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Coronary Stents Placed on India's NLEM — Are Price Controls Next?

It's ironic that at the same time India is separating out medical device regulations from pharmaceutical regulations for the first time, it will now place coronary stents on its national drug list.

The move will mean the stents will likely also fall under price controls.

After numerous meetings with stent manufacturers, cardiologists and NGOs, a government committee created in 2011 concluded that the stents are essential, and thus should appear on the National List of Essential Medicines.

The decision to put the stents on the national list was not made lightly.

Experts overwhelmingly concurred that coronary stents are reliant on constant research and development, and as such, the move to

(See **Stents**, *Page 2)*

Medicare Moving Toward UDI Acceptance for Billing

In a policy turn-about, Medicare is recommending that unique device identifiers be included in medical billing records.

Earlier this year, lawmakers had pushed the Centers for Medicare & Medicaid Services to work with the FDA to incorporate unique device identifiers into insurance claims forms, saying it would improve postmarket surveillance and curb waste.

CMS and the FDA now appear to be on the same page with that messaging. In a recent letter to the Accredited Standards Committee X12, CMS Acting Administrator Andrew Slavitt and FDA Commissioner Robert Califf urged the committee to revisit its business requirements to support capturing UDI on claim forms for high-risk devices.

Califf and Slavitt highlighted the benefits of collecting device identifiers for postmarketing safety, which would also "help

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place them under price controls should be carefully considered.

Committee members also questioned whether the quality of domestic stents could be reasonably assured. It also considered the prevalence of cardiovascular disease in the country and the percentage of patients receiving coronary stents. In making its decision, the committee considered evidence for efficacy among different types of coronary stents.

Infrastructure Needed

Experts stressed that a proper infrastructure needed to be in place for stents, such as a catheter lab and interventional cardiologists, and more investment would be required for manufacturing, distribution, follow up and training. Overwhelmingly, they agreed that the same regulatory approach given for drugs was not appropriate for the devices.

However, at the time the committee was considering the move, devices were regulated as drugs. Since that time, the government released a new framework that will see devices regulated separately. It remains to be seen if devices would have a separate essential list in the country (*IDDM*, July 8).

The committee reported that in India, the coronary stent itself represents roughly 25 percent to 40 percent of the total cost of percutaneous interventions and implantations. It stressed that patients would not benefit unless the cost of the procedure is also reduced.

Accessability and affordability remains a key concern, with patients paying out of pocket for roughly 41.38 percent of the stent procedures. The government picks up 42.8 percent, and private insurance only accounts for 17.75 percent of the cost.

Cardiovascular disease is the leading cause of morbidity and mortality in India and accounts for one-fourth of deaths.

In 2015, roughly 473,000 coronary stents were implanted in patients, and 95 percent of those were drug-eluting stents.

The committee concluded that drug-eluting stents have better efficacy, safety and performance compared to bare metal stents. "However, there is no definite superiority among currently available metallic drug-eluting stents in terms of their clinical outcomes of mortality and myocardial infarction," the report said.

It recommended that authorities differentiate between bare metal stents and drug eluting stents on the NLEM for pricing purposes. Drug-eluting stents should be classified according to the "quality of traits," the committee said.

To read the committee report, visit: www.fdanews.com/07-21-16-Indiastents.pdf.
— Tamra Sami

FDA Green Lights Medtronic's Artificial Cervical Disc

The FDA approved Medtronic's Prestige LP cervical disc for treating nerve or spinal cord compression between the C3-C7 segments of the neck.

The Prestige LP disc is designed to allow motion in the neck at the operated levels, unlike a fusion surgery that does not preserve motion.

The Prestige LP Disc is the first artificial disc on the U.S. market that showed to be superior for both one- and two-level procedures in clinical trials in almost 400 patients.

The Prestige LP patient group demonstrated superiority in overall success compared to patients treated with a two-level anterior cervical discectomy and fusion. Overall success was measured by a neck disability index, absence of serious, device-related adverse events, and absence of secondary surgeries.

