
SPECIALTY PHARMACY NEWS

REMS Benefit From Specialty Pharmacies' Core Competencies

With the FDA's recent release of draft guidance for a risk evaluation and mitigation strategy (REMS), many pharmaceutical companies may be concerned that the requirements could mean it will take much longer for a drug to reach the marketplace than it now does (see story, p. 9). However, if pharma firms work with specialty pharmacies on a REMS, this collaboration can produce value for manufacturers, as well as health plans, contend sources at specialty pharmacies.

According to the FDA's Web site, the agency had approved 89 REMS as of Oct. 30. Of these, 15 were for biologics, including Cimzia (certolizumab pegol), Enbrel (etanercept), Extavia (interferon beta-1b) and Nplate (romiplostim). Steve Russek, chief clinical officer of Accredo Health Group, a subsidiary of Medco Health Solutions, Inc., says that on the specialty side with biologics and orphan drugs, there is a higher percentage of REMS, perhaps in the 30% to 40% range, than with nonspecialty drugs. Craig Kephart, president and CEO of Centric Health Resources, Inc., tells *SPN* that he expects the FDA will exert "more regulatory control" and begin requiring even more REMS overall. "In exchange for allowing drugs to come to market faster, the FDA is layering on REMS," he says. "Almost everything in the future will have some component of a REMS."

There are two types of REMS, says Russek. About two-thirds of existing REMS have only a medication guide that provides more safety information, and others include Elements to Assure Safe Use (ETASU), which is incorporated when a drug may have a serious adverse event. An ETASU would include a goal or goals to mitigate the risk of the event, such as requiring providers to enroll patients in a registry and health care professionals to check lab values before dispensing a drug.

Requirements Are Routine for Companies

For many reasons, "the specialty pharmacy platform is the only logical choice" to execute a REMS, Kephart says. ETASUs "can be very complicated and require tight communication with physicians and patients, usually every 30 days," Russek says. "This

is what we do, so this is an extension of the specialty pharmacy model" in that these companies monitor patients to ensure these people are not at risk. He adds that Accredo includes information from the medication guides, such as signs of infection or depression, as part of its patient counseling. "We don't want to scare people, but we want them to be aware there could be a reaction," he says.

Russek says that manufacturers can contract with a hub, through which anyone receiving a particular drug must go. The hub can then refer the patient to a specialty pharmacy. Proherant Health, Inc. is Accredo's hub, but it is a separate organization from the specialty pharmacy, he explains, noting that Proherant may have patients come through who may be patients of an Accredo competitor. When a REMS requires patient registration, the hub maintains this information. The specialty pharmacy also reports patient data to the hub.

With an increasing focus on personalized medicine, manufacturers will find their markets growing smaller, Kephart asserts. Plus, he says, "it's a pretty fair bet that" the smaller the patient population and clinical trial size, "the greater the REMS requirement will be." In addition, the "margin model," in which specialty pharmacies make their money off profit margins for drugs, "is not going to survive," so these companies need to offer value that plans and manufacturers will pay for, he says. "Specialty pharmacies have the ability to control the pedigree of the product and the ability to control the patient experience," he says. "With the feds holding pharma manufacturers responsible for what happens in the marketplace, REMS are a way to mitigate" this risk, he says. These companies should design a distribution strategy that has layered in a REMS, he says. In fact, many manufacturers are already working with specialty pharmacies such as Accredo and Centric before their drugs hit the marketplace to design an effective REMS.

"We've become more of a consultant to pharma companies," asserts Nick Calla, vice president of trade relations for Walgreens Specialty Pharmacy. "With the FDA putting a lot more requirements on products as they come to market... we have less of a vendor-client relationship than a partnership."

continued

According to Kephart, independent specialty pharmacies that “focus less on volume and more on high touch” have a “great opportunity” to realize success on a national level by leveraging REMS capabilities. Many larger specialty pharmacies, he says, have invested a lot in automation and tend to have more mail-order distribution processes for numerous disease states that have larger patient populations. The challenge for pharmacies managing drugs with REMS in conditions such as multiple sclerosis or rheumatoid arthritis is those larger patient populations, he says. While Kephart points out that he’s not saying larger specialty pharmacies cannot do REMS well or that they provide bad care, he maintains that bigger numbers of patients mean the greater potential for “more points of disconnect and a greater chance of failure. Every time they hand a patient off, that is a potential point of failure.”

