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# Medical care for children living with HIV infection: the US pharmaceutical company BMS must start producing Sustiva® 100mg again!

*The pharmaceutical company Bristol-Meyers Squibb (BMS) markets efavirenz, an anti-HIV antiretroviral drug known as Sustiva® in several countries[1]. BMS admitted in March of this year that the company would stop the distribution of the 100mg paediatric capsule formulation, although this presentation of the drug is particularly well adapted for paediatrics. The HIV NGOs TRT-5[A], EATG[B] and Sidaction[C] condemn this decision which occurs in the context of a very limited number of available paediatric formulations of anti-HIV drugs. The BMS decision also goes against all official recommendations for the medical care of children and especially those living with HIV infection.*

This information was first revealed by several paediatricians (French, English, Spanish and Portuguese in particular) concerned by the ensuing reduction of treatment options for children, and was later confirmed by BMS. Having come under pressure from French[2] and European[3] drug regulatory authorities, BMS says the company is thinking about restarting production of the Sustiva® 100mg capsules. However, the disappearance of the 100mg capsules from pharmacy shelves has already become a reality in several countries. Depending on decisions of local BMS affiliates Sustiva® 100mg stops being supplied when distributor stocks have been exhausted. In fact production of the capsules has already ceased some 18 months ago, without BMS having envisaged consulting or informing neither the medical nor the patient community beforehand. This situation of fait accompli has already produced serious consequences for some of the concerned children who had to change their entire ARV regimen because of drug resistance caused by the sudden unavailability of the 100mg Sustiva® capsules.

The company has thus made the choice to deprive children living with HIV infection and their physicians of a treatment option specifically adapted to them[D]. Medical care for HIV infected children requires adapted formulations of drugs (e.g. liquids, small tablets or capsules, powders). The availability of paediatric formulations of anti-HIV drugs is today very insufficient.

According to BMS, the company decided to stop the production of the 100mg Sustiva® capsules because the volume of prescription does not allow adequate quality levels. Yet, the 100mg capsules contain the same powder used to produce the 50mg and 200mg capsules, simply conditioned into a different capsule size. Furthermore, discussions with the company made it clear that no inventory of the actual prescriptions of Sustiva® 100mg had been carried out prior to the decision and no impact study on other Sustiva® formulations been realized.[E]

Without regard for the children's needs and for the requirements and recommendations for care of these children, BMS has made the choice to stop the production of this drug formulation specifically developed and adapted for paediatric usage, with the sole priority of reducing the costs for quality control in the production of "small" batches. Furthermore BMS had not deemed it necessary to inform the concerned communities beforehand: children living with HIV infection, their families, and their health care professionals.

**TRT-5, the EATG and Sidaction condemn this interruption of availability of Sustiva® 100mg and demand that BMS reconsiders its decision which constitutes a regression in the quality of care for paediatric HIV infection and puts into peril the treatment of many HIV infected children. It is necessary that production is restarted, availability maintained in those countries where it is still available and reinstated in the countries where it has already been withdrawn in utter disregard for the children using it.**

**Otherwise it will be up to governments to decide on a compulsory license, a procedure adopted by the ministerial conference of the World Trade Organization in 2001 and which would provide for the import of a World Health Organization (WHO) certified generic version of the drug (100mg) marketed by the Indian pharmaceutical company Aurobindo.**

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[1] Efavirenz is marketed by BMS under the brandname Sustiva® *in the United States, Canada, the UK, France, Germany, Spain, Italy and the Republic of Ireland. In other countries the drug is marketed by Merck under the brandname Stocrin®.*
[2] AFSSaPS : *Agence française de sécurité sanitaire des produits de santé*, French health products safety agency
[3] EMEA : European medicines agency