The Prestige LP Disc has a ball-and-trough design and allows full range of motions.

Lax Production Processes Result In Warning Letter for Oscor

Failure to control its production processes and to validate them properly landed devicemaker Oscor an FDA warning letter for quality system deficiencies.

The June 13 letter cites the Palm Harbor, Fla.-based company for failing to develop, conduct, control and monitor production processes to ensure devices conform to specifications.

The inspector was critical of the firm's ethylene oxide (EO) sterilization process for its Maestro rechargeable system, a neuromodulator for obesity, noting that using the single lot release didn't provide sterility assurance. The firm's records didn't identify and record the quantity of samples at the appropriate stage of manufacturing, the letter said.

During the inspection, an employee told the FDA that the firm didn't maintain a controlled record documenting which device serial numbers are sterilized in each cycle for single batch release.

Sampling Not Representative

"The document provided to our investigator records product samples selected for single lot release testing did not include product samples for [certain lots.] The agency concluded that not all products representing the sterilization lot had been sampled for single lot release, even though the process control records were allocated for single lot release testing.

In addition, process control records didn't demonstrate that the operating temperature specification was met during the vacuum test phase for a sterilization run. The FDA indicated that the firm's response to revise the parameters for the operating temperature to ambient would not likely be adequate, particularly since the company didn't define "ambient temperature."

The letter notes that the firm's response that the OEM is directly involved in conducting and documenting EO sterilization processing was inadequate because the firm didn't provide documentation. Moreover, the firm did not have an explanation for a document provided to the inspector that lacked an approval signature and date.

Process control records were also found lacking for Oscor's Adelante Magnum catheters because the documents didn't describe the coating process.

The FDA also cited the firm for failure to validate a process. For example, the firm's process verification documentation for manufacturing the anterior and posterior leads of the Maestro system did not identify equipment operating parameters.

The agency said the firm "failed to validate or establish sufficient inspections or tests for the silicone injection over-molding process used for the electrodes." The FDA found the firm's response inadequate because it didn't provide supporting documentation identifying equipment operating parameters for the silicone injection over-molding process, the de-flashing process and the inspection process.

Validation activities fell short for the UV curing process for the Adelante Magnum device, the letter said. The firm's specifications indicated a cure time for the device but didn't specify appropriate UV intensity to achieve a full cure.

Procedures for in-process and final inspections only required a visual inspection for foreign matter, discoloration or flaky surfaces, and the letter said the procedure lacked adequate physical properties, specifications and testing, such as "adhesion, hardness, thickness, coefficient of friction, to support the quality of the cure."

Finally, the agency said the firm failed to establish and maintain procedures to control environmental conditions. For example Oscor didn't monitor environmental conditions such as temperature and humidity in cleanrooms for the Adelante Magnum device.

The firm did not respond to a request for comment. Read the warning letter here: www.fdanews.com/07-19-16-Oscarwarningletter.pdf. — Tamra Sami

CMS, *from Page 1*

providers and certain payers to calculate and compare total costs and outcomes based on the device model used," the letter urged.

The move would also "support program integrity" by providing better information to link the patient and device.

"CMS and FDA are hopeful that ASC X12 can complete its work on the next version of the claims form," the letter said.

The next version of the form is slated to be revised in December. The duo said they would work to assist the standards committee to develop a consensus-based standard that would capture UDIs.

The FDA is also stressing the importance of incorporating UDI into a national surveillance system for medical devices to gain maximum leverage.

Real-World Evidence

The future national medical device evaluation system — one of CDRH's 2016-2017 strategic priorities — is intended to capture and use real-world evidence to bolster regulatory decision-making.

As envisioned, the coordinating center would create opportunities for better evidence generation and sharing with a network of partners (*IDDM*, April 8).