Health management programs provide patient education, assessment and intervention and help get patients “into positive pathways for care,” says Kephart (*SPN 11/08, p. 9*). As an example, he cites pemphigus, a group of rare autoimmune blistering diseases impacting the skin and/or mucous membranes. Patients may take biologics as well as high-dose oral steroids, which can have side effects such as high blood pressure, diabetes and bone mass loss. So a REMS program for one of these biologics could include, for instance, speaking with patients about having a bone scan annually and checking their blood sugar levels regularly. “This has an economic value,” contends Kephart, if a company can demonstrate that it helped prevent diabetes in a percentage of a patient population. In addition, many biologics that have smaller patient populations do not have a lot of data by the time they hit the marketplace. Data collection through a REMS could be good for the manufacturer if concerns about a drug prove to be overblown when the drug’s effects are not as bad or as widespread as initial perceptions.

If a company has to have a REMS program anyway, it doesn’t cost that much more, Kephart says, to build in ways to determine outcomes such as whether the overall management approach helps improve quality of life and reduce hospitalizations. That way, if a company can “measure, capture and claim these outcomes as part of your value proposition, you can say that my program generates this value,” he contends.

Kephart says he encourages manufacturers to “get out of the mindset of thinking about only the therapeutic impact of their drug.” When companies can demonstrate the economic value of their programs, this “creates a win for every member of the value chain,” he maintains. Manufacturers win because they can justify their costs, payers win because the program will produce better out-

comes, and patients win because they get a better quality of life.

Although “REMS are good and something the industry needs,” one challenge with a REMS is its potential impact on cost to the health care delivery system, points out Russek. Such programs certainly add administration not just to specialty pharmacies but also to physicians, manufacturers and health plans. But, he says, considering the severe side effects of some of these drugs, including death, the key question is, “Do the extra safety measures potentially decrease costs tied to emergency room visits and hospitalizations?”

Beyond the safety aspects of patients not complying with a REMS, companies will now face some fairly pricey penalties for noncompliance. The agency will first look at the manufacturer if there’s a problem, says Calla, but the specialty pharmacy will be in the crosshairs next. So if specialty pharmacies commit to working with a manufacturer on a REMS, they must ensure that they adhere to all of the requirements.

Health plans also have a role to play with REMS, contends Russek. By placing prior authorization on these drugs, payers can “make sure the drugs are being used by the patient populations that need them,” he says. This could include not allowing a drug’s use as a first-line therapy if there are other therapies available, he explains.

Ultimately, managing a REMS “is becoming a core competency of specialty pharmacies,” adds Calla. In fact, he says, “the ability to handle these...figures very prominently” in manufacturers’ requests for proposal (RFPs). “We are judged on our ability to adhere to REMS programs,” he says, adding that even some health plans’ RFPs already include information about REMS. At this point, the discussions are “not very robust, but plans are getting their arms around this, and it will grow,” he maintains.

Contact Kephart at (866) 849-4481, Calla at (412) 325-6507 and Russek through Ann Smith at (201) 269-5984. ♦

Fines Are Among Noteworthy Parts of Proposed REMS Guidance

Although the FDA has been requesting risk evaluation and mitigation strategy submissions for a couple of years now, it has just recently released the first draft guidance for a REMS. While there weren’t any huge surprises in that Sept. 30 guidance, there were a few noteworthy aspects, industry sources tell *SPN*.

