

THE CASE FOR BIOSIMILARS

by: Aileen Soper

Biologic anticancer therapies and supportive-care treatments for oncology are likely to be a focus for generic biotechnology drug development, if U.S. Congress acts to create a regulatory pathway to approve so-called biosimilars.

Biologics are a class of medicinal products that have been derived by biological processes from natural and living substances, including humans, animals and microorganisms. Biologics may include chemotherapy, targeted anticancer drugs, and supportive-care drugs like ESAs and antiemetics, and now account for about a quarter of the U.S. prescription market.¹ The rising costs of healthcare, including the costs of branded anti-cancer drugs and treatments for other chronic and life-threatening diseases to patients and insurers, is driving demand for increased competition in the form of follow-on therapies sometimes called biosimilars or biogenerics.

The European Medicines Agency recently developed a regulatory pathway to allow sales of biosimilars in Europe. President Obama's campaign promises for healthcare reform and the outcome of 2008's Congressional races mean that similar change could be forthcoming in the United States. But it remains unclear whether there may be sufficient momentum to pass legislation in 2009 that would permit biosimilar entry into the U.S. market. Major questions on issues such as how to determine bioequivalence, requirements for confirmatory clinical trials, and how long branded innovator therapies should be guaranteed market exclusivity could be sticking points.

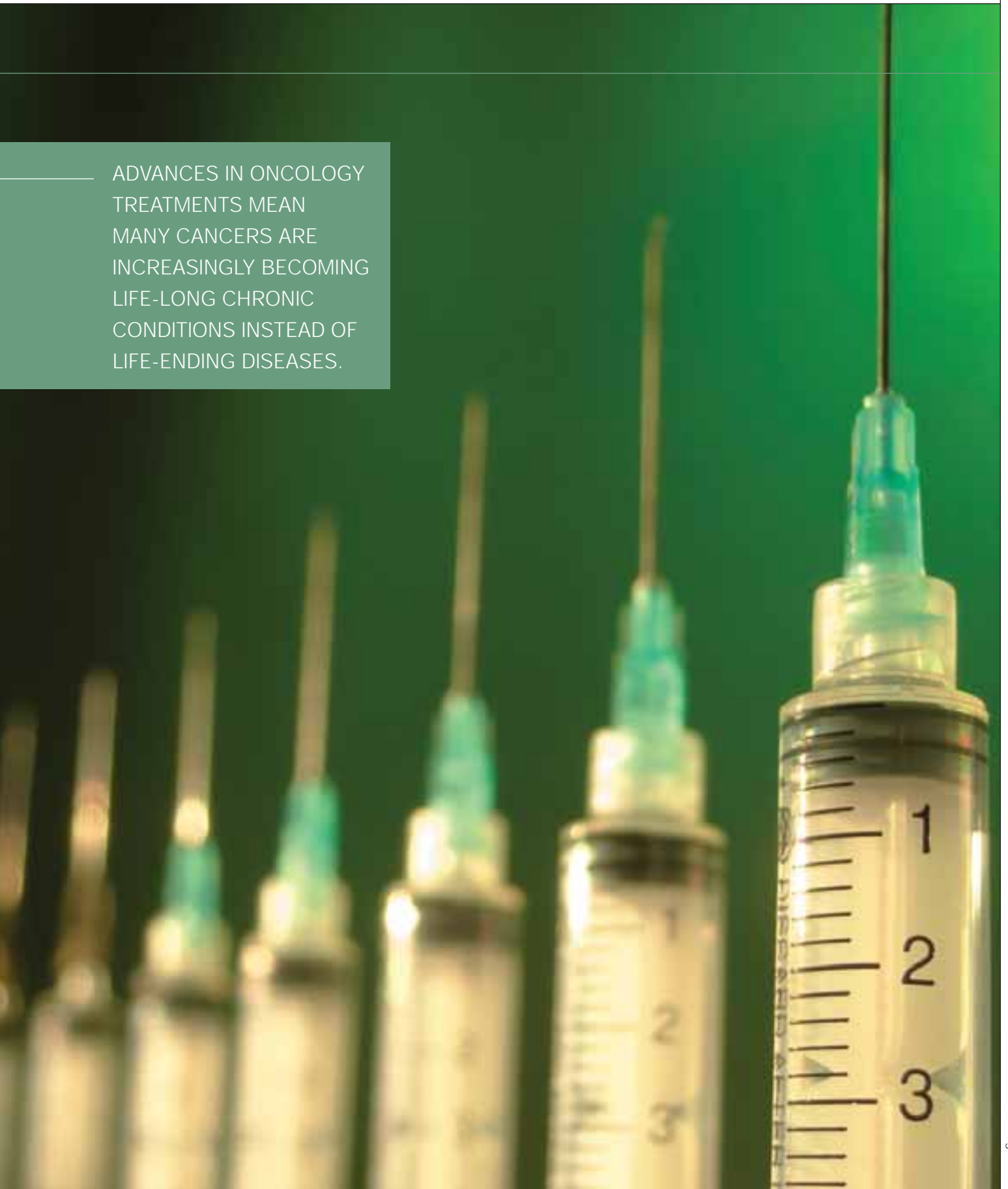
A key voice in the biosimilar debate will be that of American oncologists. They, along with patients diagnosed with cancer, may have one of the biggest stakes in the outcome of the biosimilar discussion.

