# Misoprostol drug to be withdrawn from French market

**Misoprostol drug Cytotec will be pulled from the French market on March 1, 2018, after reported adverse effects of off-label use. Barbara Casassus reports from Paris.**

Pfizer will withdraw the antigastric and duodenal ulcer drug Cytotec (misoprostol) from the French market next March 1. This follows a number of reports of serious side-effects from off-label use of the drug to induce childbirth and medical abortions.

The French branch of the US pharmaceutical manufacturer did not explain why it is taking the drug off the market in France or whether it plans to do the same elsewhere. The company takes its "decisions on a case-by-case basis" and "made [this] decision for France in full agreement with the ANSM [the French National Agency for Medicines and Health Products Safety]", a company spokesperson said in an email to *The Lancet*. They added that misoprostol is sold in 79 countries, but refused to disclose any sales figures.

The ANSM issued warnings about the gynaecological risks of Cytotec in 2005 and 2013, and the French National Authority for Health, an independent advisory body on health regulation, issued recommendations along similar lines in 2008 and 2015. The problem is that "doctors ignored [all of them]", says ANSM Director General Dominique Martin.

94% of Cytotec prescriptions in France are off label, says Alain-Michel Ceretti, president of France Assos Santé, an umbrella organisation for 75 French patients associations with more than 3 million members. Alternatives to Cytotec exist on the French market—the intravaginal drug Propess (dinoprostone) for inducing delivery, and GyMiso and MisoOne (both misoprostol) for medical abortions.

Ceretti, who has access to all the agency's data as the patients associations' representative on the ANSM administrative board, states that "money is clearly the only concern" for not prescribing the Cytotec alternatives more widely. The official price setting body factored 36€ into the 190€ fee that is charged by non-hospital doctors for medical abortions and is reimbursed by the French public health system. Cytotec costs 0·64€, whereas GyMiso, for instance, costs 36€. Ceretti says that this means that "doctors can pocket the difference".

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In many cases, practitioners have opted for vaginal, rather than oral, administration of Cytotec. This is "debatable" as the drug is indicated for oral use only, Martin told reporters on Oct 20. Known side-effects for use of Cytotec include a ruptured uterus and haemorraging for the mothers, and cardiovascular and neurodegenerative disease for their babies. Three babies are known to have died.

One issue is that the 200 µg Cytotec tablets have to be split into eight identical sections to obtain the 25 µg dose for labour induction, which means "there is a risk of overdose", says Martin. He adds that off-label prescriptions increase the risk of side-effects by 50%, but that under French law, the agency "cannot police practices […] we cannot ban what is not permitted".

For Ceretti, this is "like saying the police cannot fine drivers for speeding when they drive faster than the permitted limit". He is urging the government to make off-label prescriptions an offence when the ANSM has clearly established that a drug is dangerous if used for any purpose other than that for which it is authorised. He is also calling for Health Minister Agnès Buzyn to ask the Social Affairs General Inspectorate to investigate the Cytotec case. "About 22% of childbirths in France are induced, and I am extremely sceptical about which drugs hospitals use", Ceretti says. The Health Ministry did not respond to *The Lancet*'s request for comment.

In December, 2016, the Versailles Administrative Court ordered the Poissy-Saint-Germain Intercommunal Hospital in the Paris region and its insurer Sham to pay compensation to the severely disabled Timéo and his family for having administered an excessive dose of Cytotec and a Syntocinon (oxytocin) drip to his mother Aurélie Joux. The hospital and Sham deny liability and lodged an appeal in March.

The ANSM aims to ensure there are sufficient stocks of alternatives to replace Cytotec when it is no longer available, and to introduce a 25 µg-dosed misoprostol drug for inducing labour called Angusta in 2018, Martin says. Manufactured by Danish pharmaceutical firm Azanta, Angusta was launched in the five Nordic countries—Denmark, Finland, Iceland, Norway, and Sweden—in April, 2017.

The ANSM will hold a meeting on Nov 20 with patients associations, health-care professionals, and academic bodies to discuss any further steps to be taken in the Cytotec case.

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A previous version of this World Report has been retracted, for changes made see appendix