Shifting Specialties

New developments in specialty pharma are changing the way manufacturers, payers, docs and patients interact. **Ben Comer** looks at where things are headed

Specialty product sales are growing at a time when breaking even in other areas feels like success. New technological discoveries in drug delivery and mechanism of action have helped to bolster pipelines, and as these products are approved, new systems will need to be implemented. By 2013, global revenue from specialty products will exceed $160 billion, according to IMS Health data. That growth will catalyze necessary changes to the entire specialty pharma model, according to Pam Sauerwald, general manager, specialty offering development, and author of Changing the Channel, a new IMS Health whitepaper.

"One of the biggest challenges for pharma manufacturers is striking a balance between access for patients and control over distribution," says Sauerwald. As distribution has evolved from specialty wholesalers focused on one or two condition areas—HIV/AIDS or cancer, for example—into specialty pharmacies that offer a full range of value-added patient services, manufacturers need to decide which distribution channels are appropriate for their products, a decision that may also affect how a patient is covered by a health plan.

The real strength of specialty pharmacies, whether it's mail or walk-in retail stores, is that they help to coalesce what Sauerwald calls the four Ps: patients, physicians, payers and pharmaceutical manufacturers. For patients, a specialty pharmacy is focused on delivering the best possible treatment outcomes, and that includes providing educational resources, and clinicians to help with side effects and to facilitate compliance. Extras like toll-free, 24-hour clinical support, home delivery and help with benefits and reimbursement can improve patient outcomes.

From a physician's perspective, specialty pharmacies can function as an extension of the office, which frees up time for more patients without sacrificing level of care. Coding and billing assistance, as well as reimbursement coordination, also helps to clear out a doctor's schedule. For payers, specialty pharmacies help to maintain costs through competitive pricing, and reduce wasted product; both of which help to keep costs down.

Improving patients' access to a drug means increased sales, and pharmaceutical manufacturers are naturally keen to do both. Many specialty pharmacies offer nationwide shipping and delivery—including overnight and special handling—as can also provide Risk Evaluation and Mitigation Strategy (REMS) programs in the US, an area where best practices have yet to be fully developed.

"When a pharma manufacturer is looking for patients to be satisfied where they are already in a disease state that's perhaps frightening to say the least, it's helpful for them to have something all in one place," says Sauerwald, describing the kind of full-service care patients often require with taking specialty drugs. Treatments for conditions like rheumatoid arthritis, cirrhosis, multiple sclerosis, and Crohn's disease, for example, often have multiple side effects, so it's important to give patients an all-in-one resource for care, says Sauerwald.

Specialty pharmacies and the four Ps

One such resource, myHumira.com (for Abbott Laboratories' TNF blocker Humira) provides injection instructions and video demonstrations, starter kits and information about pen and syringe disposal. Patients can also click on a link to speak with a nurse, get medication reminders or receive tips from a panel of experts and others, all at myHumira.com. Michelle Johnson, manager of pharmaceutical public affairs at Abbott, says specialty pharmacies "work closely with patients who have chronic conditions to provide additional support services to help them with their specialty medications." For Humira, patients can enroll in the Humira Protection Plan, which provides co-pay assistance for insured patients "that can help reduce their co-pay costs to as little as $5 a month," according to Johnson, and can also provide access to "no-cost Humira for uninsured patients who qualify." These programs are important, considering the high cost of specialty products. Without insurance, Humira can cost over $1,000 for a one month supply.

Humira was the fourth best selling specialty product from September 2008 through September 2009, at $4.6 billion in global

sales, according to IMS Health. Like most of the other top selling specialties, Humira has garnered indications for several conditions, including rheumatoid arthritis, plaque psoriasis, ankylosing spondylitis and Crohn's disease. The drug is available as a self-injectable pen, as well as in pre-filled syringes. It can be administered at home, and does not require a physician for administration – a key factor in how the drug is covered by an insurance plan.

Connecting the dots

The second best selling specialty product over the same period—Centocor Ortho Biotech's Remicade (infliximab), also a TNF blocker—carries many of the same indications as Humira (Centocor is a subsidiary of Johnson & Johnson). However, Remicade is not available as a self-injectable, and must be infused and delivered via IV at a doctor's office, the hospital or at an infusion center. That changes how the drug is covered by a health plan, according to Sauerwald. "Specialty pharmaceuticals can fall under pharmacy benefits, medical benefits or both. If there is a healthcare provider (HCP) involved, or if you're in a hospital, it's going to fall under a medical benefit," says Sauerwald. "But you can infuse a product in a hospital or in a clinic, or even at home. Benefits are often parallel but not overlapping." Sauerwald admits that health plan coverage is not cut and dry, but says it's important to look at how a pharmacy benefit contracts with a pharmacy benefit manager, and how a medical benefit contracts with the health plan. "The industry itself grapples with how to connect the dots between the medical benefit and the pharmacy benefit into one set of information, in order to truly understand the cost of product."