Advances in oncology treatments mean that many cancers are increasingly becoming life-long chronic conditions instead of life-ending diseases. Many cancers are managed effectively with aggressive therapeutic regimens that are improving quality of life for people diagnosed with cancer. These treatments also bring staggering costs, which has created financial challenges for all parties and is driving demand for biosimilar development.

The most positive impact for biosimilars could be lower costs to patients, which may make access to life-sustaining and life-saving therapies a reality for more people diagnosed with cancer. Oncologists would face a separate set of challenges should biosimilars become available for currently branded anticancer and supportive care biologic therapies. These challenges may include evaluating products for safety and efficacy, and addressing patient perceptions about quality.

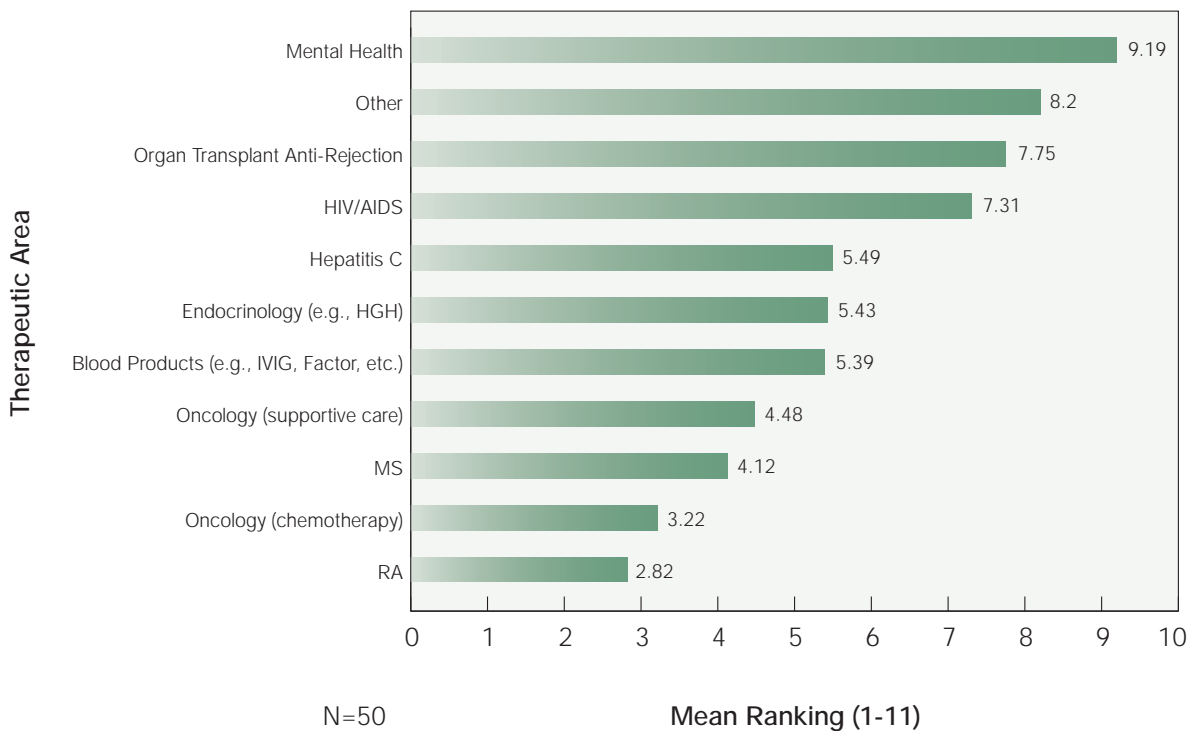
A November 2008 Managed Care Network survey of 50 pharmacy and medical directors for U.S. managed care organizations identified chemotherapy as the therapeutic area with the second highest potential (after rheumatoid arthritis) to deliver cost savings through the introduction of biosimilars. Supportive care oncology drugs ranked fourth (after therapies for multiple sclerosis).²

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reimbursement watch

Respondents were asked to rank a list of 11 therapeutic areas on a scale from 1 to 11, (with 1 being the highest priority and 11 being the lowest priority) based on where they believed a biosimilar market entry could deliver the highest potential cost savings for their plans.



