If it ain't broke, what are we trying to fix? Reprocessing devices labeled “for single use only”

The FDA wants to regulate the reprocessing of single-use devices

With little fanfare, the hospitals and doctors' offices of America just got saddled with an extra layer of Federal bureaucracy, the people who pay for health care got hit with massive extra expense, and the companies that make health care equipment stand to make a lot more money. At issue are devices that physicians and hospitals have traditionally reprocessed (cleaned, tested, and sterilized) for further service.

On August 2, 2000, the Food and Drug Administration (FDA) released a guidance document that proposes to regulate the reprocessing of single-use devices as “remanufacturing.” It will subject hospitals that reprocess these devices, as well as third-party reprocessors, to the same regulatory standards that the original manufacturers of the devices must meet, including premarket testing.

This is the government's response to scary claims by some consumer advocates and device manufacturers that reuse of devices labeled “for single use only” constitutes a threat to public health and safety.

The FDA and the General Accounting Office (GAO), in their own analyses, found this charge to be without foundation. Nevertheless, the FDA, at the urging of Congress, decided to regulate anyway because the perception that there could be a risk might undermine public confidence in our health care system.

- REASONS FOR THE SINGLE-USE LABEL

Why would the device manufacturers suddenly start labeling devices as “single-use only?” Several reasons come to mind.

Economics. A precipitating event in this controversy was a relatively recent practice by manufacturers to relabel devices (such as surgical saw blades) from multiple use to single use only. Hospitals continued to reprocess these devices just as they always had. Furthermore, if a device that has previously been used safely up to five times (especially an expensive one, such as a lumenless cardiac electrophysiology mapping catheter or a radiofrequency ablation catheter) now can only be used once, the manufacturer can sell five times as many catheters and make five times as much money. Not a bad day's work for just adding a phrase to the label.

Product liability. If an injured party can successfully sue the deep-pocketed manufacturer of a product used in a medical procedure that caused an injury, that's scary, especially since the manufacturer has no control over what happens to the product once it is shipped to the hospital or physician who purchased it.

Safety. Some devices cannot be adequately cleaned without damaging them to the point of unreliability. For example, certain gastrointestinal biopsy forceps don't work as well after cleaning and sterilization, and some studies suggest that they really can't be adequately cleaned. On the other hand, many devices can be safely reprocessed and reused.

- WHY SHOULD WE CARE?

The GAO acknowledged in their recent report that there is no evidence that reprocessing of single-use devices is a threat to public health. One thing neither the GAO nor
the FDA included in their respective reports is a recommendation for the development of criteria for application of the "single-use only" label. Why should providers or anyone else care?

**It is wasteful.** Hospitals and physicians are currently operating under strong mandates to eliminate unnecessary costs from their procedures and practices. It is clearly wasteful to discard an expensive piece of equipment that can be safely and economically reused. When the cost of using a serviceable, safe, reprocessed item is less than the cost of using a new one, why would we not want to do this? Cost-effectiveness is one of the linchpins of health care reform, and we must continue to increase it.

**It will consume resources better directed toward quality improvement.** Maintenance and improvement of quality are the hallmarks of modern health care. Current initiatives throughout the system to track and prevent errors are a part of this, and providers must keep the pressure on to assure that there are resources to beef up these efforts.

Such initiatives provide the data which prove the safety of current reprocessing methods, and we should not consume the valuable resources that fuel this process by arbitrarily driving up the expenses associated with clinical practice.

**It will generate more medical waste.** Recycling is one of the cornerstones of modern waste management. Medical waste is a particularly nasty byproduct of the health care system, for which nearly every practical method of disposal has come under serious criticism. A better solution is to reduce the generation of waste through recycling.

**It is not necessary.** As the GAO report on reprocessing confirmed, there is no evidence that reprocessing and reuse of single-use devices, as it is now practiced, has produced any significant problems.

Even new devices occasionally fail, and nothing suggests that reprocessed devices fail at a greater rate than new ones. Infection from inadequately sterilized devices is a theoretical problem that has not been encountered in practice. So why institute a process that will definitely add cost but cannot improve quality?

**FDA RULING WAS A COMPROMISE**

The involvement of the FDA came about in an attempt to find a compromise between banning the reuse of single-use devices vs doing nothing in response to the issues raised by the device manufacturers. On the face of it, this makes sense, because the focus of FDA oversight would be on patient safety rather than on economic benefits for the manufacturers. Reprocessing, whether by hospitals or third-party reprocessing companies, would be permitted, but it would only be allowed to occur under strict FDA supervision. There are several reasons why this compromise is not optimal.

**These devices are not really remanufactured.** To refer to the process of cleaning, testing, and resterilization by the term "remanufacturing," as the FDA does, is more than a little pretentious, not to mention misleading. Throughout modern history, hospitals have been and remain in the business of resterilizing equipment used in the operating room and elsewhere, and this is not at issue. It is only understandable in the context of what the FDA wants to require of those who reprocess equipment marked, arbitrarily in many cases, "for single use only." The proposed requirements are essentially the same as those posed to the original manufacturers, including premarket testing, etc.