Remicade mostly falls under a medical benefit, since it must be handled by an HCP prior to administration. "[Remicade] is infused at the doctor's office, and there is also a buy and bill component there, so the doctor is somewhat incentivized, and may also feel that he or she has more control over true compliance—not just that a patient has picked something up [from a pharmacy]," says Sauerwald. Although Remicade, unlike Humira and the top-selling specialty drug, Enbrel, is not available for self-injection, Centocor received FDA approval for two new biologics in 2009 that could potentially fill the gap. Simponi (golimumab) was approved in April for rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, and is "more or less" a self-injectable formulation of Remicade, developed at least in part so that Centocor can "move more into the home health or self-injectable space," according to Sauerwald.

The second approval for Centocor and J&J came in September, with Stelara (ustekinumab), an HCP administered infusion for moderate to severe plaque psoriasis. A study published January in the *New England Journal of Medicine* found Stelara to be more effective than Enbrel in treating psoriasis—the two drugs have completely different mechanisms of action.

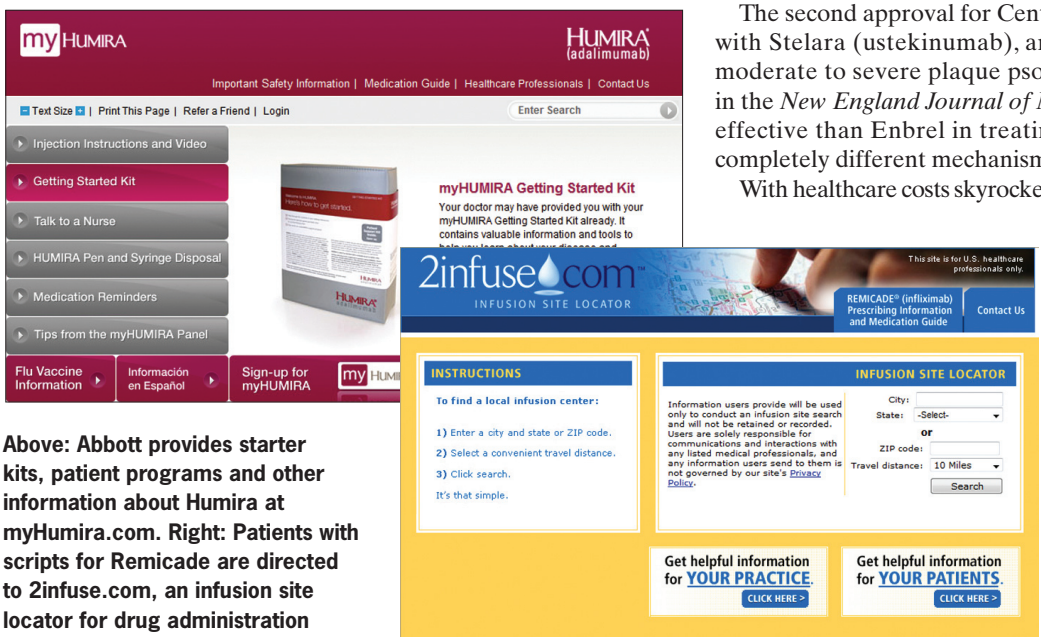
With healthcare costs skyrocketing, payers are increasingly focused on ways to bring down costs. Cost containment measures listed in the whitepaper include determining access to a given drug based on diagnostic tests, adherence to evidence-based clinical guidelines, seeking prior authorization, requiring step therapy, monitoring the duration of therapy and minimizing off-label use: all of which will serve to constrict product sales, writes Sauerwald.

Manufacturers are already required to demonstrate a product's value through health eco-

Top 10 global specialty pharma categories (2008)

Specialty pharmaceuticals	100.0
Oncologics (e.g., AvastinTM, Erbitux®, Herceptin®, RetuxinTM, Sutent®, Taxotere®, Xeloda®)	35.7
Antivirals: HIV/AIDS (e.g., Atripla®, Kaletra®, TruvadaTM)	9.1
Immunosuppressants (e.g., Prograf®, Cellcept®, Rapamune®)	9.1
Erythropoietins (e.g., Aranesp®, Procrit®)	8.5
Autoimmune biologics (e.g., Enbrel®, HUMIRA®, Remicade®, Orencia®, Kineret®)	8.2
Immunostimulants (excl. Interferons-e.g., Neulasta®, Copaxone®, Neupogen®)	6.6
Autoimmune Modulators (e.g., Roferon®, Avonex®, Betaseron®)	4.2
Immunoglobulins (e.g., Gamimmune®, Gamunex®, Octagam®)	3.7
Blood coagulation (e.g., Helixate FS®, Koate®)	3.0
Interferons for Hepatitis C (e.g., Rebetol®, Copegus®, Baraclude®)	2.9
TOTAL OTHERS	9.0

