Italian Law Compelling Off-Label Use May Spread In EU, Worries Pharma

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Executive Summary

Moves by Italian and French lawmakers to compel doctors to prescribe drugs off-label in indications where there are approved medicines available already effectively will bypass the EU’s rigorous regulatory framework and put patients at risk, and pharma warns the trend could spread in the region.

Europe’s biopharma sector has appealed to the European Commission to intervene and force the removal of an Italian law promoting use of medicines beyond their authorized indications because they are less expensive than those authorized in specific indications.

Warning that the Italian legislation threatens health care provision in the region, the European Federation of Pharmaceutical Industries and Associations (EFPIA), the European Confederation of Pharmaceutical Entrepreneurs (EUCOPE) and the European association for Bio-industries (EuropaBio) filed a complaint Jan. 28 to the commission saying that the law will “infringe and undermine” Europe’s marketing authorization system.

The law also goes against a judgment by the European Court of Justice stipulating the EU’s 28 member states may not revert to off-label use as a cost-containment measure in cases where approved alternatives exist.

The Italian law decree, pushed relatively quickly through the National Assembly, came into force May 21 allowing off-label drugs to be reimbursed there by the country’s National Health Service. The decree expanded on previous rules saying drugs could be reimbursed only if they were on a list approved by the national medicines agency, AIFA.

Under the new rules, drugs may be prescribed off-label even if an authorized alternative exists. This empowers the Italian regulatory authority AIFA to assess the safety and efficacy of a given medicine in the off-label indications, taking into account the relative burden of the licensed medicine on the health care system. It also threatens to name and shame drug makers that do not agree with the off-label use of their medicine. Pharmaceutical companies are strictly forbidden from promoting off-label use of their medicines.
“AIFA’s position before this law was enacted was that it would not be acceptable to compel doctors to prescribe less expensive medicines off-label,” noted Richard Bergstrom, director general of EFPIA. “This new law makes things very difficult for the Italian agency: They first apply certain standards for authorization, and here suddenly they have to apply a different one,” he said in an interview.

The Italian law has zeroed in on Novartis AG’s Lucentis (ranibizumab) and Roche’s less expensive Avastin (bevacizumab) for age-related macular degeneration. “This is not about me-too drugs, it’s about different products that might have similar mechanisms of action or in the case of Lucentis which is a fragment of Avastin. Both drugs have been around for some time. And you’ve seen off-label use of Avastin in place of Lucentis in different countries in Europe, but not by decree.”

**Growing Trend In Europe**

A proposed French law to significantly widen off-label use of prescription drugs meanwhile is being pushed through France’s parliament by the country’s left-wing government, putting patient safety at risk, according to the country’s pharmaceutical industry association, LEEM. Similar legislation also is being considered by lawmakers in Denmark.

“Legislative action like this puts us on a slippery slope and represents the thin edge of the wedge for potentially undermining the functioning system here underpinning health care. It poses an unpleasant can-of-worms to all participants,” Bergstrom said.

“Off-label use of medicines should always be limited to individual decisions of the treating physician based on medical needs when patients cannot be treated,” said Alexander Natz, secretary general of EUCOPE. “We have no problem with off-label use where it’s needed such as in oncology, but we should restrict it to where there’s no therapy alternative on the market and not just impose that decision by law,” Natz said in an interview.

The threat this poses to Europe’s regulatory framework and innovation process has prompted EFPIA, EUCOPE and EuropaBio to formally ask the commission to step in.

“We feel pretty confident that the commission will agree with our assessment because we basically stand on two pillars in order to make this innovation system work for the benefit of all – one is the regulatory system, which has for 50 years given Europe clarity and predictability, and this is a huge departure from the model under which we’ve operated for half a century,” Bergstrom said.

Confrontational legislation aimed at drug makers eventually could hurt the end users – patients – if companies take fright and don’t make their cutting-edge medicines available there. It also would be bad for business. “If countries in Europe push through legislation like this, then the region runs the risk of becoming a “no-go” area for companies that look to do business in a predictable fashion. IP and the regulatory process are the needed pillars to do predictable business, “EuropaBio Secretary General Nathalie Moll said.

“The message that this conveys to drug makers is that you don’t need to get your product approved because you can get it used anyway for economic reasons. It makes the situation shaky not just for businesses but also for consumers,” she said in an interview.
Moves Against High Prices

There are other trends in Europe that worry the pharma sector, not least a growing reaction against high-priced drugs. The French non-governmental organization Médecins du Monde is stimulating a debate in France and other countries about the affordability of high-priced medicines like sofosbuvir and has opposed a company’s European patent to make its point ("Opposition to Gilead’s Sovaldi Patents And Price Spreads In Europe" — "The Pink Sheet" DAILY, Feb. 10, 2015).

“I understand that people get concerned about the high prices of some of these breakthrough drugs – but the answer isn’t silly legislation that undermines the system; rather what’s needed is governments and payers need to sit down with pharma companies and talk things over and try to find a middle ground,” Bergstrom said.

“There’s no reason to break the system using irrational measures. Keep patent protection and agreed regulatory pathways in place and use tools to inform and guide us in negotiations such as relative-effectiveness assessments, cost-effectiveness assessments and that way we’ll preserve the innovation system.”