% of brand (with 1 competitor)
 - » Brand raises price in 1st year and lowers price thereafter

■■■ Share of Estimated Effect That Is Federal (versus Other Payers)

- Savings from FOBs will accrue to multiple payers
- Majority of biologics baseline of \$31.5 billion is paid for by non-Federal payers
- National Health Expenditures data project that approximately 40% of pharmaceutical spending is Federal

Problems with Prior Estimates

- Assume immediate savings
 - » Do not take into account time for passage of legislation, promulgation of regulation, application review, and FOB manufacturing and marketing
- Assume erroneous level of off-patent products
 - » Only one of the 5 biologics in one report, representing 30% of biologics revenues, will be off patent during the budget window
- Assume all off-patent products will have FOB competitors
 - » FOB competitors will likely target only biologics with large and medium revenues
- Assume high levels of interchange
 - » Implying immediate physician and patient acceptance of new technology
 - » Implying pharmacy-level interchange facilitated by state laws
- Assume market penetration similar to small molecule generics
 - » Complexity of FOBs indicates products will be alternatives not substitutes

Avalere Model Key Steps

- Based on aggregate spending for biologics projected forward over 10 year budget window
 - » The model calculates the difference between baseline spending projections and spending under FOB policy for cost estimate
- Baseline spending calculated using actuals with 20% growth rate based on historical rates
 - » Gross baseline modified to account for pipeline products and exclusion of insulin and human growth hormone
- Assumes first FOBs enter market in FY2013 (after passage of legislation, implementation of regulations, submission of FOB application, and FDA approval of application)
- Model incorporates data on typical patent life and distribution of market size for biologics
 - » Assumes 10% of biologics annually become subject to FOB competition
 - » Assumes biologics with larger revenues are more likely to have FOB competition
 - 0-3 FOB entrants depending on market size
- Assumes FOBs reach market saturation (60% share) over three years, at 70-90% of innovator price

Alternative Model / Results

- Model output: Estimated Federal savings of \$3.6 billion over 10 years (2008-2017)
 - » No savings estimated from 2008-2012 due to time elapsing for FDA regulation promulgation and review of initial applications
- Savings would be reduced if these additional levers were included in model:
 - » An expected increase in utilization due to availability of lower priced therapeutic alternatives
 - » An expected degrading of market size for both off-patent and FOB products when new innovator products come on the market
 - Also potential effect of innovator small molecule drugs on off-patent/FOB markets