In a recent JAMA editorial, which was posted to the CDRH website July 19, Califf and CDRH Director Jeffrey Shuren stressed that clinicians routinely under report adverse events, and that a more strategic approach to linking clinical registries, electronic health records and claims data, could reduce the burdens of obtaining appropriate evidence across the life cycle of a device.

By leveraging clinical data and applying advanced analytics, they said, a more "comprehensive and accurate framework could be created for assessing the risks and benefits of devices."

Stakeholders have also recommended developing a virtual system for evidence generation by "creating strategic alliances among data sources including registries, EHRs, payer claims, and other sources; incorporating unique device identifiers (UDIs) over time; and activating multiple linkages among data sources to address specific questions," the editorial said.
— Tamra Sami

Medtronic Issues Alerts For DBS Pocket Adaptors

Medtronic Australasia, in consultation with Australia's Therapeutic Good Administration, issued a hazard alert for two models of its Neuromodulation Deep Brain Stimulation system pocket adaptors in Australia.

The pocket adaptors (model numbers 64001 and 64002) are used with Activa PC and Activa RC neurostimulators.

Globally, 16 Medtronic Neuromodulation DBS system pocket adaptors have been returned due to high impedance, resulting in decreased current being conducted through the device.

Some of the reported cases involved loss of therapy, return of symptoms, rebound effects and potential revision surgery to replace the device. There have been no incidents reported in Australia.

Analysis of the returned devices found the cause of the high impedance to be conductor wire fractures near where the wire exits the neurostimulator connector block.

In two cases, the issue was identified during implantation surgery, while the other 14 were identified after implantation and resulted in revision surgery.

DBS devices are implantable, programmable devices that deliver electrical stimulation to the patient's brain. The devices are used to treat symptoms associated with movement disorders such as epilepsy and Parkinson's disease.

Q&A: How to Effectively Manage Medical Device Complaints

Any complaint involving alleged failure of a device, its labeling or its packaging must be investigated.

Due to new guidance, these records must now include the unique device identification and the unique product code, Ombu Enterprises President Dan O'Leary said during a recent FDAnews webinar. The following Q&A with O'Leary was excerpted from the webinar:

Question: *Must the unique device identifier number be listed as part of the complaint file, or is it acceptable to reference the location of the UDI number, such as the label?*

Answer: The requirement is that the complaint file contain specific information, and it could either be written in the file or you can point to it. But the problem is that if you point to the label then, depending upon how you set up your UDI, the label may change with every lot. The device identifier portion may stay constant, but the date of manufacture, the lot number, and the serial number are going to change dynamically. And so you would have to point to exactly the correct label. That's probably not going to work unless you can point to the unique label that's represented in your system. But if you can do that, then a pointer would be acceptable.

Q: *What happens if at the date of a complaint no information has been provided that alleges that a complaint may be reportable but the information is provided 10 days later? Which date is valid for reporting purposes?*

A: It's going to be the date you become aware. What typically happens is that the FDA investigator is going to say that you have 30 days in order to make your initial report, and the 30-day clock is going to start when you receive the complaint. But it may be that you become aware after the investigation, so you would need to document the date when you became aware, and then that's when the clock starts. And then you have 30 days in order to submit.

I recommend that you don't take the full 30 days. Because now you're submitting eMDRs, and you've got to go through the gateway, which means if the system goes down or there's a hiccup, you're going to have to troubleshoot that.

Q: *What other feedback sources should be considered for postmarket risk management besides complaints?*

A: When you get a complaint you know about your devices, but it can be helpful to know what your competitors are up to. You can go to the FDA's website and access Total Product Life Cycle reports, and you can analyze the complaint codes that are showing up in MDRs.

You want to analyze any recalls to see whether or not the reason that somebody else has initiated a recall could apply to your company. The TPLC report is full of hyperlinks, so you can see how often certain problem codes are occuring. It's sorted so that the most frequent occurrences are at the top. From those hyperlinks you can get to any individual MDR report or any individual recall report. So, that's probably the most powerful source.

