



# Biosimilars Series: Strategic Issues

Potential remains uncertain

Barriers to entry into the biosimilars market are high. High costs of development and promotion compounded with the need for specific expertise and financial backing favor big players and are likely to deter smaller companies. Smaller specialist players are more likely to enter this market via collaboration agreements with established generics companies.

Acceptance by key stakeholders is crucial for market uptake of biosimilars. The pricing and reimbursement environment is different than for generics at least in the short term but has a big impact on profitability. Thorough understanding of the marketplace is critical for success. Originators are responding to the imminent threat of biosimilars by a combination of lifecycle management strategies and intense lobbying of regulatory bodies and physician detailing.

Reference Code: DMHC2337

Publication Date: 10/2007

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market. Furthermore the launch of Roche's once-a-month pegylated epoetin Mircera will present a challenge to biosimilars although to what extent will depend largely on Mircera's price.

Differences in epoetin markets between Europe and the US are significant — two entirely different environments exist. In the US Aranesp's more convenient dosing regimen has made it the treatment of choice and it is the leading epoetin treatment. Therefore biosimilar epoetins are expected to attain lower market share in the US. However Epogen is patent protected until at least 2012 in the US and is under no immediate threat from biosimilars.

### *Restrictions on epoetin use in the US will impact the overall market size*

The US is the major market for epoetin products (apart from NeoRecormon, which is marketed only in Europe). Currently there is no regulatory approval pathway that would allow biosimilar epoetin to be approved (original epoetin products were approved under BLAs). Once such a pathway is established, however, biosimilar epoetins will enter this market (provided biosimilar manufacturers can successfully challenge Amgen's patents) and their success will largely depend on whether they get preferential status with payers. Following safety concerns regarding the use of erythropoiesis stimulating agents, the FDA issued a black box warning for all epoetins used for anemia associated with cancer. Consequently the use of epoetin therapy for Medicare and Medicaid patients has been restricted and several insurance companies have cut their coverage of epoetin therapy. Although physicians are protesting against these restrictions they are unlikely to be lifted. Therefore, the arrival of biosimilar epoetins may be welcomed by payers. Aggressive price discounts could result in increased payer uptake. Considering the higher price of drugs in the US compared to Europe, biosimilar epoetins could generate high revenues even after large discounts. However, there is the possibility that originators will defend their products by offering significant discounts, even in the US. Innovators will be likely to drop their prices (as epoetin margins are high) in order to maintain their market share. The tender process has demonstrated that the price elasticity of epoetin is great. If originators respond to competition from biosimilars with even greater price discounts, there will be serious implications for the total revenue potential of biosimilar epoetins.

### *Launch of first biosimilar epoetin alpha in Europe is imminent*

In August 2007 Sandoz received marketing approval for its epoetin alpha biosimilar Binocrit. Sandoz is also marketing its product through its German subsidiary, Hexal, and through a licensing deal with another German company, Medice Arzneimittel Pütter. Sandoz has stated that its epoetin alpha biosimilars will be priced at a 25–

second-generation products. However if the Biologics Price Competition and Innovation Act becomes law it will allow a highly litigious environment in the US. According to the bill the biosimilar manufacturer will have to give notice to the originator company, including data on process and product, so that it can consider suing for patent infringement. The reference product sponsor then has 60 days to provide the biosimilar producer with a list of patents that it believes are being infringed. The biosimilar manufacturer has a further 60 days to respond. This exchange of information allows the biosimilar manufacturer to challenge validity of patents and gives the BLA holder the opportunity to sue for patent infringement. The biosimilar manufacturer also has to give the reference product sponsor at least 180 days notice before the first commercial marketing of the follow-on biologic product. This allows the reference product sponsor to seek a preliminary injunction preventing the biosimilar manufacturer from engaging in commercial manufacture or sale of the product before any patent dispute is settled. Therefore the strategies the innovator can use maximize revenue through patent regulation include:

- sue only the first biosimilar filer and negotiate settlement;
- assert willful infringement in filing for a biosimilar or litigation misconduct;
- assert copyright infringement;
- sue upon launch of biosimilar;
- obtain additional patents, including process and third-party patents;
- obtain patent extension through new indication approval;
- file Citizen Petitions (although the generics industry is lobbying the US government to introduce legislation that would prevent Citizen Petitions from delaying approval of biosimilars).

### **Pricing strategies**

Payers will invariably find the discounts offered by biosimilar manufacturers very attractive especially with increasing cost-containment pressures and originators will have to use different strategies to prevent switching. These strategies will include:

- offering rebates to PBMs and MCOs (in the US);
- capping total cost per year per patient as seen with Avastin;

even before any biosimilars appear on the market it could make the market less attractive for biosimilars producer and would make it harder for them to enter it.

Furthermore development of second generation products is not so easy – Roche had to temporarily suspended its phase II trials for a pegylated epoetin Mircera (CERA as a result of imbalance of deaths among treatment arms (Generics industry urged to focus on science for biosimilars, 2007). Roche is also facing tough patent dispute with Amgen over Amgen's epoetin patents.

### Innovative delivery systems

As most biologics are injectables delivery devices play an important role in the branding strategy of both biosimilar and innovative companies. Innovative delivery devices can provide both a barrier to entry and differentiate originators' products. Innovators are constantly improving their delivery devices making them more patient friendly. Ease of use and discomfort during administration can affect both patient compliance and product uptake. Therefore companies are looking to use devices that are easier to use (fewer steps) or allow less painful administration (needleless devices). Companies offering a range of delivery devices suited to different preferences and lifestyles are more likely to succeed in maintaining their market share. However, biosimilar companies are also partnering with developers of advanced delivery devices and competition is likely to get stronger. Therefore use of superior patent-protected delivery devices is recommended.

### Innovation, innovation, innovation

Some companies recognize that in the future biosimilars will be a normal part of the product's life cycle and that focus will be on what innovative companies are good at: continuous innovation and product improvement. Despite the current productivity crisis innovative pharmaceutical and biotechnology companies have the expertise, experience, organizational and financial capabilities to develop and market new medicines. Once new therapies are introduced onto the market treatment practices will change and biosimilars will not have the same role. Therefore continuous innovation is seen as the simplest way forward.