Furthermore, the FDA has classified the reprocessed equipment to be overseen into minimal (class I), intermediate (class II), and high (class III) risk. Included in the class II category are blood pressure cuffs. On the face of it, this seems ludicrous, and the whole business could use a dose of common sense.

**No evidence there is a problem.** If there is no problem (as confirmed by the GAO), how will we know if the FDA process has been successful? If after a few years there have been no infections, for example, is someone going to claim that the FDA’s oversight process is responsible for that?

**New bureaucracy.** The FDA is restricting its initial oversight to hospitals and third-party reprocessors. They acknowledge that many of the same activities they plan to regulate also take place in physicians’ offices, but...
they do not as yet have the manpower to deal with these settings.\textsuperscript{1} You can bet they will correct that as quickly as they can.

\textbf{Additional burdensome regulation}. Hospitals and physicians' offices already carry a heavy regulatory burden. They get inspected by multiple federal and state agencies as well as by accrediting organizations, such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) and the National Committee on Quality Assurance (NCQA). If there were a way to combine some of these inspections, that would at least be somewhat helpful.

\textbf{Conflicting message.} The government has a hard time getting agreement among its various departments and agencies as to what they really expect of health care providers, and many conflicting messages and initiatives, not all of which are clearly articulated, keep pouring forth. Are we supposed to be cost-effective or to avoid any activity that might have the nefarious purpose of saving money? Are we supposed to protect the environment or load it up with perhaps five times the amount of waste we now generate?

\textbf{HOSPITALS, OFFICES WILL HAVE TO CHOOSE}

It seems pretty clear that, at least for the present, hospitals that currently reprocess certain equipment will have some choices to make. If they wish to continue reprocessing, they will need to gear up to meet the new FDA requirements. The other choices are to stop doing the procedures altogether (unacceptable), use the equipment only once and discard it (expensive and wasteful), or to send out the used equipment to third-party reprocessors. While none of these options is particularly attractive, the last one may be the least of the evils for hospitals. The best option for individual physicians' offices, when it comes to that, is less clear. Cost and turnaround time (especially for expensive equipment) are the main problems with the last option, and hospitals will need to carefully consider the relative importance of these and other factors in making their decisions.

\section*{REFERENCES}

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Brief Summary
NORVASC® (amlodipine besylate) Tablets

For Oral Use

CONTRAINDICATIONS: NORVASC is contraindicated in patients with known sensitivity to amlodipine.

WARNING: Increased Angina and/or Myocardial Ischemia: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

PRECAUTIONS: General: Since the vasodilatation induced by NORVASC is gradual in onset, acute hypotension has rarely been reported after oral administration of NORVASC. Nonetheless, caution should be exercised when administering NORVASC as any other peripheral vasodilator particularly in patients with severe aortic stenosis.

Use in Patients with Congestive Heart Failure: In general, calcium channel blockers should be used with caution in patients with heart failure. NORVASC (5-10 mg/day) has been studied in a placebo-controlled trial of 1153 patients with NYHA Class III or IV heart failure on stable doses of ACE inhibitors, beta-blockers, digoxin, and diuretics. Follow-up was for 6 months, with a mean of about 14 months. There was no overall adverse effect on survival or cardiac morbidity (as defined by life-threatening arrhythmia, acute myocardial infarction, or hospitalization for worsened heart failure). NORVASC has been used in elderly patients aged 65 and over in 6-12 week studies of patients with NYHA Class III heart failure, involving a total of 697 patients. In these studies, there was no evidence of worsened heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or LVEF.

Beta-Blocker Withdrawal: NORVASC is not a beta-blocker and therefore gives no protection against the consequences of abrupt beta-blocker withdrawal. Any such withdrawal should be by gradual reduction of the dose of beta-blocker.

Patients with Hepatic Failure: Since NORVASC is extensively metabolized by the liver and the plasma elimination half-life (1.5-3) is 56 hours in patients with impaired hepatic function, caution should be exercised when administering NORVASC to patients with severe hepatic impairment.

Drug Interactions: In vitro data in human plasma indicate that NORVASC has no effect on the protein binding of drugs tested (digoxin, phenytoin, warfarin, and indomethacin). Special studies have indicated that there is no significant effect of NORVASC with digoxin on digoxin levels in patients on maintenance doses of digoxin given under normal renal clearance in normal volunteers; that co-administration with cimetidine did not alter the pharmacokinetics of amlodipine; and that co-administration with warfarin did not change the warfarin prothrombin response time.

In clinical trials, NORVASC has been safely administered with thiazide diuretics, diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.

Drug/Laboratory Test Interactions: None known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Rats and mice treated with amlodipine in the diet for two years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg/kg showed no evidence of carcinogenicity. The highest dose (for mice, similar to, and for rats twice) the maximum recommended clinical dose of 10 mg on a mg/m² basis) was close to the maximum tolerated dose for mice but not for rats.

Mutagenicity studies revealed no drug-related effects at either the gene or chromosomal levels.

There was no effect on the fertility of rats treated with amlodipine (males for 64 days and females 14 days prior to mating) at doses up to 10 mg/kg/day (8 times the maximum recommended human dose of 10 mg on a mg/m² basis).