Q: *How important is it that manufacturers institute the UDI system for traceability?*

A: Requirements for the manufacturer are that you have to include it on all your labels, and that's part of labeling inspection. It's included in the device history record, the master device record and all of the complaint files. And it's included in any corrections or removals reports that you make. So, what this means is that UDI as a manufacturer is going to hit all of those systems, and you are supposed to have them all implemented.

This means that if you have information in an old system you're going to have to create fields to hold that information, and those fields are then going to be part of a software package that gets validated. A lot of companies are finding this to be a relatively large task. But FDA investigators are going to start checking, particularly after Sept. 24, for Class II devices.

CAPA, Validation Found Lacking at Canada's RS Medical

Vancouver-based RS Medical was handed a 483 following a February inspection that found CAPA procedures and validation activities lacking. The company manufactures electrotherapy pain products.

The FDA found that only four out of 11 CAPA records from January 2014 to February 2016 were reviewed. One CAPA was opened "to address a systemic lack of understanding regarding storage requirements for rechargeable batteries" used in electrical nerve stimulation devices, the 483 says.

An action plan included revisions for material handling and storage and preservation, but it did not include charging requirements for the rechargeable batteries. In addition, the CAPA was closed but it didn't include a verification check that the procedures were effective.

The 483 also cited the firm for not documenting software validation activities associated with the quality system.

Inspectors also found fault with the firm's document control procedures and training activities. For example, changes to the device master record for the RS-41 Plus sequential stimulator were not approved through the document control procedures.

In addition, inspectors observed that the firm's training activities lacked appropriate documentation. The firm's SOP stipulates that new employees are assigned training by the department supervisor based on their responsibilities and that the training be completed in a timely manner.

But during the inspection, the investigator discovered that training records were dated the same day as the inspection for a quality assurance technician whose responsibilities include receiving, inspecting, quality testing and initiating out-of-specification reports.

RS Medical did not respond to a request for comment. Read the Form 483 here: www.fdanews.com/07-21-16-RSMedical483.pdf.
— Tamra Sami

Transatlantic Treaty Annex Highlights Global UDIs, Standards

American and European regulators are moving toward more regulatory convergence under the newest iteration of the Transatlantic Trade Investment partnership.

The FDA and its European counterparts have worked closely together over the years to hammer out international standards and to share data amongst themselves.

That effort appears to be paying off. A new annex on medical devices supports international efforts to establish a globally accepted unique device identification system for devices.

The annex lays out principles and objectives that focus to promote convergence of technical and clinical requirements for medical devices. The agreements would remove unnecessary duplications of data submissions and device testing and manufacturing site inspections.

Standards play a key role in the convergence process, and the agreement calls for recognition of international organizations such as the International Medical Devices Regulators Forum (IMDRF) , the International Organisation for Standardisation (ISO) and the Global Medical Device Nomenclature.

Both sides are expected to participate in developing scientific and technical guidelines for regulating devices in IMDRF. Cooperation is expected to result in more international standards, guidelines and joint initiatives.

FDA noted that EU counterparts also acknowledged the importance of the Medical Device Single Audit Program, and the EC would continue to coordinate and support efforts in EU member states.

Read the TTIP device annex here: www.fdanews.com/07-19-16-TTPdeviceannex.pdf. — Tamra Sami

FDA Holds Public Workshop on Third-Party Refurbishing of Devices

The FDA is holding a public workshop Oct. 27 to Oct. 28 to discuss stakeholder input on refurbishing and reconditioning medical devices by third parties.

The agency had sought public comments on the challenges third-party entities face in maintaining or restoring devices to their original or current specifications.

The FDA said the request for comments was prompted by stakeholder concerns that some third-party entities may use unqualified personnel to perform service, maintenance, refurbishment and device alterations on their equipment and that the work may not be adequately documented (*IDDM*, March 4).

