NEWS FEATURE

Finding new formulas for pharma success

Reformulating existing drugs has become an increasingly popular strategy for tackling productivity shortfalls. David Bradley investigates the trend.

Finding new markets for old drugs or ways to modify a formulation to allow it to enter a new market could be the key to keeping productivity from stalling as markets for older products dry up, patents expire and profit margins continue to be eroded by market pressures, competitor products and generic alternatives.

According to a report from Datamonitor (Reformulation Strategies — Comparisons of Past and Future Reformulation Strategies, September 2006), reformulation has become an almost ubiquitous product lifecycle management technique. The top 50 manufacturers used reformulation for almost two thirds of product launches during 2002–2005.

Cardiovascular health, central nervous system, diabetes and women's health products have seen the widest degree of reformulation, but companies are keen to reformulate in the emerging area of alimentary and metabolic drugs too. All of these areas represent a huge patient base, and entry offers high commercial value and significant return on investment for companies that successfully market reformulations.

Tim Atkinson, Director of Research and Analysis at Spectra Intelligence and the author of an independent Global Business Insights report on drug reformulation explains why this approach has become popular. "Drug reformulation has proven to be an essential method for extending the lifecycle of patented drugs," he says. He suggests that re-engineering old favourites or less successful products generally improves therapeutic efficacy, compliance and clinical outcomes. Pfizer's extended-release formulation of its antihypertensive nifedipine, Procardia XL, is a classic example of the art in action — it yielded US$8 billion in additional sales from 1990 to 1998.

Other companies hope to emulate this success. For instance, Johnson & Johnson (J&J) has developed an extended-release follow-up to its antipsychotic blockbuster Risperdal (risperidone), known as Invega, the active ingredient of which is the major active metabolite of risperidone. Following its recent approval, commentators at Datamonitor anticipate that J&J will aim to switch as many patients as possible from Risperdal to Invega before the Risperdal patent expires in 2008. To do so successfully, J&J must overcome the higher price barrier relative to generics by demonstrating a significant therapeutic advantage.

The reformulation of methylphenidate, a stimulant used to treat attention-deficit/hyperactivity disorder, to Concerta represents a past successful market grab for J&J. By contrast, Lilly's Symbyax for bipolar depression, a reformulation combining the blockbuster antipsychotic Zyprexa (olanzapine) with the antidepressant fluoxetine, has yet to demonstrate its niche grab, perhaps because of strong generics, say the report's authors.

More recent ongoing success stories involve the emerging field of nanotechnology. "Cancer drugs may benefit particularly from reformulation," highlights Atkinson, who also reported for Spectra recently in Chemotherapy Market Insights. He says at least 35 nanotechnology drug reformulations are in development. "Such technologies may not only bring about a new generation of novel drugs," he adds, "but will also greatly facilitate the redevelopment of drugs in current use to greater therapeutic efficacy." According to Atkinson, Abraxis BioScience's injectable paclitaxel (Taxol) particulate formulation, which is therapeutically superior to the previously patented version, is a good example.

Another example of nanotechnology anticancer strategies is provided by research from Dennis Discher of the University of Pennsylvania, who has demonstrated that biodegradable nanoparticles — polymerosomes — act as 'Trojan horses' for potent cancer-fighting drugs, paclitaxel and doxorubicin, carrying them into human breast tumour cells, making them more effective than the stand-alone drugs. "Understanding and development of relevant nano-assemblies have grown over the last decade," Discher says. "It is therefore almost certain that new nano-based approaches will be used increasingly."

Indeed, there are numerous research teams in academia and industry working on nanotechnology as a reformulation approach. Rochelle Wagner, Senior Research Scientist in Life Sciences at Altairnano, a company that works on microparticles and ceramic nanomaterials, explains the potential of nanotechnology for cancer therapies: "Reformulations in cancer chemotherapy include targeting of molecules in such a manner that the usual severe toxicity to normal cells is averted," she says. "For example, a nano-sized 'encapsulation', if you will, of agents that allows targeting to a cancer cell via a molecule preferential to the cancer or via a molecule that can bind for normal passage throughout the blood stream." Additionally, she says, "exciting advances have been made in breaking the barriers of cancerous tumours that ensure their success by using the nanoparticle as the delivery agent instead of the drug itself."

Altairnano is investigating nanotechnology formulation of novel compounds, but its technologies could be equally applicable to reformulation. "We have successfully used spherical nanoparticles of Renalan [lanthanum-based phosphate binders] for end-stage kidney disease. The enormous surface area to volume ratio reduces drastically the required dose," Wagner explains. "The main advantages are multi-faceted," she says, "selectivity, lower dose, increased specific dosing, lower toxicity." She adds that, "combining an organic nanoparticle with a drug allows the drug greater access to appropriate tissues while combining an inorganic nanoparticle with a drug could extend the time of action due to decreased catabolism."