Cryoprecipitate should not be the essential medicine recommended by the WHO to treat hemophilia

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Dear Editor,

In their commentary in Blood Transfusion, Epstein and colleagues[1] justify the inclusion of pathogen reduced and native cryoprecipitate on the WHO essential medicines list for the treatment of hemophilia A[2]. The WHO recommendation seems to ignore the enormous progress in hemophilia treatments over the last 30 years, the prices that can be achieved with tendering for FVIII concentrate, and most importantly the continued potential for transfusion transmitted infections especially HIV, hepatitis B and hepatitis C by native cryoprecipitate.

The authors state that "The use of native cryoprecipitate in these areas (*low and lower-middle income countries*) carries unacceptable risks due to the prevalence of these infections in blood donors, suboptimal donation testing, and the additive infectious risks from repeated exposures to products prepared from small plasma pools". Yet despite this, they end up agreeing with the inclusion of this product on the essential medicines list for use when pathogen reduced cryoprecipitate is not available.

We accept that the commentary argues that pathogen reduced cryoprecipitate is safer than the native product, and do not dispute that implementation of the technology to produce it is desirable. However, the essential medicines list should not be about what will be desirable in the future because the reality is that, as far as we know, only two LIC/LMIC countries (Egypt and Thailand) have the product available today. The result is that for the vast majority of LIC/LMIC that rely on the essential medicines list to guide their procurement, only native cryoprecipitate is available to treat hemophilia A.

Cryoprecipitate, whether native or pathogen reduced, has many limitations besides the infection risk. It requires frozen storage at –20°C, must be administered at a medical facility and contains relatively low levels of FVIII. In contrast FVIII concentrate can be stored at room temperature, provides significantly higher amounts of clotting factor per vial, and can be administered at the patient's home. In practice, low dose prophylaxis to prevent bleeding in hemophilia is achieved using concentrate rather than cryoprecipitate.

Our final comment concerns the area of expertise of those who advise the WHO in this specific area. The guidance has largely come from individuals working in Blood Transfusion rather than hemophilia treatment. As hemophilia treaters, we believe that the WHO essential medicines list product for the treatment of hemophilia should be FVIII concentrate, as native cryoprecipitate is unsafe and should have no role in

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the current treatment of the disease. By prioritizing a secure plasma derivative for which there are now multiple alternatives which are increasingly available in many LIC/LMIC[3], the WHO jeopardizes access to innovative therapies.

DECLARATION OF INTERESTS

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