Pregnancy Category C: No evidence of teratogenicity or other embryotoxic/fetal toxicity was found when pregnant rats or rabbits were treated orally with up to 10 mg amlodipine (respectively 8 times and 23 times) the maximum recommended human dose of 10 mg on a mg/m² basis) during their respective periods of major organogenesis. However, litter size was significantly decreased (by about 50%) and the number of intrauterine deaths was significantly increased (about 5-fold) in rats administered 10 mg amlodipine for 14 days before mating and throughout mating and gestation. Amlodipine has been shown to prolong both the gestation period and the duration of labor in rats at this dose. However, there are no adequate and well-controlled studies in pregnant women. Amlodipine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether amlodipine is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while NORVASC is administered.

Pediatric Use: Safety and effectiveness of NORVASC in children have not been established.

ADVERSE REACTIONS: NORVASC has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with NORVASC was well-tolerated at doses up to 10 mg/day. Most adverse reactions reported during the clinical trials were of mild or moderate severity and were not considered drug related.

For several adverse experiences that appear to be drug and dose related, there was a greater incidence in women than men associated with amlodipine treatment as follows: edema (5.6% in men, 14.4% in women, compared with a placebo incidence in men of 1.4% and 5.1% in women); flushing (1.5% in men, 4.5% in women, compared with a placebo incidence of 0.3% in men and 0.5% in women); palpitations (1.4% in men, 3.3% in women, compared with a placebo incidence of 0.9% in men and 3.9% in women); and somnolence (1.3% in men, 1.6% in women, compared with a placebo incidence of 0.8% in men and 1.6% in women).

The following events occurred in ≤1% but >0.1% of patients in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain; they are listed in the following table (peripheral vascular adverse reaction incidence of NORVASC: dry mouth, sweating increased; metabolic and nutritional; hyperglycemia, thirst; hemopoietic: leukopenia, purpura, thrombocytopenia).

The following events occurred in ≤0.1% of patients: cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dermatis, muscle weakness, twitching, ataxia, hypertonia, migraine, cold and clammy skin, apathy, agitation, anemia, gastritis, increased appetite, loose stools, coughing, rhinitis, dysuria, polyuria, paroxysm, taste perversion, abnormal visual accommodation, and xerophthalmia.

Other reactions occurred sporadically and cannot be distinguished from medications or concurrent disease states such as myocardial infarction and angina.

CONTRAINDICATIONS: NORVASC has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, HDL cholesterol, uric acid, blood urea nitrogen, or creatinine.

The following postmarketing event has been reported infrequently where a causal relationship is uncertain: gingival hyperplasia, allergic reaction, asthma, back pain, hot flushes, malaise, pain, rigors, weight gain; musculoskeletal system: arthralgia, arthrosis, muscle cramps; alimentary: nausea, vomiting, gingival hyperplasia; general: allergic reaction, asthma:** back pain, hot flushes, malaise, pain, rigors, weight gain; musculoskeletal system: arthralgia, arthrosis, muscle cramps; psychiatric: sexual dysfunction (male** and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization; respiratory system: dyspnea,** esthesia; skin and appendages: angioedema, erythema multiforme, pruritus,** rash,** rash erythematous, rash maculopapular; special senses: abnormal vision, conjunctivitis, diplopia, eye pain, blindness; urinary system: infection frequency, infection duration, incontinence, autonomic nervous system: dry mouth, sweating increased; metabolic and nutritional: hyperglycemia, thirst; hemopoietic: leukopenia, purpura, thrombocytopenia.

OVERDOSAGE: Single oral doses of 40 mg/kg and 100 mg/kg in mice and rats, respectively, caused death. A single oral dose of 4 mg/kg or higher in dogs caused a marked peripheral vasodilatation and hypotension.

Overdose might be expected to cause excessive peripheral vasodilatation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional oversedation of NORVASC in limited. Reports of intentional overdose include a patient who ingested 250 mg and was asymptomatic and was not hospitalized; another (120 mg) was hospitalized, underwent gastric lavage and remained normotensive; the third (105 mg) was hospitalized and had hypotension (90/50 mmHg) which normalized following plasma exchange. A patient who took 70 mg amlodipine and an unknown quantity of benzodiazepine in a suicide attempt developed shock which was refractory to treatment and died the following day with abnormally high benzodiazepine plasma concentration. A case of accidental drug overdose has been documented in a 10-yr-old male who ingested 30 mg amlodipine (about 2.0 mg/kg). During the emergency room presentation, vital signs were stable with no evidence of hypotension, but a heart rate of 186 bpm. Ipecac was administered 3.5 hours after ingestion and on subsequent observation (overweight) no sequelae noted.

If massive overdose should occur, active cardiac and respiratory monitoring should be instituted.

Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockage. As NORVASC is highly protein bound, hemodialysis is not likely to be of benefit.

* Based on patient weight of 50 kg.

** These events occurred in less than 1% in placebo-controlled trials, but the incidence of these side effects was between 1% and 2% in all multiple dose studies.

More detailed professional information available on request.

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