**Complementary information:**

**[A] What is TRT-5?**

TRT-5 (Traitements & Recherche Thérapeutique / Treatments & Clinical Research) is a coalition of treatment activists representing eight French Aids/HIV NGOs (Actions Traitements, Act Up, AIDES, ARCAT, Dessine-moi un mouton, Nova Dona, Sida Info Service & Solensi). Created in 1992, it promotes the needs of PLHAs and advocates on their behalf in the areas of clinical research, standard of care, governmental institutions and the pharmaceutical industry.
The coalition's and its member organizations' websites : www.trt-5.org www.actions-traitements.org www.actupparis.org www.aides.org www.arcat-sante.org www.dessinemoiunmouton.org www.sida-info-service.org www.solensi.asso.fr

**[B] What is the EATG?**

Founded in 1991 as a co-operative structure of people from different nationalities, the European AIDS Treatment Group is a growing group of treatment activists from 31 European countries. To secure its impartiality the EATG receives funding from a variety of private and public funders. One of our guiding principles is to reflect the diversity of people living with HIV and their advocates.

**[C] What is Sidaction?**

Sidaction is a French NGO whose objective is to develop programmes for the fight against HIV/Aids. It is the most important private provider of support for the fight against HIV/Aids in France and it is the only French NGO providing financial support for scientific and medical research. In addition to its activities in favour of prevention projects and support for PLHAs in France, Sidaction provides support to more than sixty organisations in 29 developing countries. These interventions concern, for some of them, projects which aim to improve care for children with HIV infection, as is the case for the project "Grandir" (Growing up) set up in collaboration with Initiative Développement, SolenSi and with the support of the French Ministry of Foreign Affairs.

**[D] Why is the disappearance of Sustiva® 100mg problematic for the care of children with HIV infection?**

Over and above the problems created by the shocking failure of BMS communicating beforehand, the disappearance of this drug formulation poses other serious problems:
Among the different existing formulations of Sustiva®**, the 100mg capsule is the one which is most suited for paediatric usage as it is the optimal compromise between capsule size and dosage.**

- The 600mg tablets and the 200mg capsules are bigger in size than the 100mg capsules and thus pose more problems with swallowing.
- The liquid version is more problematic both to conserve and to administer. Its taste is a problem for some children and it has a lower biovailability than the capsule formulations.
- The 50mg capsules containing half as much of the drug, their usage means a doubling of the number of capsules to be taken by the children each time.

Example: a child with a weight of 22kg taking 300mg of efavirenz each day:

- If he/she is able to swallow the 200mg capsule: instead of one 200mg capsule and one 100mg capsule, he/she will have to swallow one 200mg and two 50mg capsules each time.
- If he/she is unable to swallow the 200mg capsule: instead of taking three 100mg capsules, he/she will have to use six 50mg capsules each time.

These formulations, when used in situations in which they are not adapted cause difficulties : difficulties of ingestion for the liquid form or the bigger tablets and capsules, big number of capsules to be swallowed for the smallest ones. These difficulties will have consequences on adherence to treatment, while it has a major imput on its efficacy.
The suppression of this formulation goes against the European rules on paediatrics, effective since January 2007 with the objective of easing clinical development of new paediatric drugs. It also is contrary to the recommendations issued in February 2008, of the American "Paediatric guidelines", demanding adapted paediatric formulations for all ARVs. Finally, it is also contrary to the French guidelines for care & treatment of people living with HIV, insisting on the necessity of "inciting the pharmaceutical industry to continue to search for formulations adapted to children."

**[E] What are the consequences of BMS lack of interest for prescription and consummation of its drug?**

This lack of interest for the real use of Sustiva® 100mg not only is the sign of a unacceptable thoughtlessness from BMS when taking this decision. Neither the consummation in the concerned countries, nor the needs in the other formulations that would follow the disappearance of 100mg were evaluated by the company. The consequence was stock exhaustion of the 50mg capsules as well in some places. This absence of consideration for the consequences of the 100mg capsules withdrawal even caused treatment discontinuations, with subsequent appearance of resistance, and, at the end of the day, a necessary complete change of treatment.