Key questions must be answered in the ongoing debate over biosimilars. Among them:

- How will federal regulators and oncologists evaluate clinical efficacy, safety, and equivalence for biosimilar therapies?
- How might payers like Medicare, Medicaid, the Veteran's Administration, and private managed care organizations challenge provider prescribing preferences and push biosimilar generic substitution requirements?

- How much savings might patients realize through use of biosimilars and how will potentially lower costs impact utilization?
- How would the approval of biosimilars impact reimbursement given the current average sales price (ASP) payment methodology for Medicare Part B-covered drugs?
- How long will new formulations for branded biologic therapies be able to retain market exclusivity?

One of the focuses of disagreement has centered on the length of time that pharmaceutical manufacturers who develop innovative, new biologic therapies would need to retain market exclusivity in order to recoup their initial investment. Recent competing studies have estimated that time span as ranging from 7 to 14 years.³ It is worth noting that for novel therapies oncology is one specialty that depends on a constant flow of new research and drug development from pharmaceutical manufacturers. The impact of any cap on market exclusivity would need

to be weighed against the possibility that such reform might dilute incentives for companies to produce new, innovative therapies.

The current generic drug approval system was established under the Drug Price Competition and Patent Term Restoration Act of 1984, sometimes called Hatch-Waxman, after the Act's legislative sponsors. Under this Act, a generic drug manufacturer may submit an abbreviated new drug application (ANDA) to the FDA that allows them to



market a generic drug without first producing the same evidence of extensive preclinical and clinical testing to demonstrate safety and efficacy that would be required to support approval of the original, branded drug. Rather, generic manufacturers must show that the generic product is "bioequivalent," meaning that it enters the bloodstream at a rate and offers systemic exposure that is comparable to the innovator therapy.

MANAGED CARE ORGANIZATIONS WOULD EXPECT CONSIDERABLY LOWER PRICES VERSUS INNOVATOR DRUGS IN ORDER TO GIVE BIOSIMILARS FAVORABLE TIER PLACEMENT OR TO RELAX UTILIZATION RESTRICTIONS COMMON FOR BRANDED BIOLOGICS.

Bioequivalence is often substantiated by administering the generic to small groups of volunteers and measuring the drug's metabolic impact. It is a considerably shorter and less expensive testing process than the clinical trials and regulatory requirements of the standard drug-approval process.⁴ Some industry groups including the American Society of Clinical Oncology (ASCO) maintain that since biologics are vastly more complex in their molecular structure than traditional drugs, the complexity of both the composition and manufacturing behind biologics could pose problems for producing reliable copies and even compromise safety and efficacy. ASCO, in a 2008 position paper, noted that

"even the most seemingly insignificant changes in drug formulation can result in a product that has severe health consequences."⁵

The U.S. Congressional Budget Office has predicted that biosimilars could save the United States \$25 billion in healthcare costs over 10 years. One piece of recent legislation, the Biologics Price Competition and Innovation Act of 2007, passed the Senate Health Committee but never went to a full vote. It proposed 12 years of market protection for new biologics and would have given the FDA the authority to approve interchangeable biosimilars.

Even if legislation gets passed in 2009, it would likely be years before a biosimilar therapy is for sale on the U.S. market.⁶ One recent study estimated that it would take a pharmaceutical manufacturer a minimum of three years to launch a viable biosimilar therapy following the passage of legislation clearing biosimilars for the U.S. market.⁶

One consideration is how financially viable the development of biosimilars might be to a pharmaceutical manufacturer, considering the expense that may be involved in replicating clinical trials and a reliable manufacturing process. Managed care organizations would expect considerably lower prices versus innovator drugs in order to give biosimilars favorable tier placement or to relax utilization restrictions common for branded biologics. In the November 2008 MCN survey, a majority (40%) of managed care representatives indicated they would expect to realize savings of 20-30% in order to favor therapeutically equivalent biosimilars over brand competitors.

The Obama Administration and Democratic majority in Congress have the potential to pass biosimilar-friendly legislation in 2009. At the same time, the momentum to introduce bioequivalent therapies to the U.S. market could be eclipsed by other pressing demands, such

as the adoption of health information technology. Oncologists will need to monitor any proposals to ensure that safety and efficacy take first priority in the creation of a regulatory process for biosimilar approval. The creation of clinical standards and a regulatory process to measure bioequivalence will require buy in from the oncology community as a whole. ■



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Xcenda, a national healthcare consulting company, will publish a comprehensive report on biosimilars in the spring of 2009. The report will leverage primary survey data gathered through the Managed Care Network and through a separate survey of community oncologists on the topic. For more information on the report, contact Barb Lennert from Xcenda at barb.lennert@xcenda.com.