Re: Rifapentine (Addition) – EML and EMLc

Dear Expert Committee:

We are writing to express our strong support for the addition of rifapentine to the World Health Organization Model List of Essential Medicines for adults (EML) and children (EMLc). As an agent with the potential to shorten therapy for drug-sensitive TB (DS-TB) and latent tuberculosis infection (LTBI), rifapentine will play an increasingly important role in country efforts to achieve the ambitious targets set forth in the WHO’s post-2015 Global TB Strategy, endorsed by Member States at the 67th World Health Assembly in May 2014.

We write as members of the Community Research Advisors Group (CRAG), an international, community-based advisory body that works to ensure the meaningful participation and engagement of TB-affected communities in research conducted by the U.S. Centers for Disease Control and Prevention’s (CDC) Tuberculosis Trials Consortium (TBTC). The TBTC conducted Study 26, the phase III trial that established the safety and efficacy of using rifapentine together with isoniazid—the so-called 3HP regimen—to treat LTBI. Rifapentine’s use for treating TB infection was recently approved by a stringent regulatory authority (the U.S. FDA) in November 2014. Through our advisory capacity to the TBTC, we have participated in the development of rifapentine for nearly a decade. This letter reflects our longstanding experience evaluating the place of rifapentine in TB treatment from the perspective of TB-affected communities.

The publication of the first-ever WHO Guidelines on the Management of Latent Tuberculosis Infection makes this an important moment to add rifapentine to the EML and EMLc. The Guidelines include the 3HP regimen as one of the recommended regimens for treating LTBI, and many countries may prefer its 3-month duration to the 6- and 9-month regimens of daily isoniazid (6H and 9H) that the Guidelines panel judged equivalent. Access to rifapentine for LTBI treatment will be especially important to the 33 countries and territories covered by the WHO’s TB Elimination Action Framework for Low-Incidence Countries. In TB high burden countries, rifapentine’s potential to shorten LTBI treatment could make therapy easier to tolerate and complete for high-risk populations including children.

Available clinical evidence also supports the addition of rifapentine to the EMLc. In the application before the Committee, the WHO notes that an extension of TBTC Study 26 enrolled 1058 children between the ages of 2 and 17 years old, which not only confirmed the safety and tolerability of 3HP in children, but also provided evidence of efficacy consistent with
the main TBTC Study 26 population of adults. Sanofi, the manufacturer of rifapentine, is
developing pediatric-friendly formulations of 3HP—including a water-dispersible, fixed-dose
tablet (isoniazid 150mg/rifapentine 150mg) and a water-dispersible, stand-alone tablet
(rifapentine 100mg)—to allow for simple dosing adjustments in younger children. TBTC Study
35 will evaluate the pharmacokinetics and safety of the rifapentine/isoniazid fixed-dose
combination in children 0–12 years old, lending further evidence to the safety of rifapentine’s
use in pediatric regimens.

In 2015, the TBTC will initiate a phase III study to evaluate whether rifapentine can shorten the
duration of DS-TB treatment from six months to four months when used as either a substitute
for rifampicin or in combination with moxifloxacin in substitution for ethambutol. Should this
trial demonstrate the safety and efficacy of a 4-month rifapentine-containing regimen for DS-
TB, ensuring that countries are prepared to access rifapentine will become even more
imperative for achieving the goals of the WHO’s Global TB Strategy. Including rifapentine on
the EML and EMLc will lay the groundwork for facilitating greater access in the future.

We draw your Committee’s attention to the public financing that has underwritten the majority
of studies of rifapentine. Developed through a series public-private partnerships between
Sanofi and research groups in the US, UK and South Africa, rifapentine has the potential to
become a true “public health good,” and its introduction as a treatment-shortening therapy for
LTBI in the US has sparked robust civil society- and patient-led advocacy to ensure the drug’s
affordability. A coalition of stakeholders from academic institutions, non-governmental
organizations, public health programs and patient groups successfully advocated for Sanofi to
lower the price of rifapentine from US $71/32-tablet blister pack to US $32/32-tablet blister
pack under 340b public health service pricing. This 51% price reduction is greater than the
historic 20% reduction of the HIV drug azidothymidine (AZT) by Burroughs Wellcome in 1989
and makes rifapentine a more affordable treatment option for US TB programs.

A cost-effectiveness analysis conducted after the price reduction found that, at the lower price,
using 3HP instead of 9H to treat LTBI is cost-saving. The 3HP regimen has the potential to
offer even greater cost-savings if on-going research by the TBTC shows that the regimen can be
safety self-administered by patients. Under patient self-administration, U.S. TB programs would
save $141 per individual treated by switching from 9H to 3HP. From a societal perspective,
switching to 3HP would save the U.S. economy $231 per individual treated over a 20-year
period. U.S. TB programs have already begun to switch to rifapentine-based 3HP, and the U.S.
Federal Bureau of Prisons recently announced that it is now using the 3HP regimen in place of
9H as its preferred option for treating LTBI.

While the price of rifapentine outside of the U.S. remains unknown—as the drug has not yet
been registered in other countries—the successful price reduction in the U.S. signals that Sanofi
is willing to negotiate on price. Additionally, the U.S. price should set a ceiling price for the sale
of rifapentine globally, according to the tiered pricing framework Sanofi uses to set drug prices
across high-, middle- and low-income countries.

We are keenly aware that access to rifapentine outside of the United States remains limited by
the drug’s lack of registration with regulatory authorities other than the U.S. FDA. However, we
agree with the statement in the application submitted by WHO that adding rifapentine to the
EML and EMLc will “greatly widen access to the drug by soliciting and possibly encouraging
the manufacturer of RPT to submit approval applications to all relevant regulatory authorities
world-wide.” Our recent communications with Sanofi suggest that the company has already taken steps to register rifapentine in additional countries including South Africa, Peru and Brazil. The addition of rifapentine to the EML and EMLc would encourage moves toward wider registration by sparking greater demand for the drug from national TB programs and country governments.

Given the strong clinical evidence of safety and efficacy, coupled with the manufacturer’s willingness to work with civil society and governments on affordability, we encourage your Committee to add rifapentine to the EML and EMLc. We welcome the opportunity to discuss this issue further and ask that you please contact Laia Ruiz Mingote (rmingotelaia@gmail.com) with questions or future communications.

Sincerely,

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