Source: IMS Health



Above: Abbott provides starter kits, patient programs and other information about Humira at myHumira.com. Right: Patients with scripts for Remicade are directed to 2infuse.com, an infusion site locator for drug administration

nomics and outcomes research (HEOR), but "specialty pharmacy providers will soon be able to weigh in on the issue of a product's value with feedback on its comparative effectiveness in the real-world setting," writes Sauerwald. "For better or worse, manufacturers must brace themselves for the availability of such information, because it is coming."

Payers have already been able to extract guarantees from manufacturers on product performance—the National Health Service contracted with J&J to pay for Velcade treatment in only those patients for whom it proved effective, Sauerwald writes—and this is an area where specialty pharmacies can help.

In recent years, specialty pharmacy providers have partnered with pharmacy benefit managers to serve as "clinical advisors to patients and cost controller for payers," according to Sauerwald. "It's well known in the industry that the two of the largest [specialty pharmacy] players are aligned with pharmacy benefit managers," says Sauerwald. Medco, which was originally created by Merck as an in-house pharmacy benefit manager, became independent in 2003 and acquired Accredo Health, a specialty pharmacy, for $2.2 billion in 2005. Similarly, Express Scripts acquired the specialty pharmacy CuraScript in 2004. CVS purchased Caremark in 2007, a deal that came with specialty pharmacy Caremark Therapeutic Services (CTS). Other retail pharmacies like Walgreens have steadily picked up smaller specialty pharmacies.

These kinds of consolidations will continue as higher safety standards and a greater participation among patients as the healthcare process continues. "I think there will be more and more vertical integration with some of the pharmacy providers picking up infusion houses, for example, because it just makes fiscal sense for them," says Sauerwald.

Enbrel's product site offers patients interactive diagrams, step-by-step how to's, online assistance and support for safe self-injection

In order to control costs further, governments are exploring possible regulatory pathways for biosimilars. Sauerwald says a framework is in development, and is also a part of the healthcare reform bill, but isn't finalized. In Europe, biosimilars have been developed for erythropoietins, and the US framework will most likely follow the European model, according to Sauerwald.

Top 15 specialty products in global sales (September 2008 – September 2009)

Product	Manufacturer	Sales in billions
Enbrel	Immunex Corp.	$5.6
Remicade	Centocor Ortho Biotech	$5.2
Avastin	Genentech	$4.7
Humira	Abbott Laboratories	$4.6
Mabthera	Roche	$4.5
Herceptin	Genentech	$3.7
Neulasta	Amgen	$3.6
Glivec	Novartis	$3.2
Epogen	Amgen	$3.0
Aranesp	Amgen	$2.7
Tazotere	Sanofi-Aventis	$2.6
Eryp	Oanssen-Cilag	$2.5
Copaxone	Teva	$2.3
Truvada	Gilead	$2.3
Atripla	Bristol-Myers Squibb/Gilead	$2.1

Source: IMS Health

There isn't any one way to partner—or acquire—a biotech manufacturer or drug candidate, says Sauerwald. If a given drug has a very small population of potential patients, and the manufacturer has production issues, it may be wise to have one exclusive partner relationship. Disease management could then be parceled out between the manufacturer and partner. Manufacturers would need to create physician referral programs that work with a specialty pharmacy, and opt-in registries for patients, says Sauerwald. "The manufacturer itself cannot deliver directly to the patient, and would need to triangulate between the prescriber, the pharmacy and the patient."

Much of the low-hanging fruit—drugs that are closer to complete development—have been snatched up already. "You're getting further up the stream from an R&D standpoint, so it becomes a little bit more difficult to see how it's going to benefit an individual company," says Sauerwald, adding that despite risks, acquisitions of biotechs with promising pipelines will likely continue.

Safety concerns

FDA is requiring that more drugs have Risk Evaluation and Mitigation Strategy (REMS) programs, and some companies are voluntarily preparing for them, Sauerwald writes in the white paper. REMS was launched under the Food and Drug Administration Amendments Act of 2007, and FDA can require manufacturers to submit a REMS when a drug first comes on the market, or later if FDA becomes aware of new safety data. FDA can also require REMS for a product that doesn't necessarily present significant risks in clinical trials, but is in the same category as another drug that received a REMS requirement. Though FDA has used the program sparingly so far, Sauerwald says best practices are needed. "I think [REMS] is an opportunity for specialty pharmacy and specialty manufacturers to work closely together," she says. "The FDA still has some backlog, but not any very specific rules and regulations about how to go about creating a REMS." ■