The FDA can require REMS with new drug applications (NDAs), abbreviated new drug applications (ANDAs) and biologics license applications (BLAs). Ac-

cording to the FDA's Web site, the agency had approved 89 REMS as of Oct. 30, 15 of which were BLAs, including PegIntron (peginterferon alfa-2b), Simponi (golimumab) and Stelara (ustekinumab). The Food and Drug Administration Amendments Act of 2007 (FDAAA) authorized the FDA to require a REMS as part of a drug application if the agency determined that it needed to ensure that the benefits of the drug outweighed the risks. Before the FDAAA, a risk minimization action plan (RiskMAP) was used when more stringent risk management strategies were needed beyond labeling and reporting requirements. The multiple sclerosis and Crohn's disease therapy Tysabri (natalizumab), for example, has a RiskMAP because of patients' risk of acquiring progressive multifocal leukoencephalopathy, a potentially fatal viral infection of the brain.

In 2005, the FDA issued guidance for RiskMAPs, much of which is similar to the issued REMS guidance as well as future REMS documents, according to the FDA. The REMS guidance notes that unless new safety information on an approved drug comes out, the RiskMAP guidance will still apply to products with an existing RiskMAP, as well as to drugs approved under ANDAs whose reference product has a RiskMAP. ANDAs that have a reference drug with a REMS likewise will be required to have a REMS with the same elements as the reference drug's.

Companies can voluntarily submit a REMS if they think it necessary, and those REMS will be subject to the same requirements as an FDA-required REMS.

The document offers guidance on the following:

- ◆ **Format and content of proposed REMS**, including supporting documentation;
- ◆ **Content of assessments and proposed modifications** of REMS already approved;
- ◆ **Identifiers to use on REMS documents**; and
- ◆ **Communications with the FDA about a REMS.**

The FDA noted that it will issue additional REMS guidance documents, but it did not give a timeline.

FDA Means Business With Penalties

While the requirements for a REMS may seem onerous at first blush, this approach could allow a drug onto the marketplace when it might otherwise have posed too great of a safety risk without a REMS. The guidance is pretty much "what we really know already," says Nick Calla, vice president of trade relations for Walgreens Specialty Pharmacy. But there are some noteworthy aspects of it.

For one, the noncompliance penalties "give the FDA a lot of power" to enforce a REMS, says Steve Russek, chief clinical officer of Accredo Health Group, a Medco

Health Solutions, Inc. subsidiary. The guidance proposes a minimum fine of \$250,000 per violation, up to \$1 million in a single proceeding for a person who violates a REMS requirement. If the violation continues for more than 30 days after FDA notification of the violation, the penalties double and then "continue to double for subsequent 30-day periods, up to \$1 million per period and \$10 million per proceeding," says the guidance. "I think we will see penalties handed out, and they'll be significant," says Calla.

The guidance also says that a REMS must state one or more overall goals of the program. "REMS goals should target the achievement of particular health outcomes or knowledge related to known safety risks and should be stated in a way that aims to achieve maximum risk reduction," it explains. Companies should "assume we need to measure everything," says Craig Kephart, president and CEO of Centric Health Resources, Inc. This means they'll need a way to quantify whether patients and physicians understand the information given to them, he says.

The guidance also gives a timetable for companies to submit assessment data. "Each timetable for submission of assessments of a REMS must at a minimum include assessments submitted by 18 months and by 3 years after the REMS is initially approved, and in the 7th year after the REMS is initially approved, with additional dates if more frequent assessments are necessary to ensure that the benefits of the drug continue to outweigh the risks," it says. "I'm glad to see this is not just a safety program with no one assessing" any outcomes, says Russek.

"This seems well thought out," he says. "The elements of the guidance...give the industry the flexibility to work with the FDA. Different elements are brought into use depending on the drug." Because the manufacturer is responsible for a lot of documentation, "a specialty pharmacy becomes an important partner," he adds (see story, p. 6).

The guidance was published in the Oct. 1 *Federal Register*, and comments are due by Dec. 30. View the proposed guidance at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM184128.pdf. View the RiskMAP guidance at www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM071616.pdf. View a list of approved REMS at www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111350.htm. Contact Kephart at (866) 849-4481, Calla at (412) 325-6507 and Russek through Ann Smith at (201) 269-5984. ✦