The agency received 73 comments on the docket. The issue has been a contentious one among original equipment manufacturers and companies that service and refurbish equipment.

For example, the International Association of Medical Equipment Remarketers and Servicers said in its comments that if there is a lack of uniform performance, it is likely due to the OEM's failure to supply the remanufacturer with required information.

The ECRI Institute said in its comments that an extensive search of its internal databases as well as the FDA's Manufacturer and User Device Experience database, revealed no compelling evidence "that a safety problem exists with the servicing, maintenance and repair of devices by either third-party organizations or OEMS."

Siemens said in its comments that it believed all parties in the supply chain should be governed by quality system regulations under 21 CFR 820.200. Under current regs, the OEM is responsible for QSR compliance.

The FDA hopes to establish working definitions for third-party and original equipment manufacturer activities at the workshop. It also plans to identify best practices and to discuss alternative methods to mitigate risks associated with activities performed by third parties.

For more information, visit: www.fdanews.com/07-21-16-FDArefurbworkshop.pdf. — Tamra Sami

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FDA Holds NGS Webinars

The FDA will host two webinars on July 27 to provide details on its guidances on next-generation sequencing technologies.

The draft guidances are part of President Obama's Precision Medicine Initiative, which aims to take advantage of genomic testing to accelerate the development of new personalized treatments.

The agency released two complementary draft guidances earlier this month that set a foundation for a flexible regulatory pathway for genomic tests. The pathway streamlines submission and review of data supporting clinical validity of NGS-based in vitro diagnostics (*IDDM*, July 15). For information on how to register, visit: www.fdanews.com/07-21-16-NGSwebinars.pdf.

FDA Seeks Patient Feedback

The FDA's Center for Devices and Radiological Health is hosting an Aug. 1 workshop to solicit feedback from patients about their experiences with neurostimulation devices.

The workshop will explore patient experiences regarding the usability, benefits, and desired features of assistive and neurostimulation devices associated used to treat diabetes, macular degeneration and neurological diseases. For information, visit: www.fdanews.com/07-21-16-FDApatientworkshop.pdf.

BMS Launches Orencia Combo Product

Bristol-Myers Squibb launched its combination Orencia ClickJect for adults with moderate to severe rheumatoid arthritis. The Orencia auto injector delivers 125 mg subcutaneously via push button operation and injection confirmation, which may reduce user errors.

Orencia is the only RA biologic that offers three administration options: IV infusion, prefilled syringe and Autoinjector.

WHO Prequalifies Alere HIV Test

Alere's HIV combo test received World Health Organization prequalification status. The fourth-generation test detects both HIV-1/2 antibodies and the HIV-1 p24 antigen. The WHO prequalification status means it will be available for public sector procurement in poorer nations.

Essential Medicine Gains CE Mark

Essential Medicine's Manta gained CE Mark clearance in the European Union.

The large bore vascular closure device improves access site management for large-bore interventions. It is designed to close punctures after cardiac catheterization procedures.

Closure of large bore femoral access sites has been associated with significant morbidity including long times to achieve hemostasis, extended procedure time, need for a vascular surgeon in the catheterization lab, delayed ambulation, higher rate of complications and higher total cost of care.

FDA Approves Celt ACD

The FDA granted premarket approval to Irish devicemaker Vasorum's vascular closure device Celt ACD. The single-use device for closing femoral artery punctures comes in three sizes. It can be used in both diagnostic procedures and for interventional cardiology and radiology procedures.

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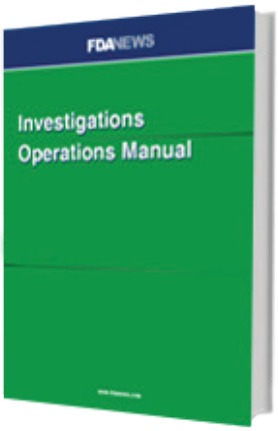

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