Removal of non-pathogen reduced cryoprecipitate from the EML and EMLc

Background:

In 2023, the Expert Committee considered an application from the International Society of Blood Transfusion for the addition of pathogen-reduced cryoprecipitate (cryoprecipitate-PR) to the EML and EMLc for replacement of coagulation factors in cases of massive haemorrhage, von Willebrand disease and deficiency of coagulation factor XIII, and as a therapeutic alternative to coagulation factor VIII for treatment of haemophilia A in settings where coagulation factor VIII is not available or affordable. Listing was proposed as a 'square box' listing for cryoprecipitate-PR, with non-pathogen reduced cryoprecipitate specified as a therapeutic alternative.

A copy of the application is available here.

2023 Expert Committee recommendation:

"The Expert Committee recognized that insufficient access to clotting factor replacement products contributes to early death in patients with bleeding disorders. Accessibility to these products is especially problematic in low- and middle-income countries where many patients have no access to treatment.

The Committee considered that the evidence and extensive clinical experience suggest that cryoprecipitate is superior to plasma for replacement of certain clotting fctors in a variety of indications in adults and children. However, the Expert Committee noted that concentrated clotting factors remain the preferred treatment for many bleeding disorders and should be prioritized for selection and use wherever possible. The Committee noted and agreed with the WHO Blood Regulatory Network position statement and emphasized that cryoprecipitate-PR ought only to be used in settings where commercial clotting factors are unaffordable or unavailable. The Committee was not in the position to recommend specific methods of pathogen reduction but considered that cryoprecipitate-PR developed using validated, approved pathogen-reduction methods should be ensured.

The Committee also noted that comparative evidence for cryoprecipitate-PR versus non-pathogen-reduced cryoprecipitate was limited but acknowledged that pathogen reduction can eliminate major risks of transmission of bloodborne infectious agents and increase the safety of administration. While there is a risk of alloimmunization and allergic transfusion reaction, these adverse events are lower than rates reported for other blood components, including fresh frozen plasma.

The Expert Committee therefore recommended the inclusion of cryoprecipitate-PR on the core list of the EML and EMLc for use in the replacement of coagulation factors in cases of massive haemorrhage, von Willebrand disease and deficiency of coagulation factor XIII. It may also be used as an alternative to coagulation factor VIII concentrate for patients with haemophilia A in settings where this product is unavailable of unaffordable. The Committee also recommended that non-pathogen-reduced cryoprecipitate be included in the Model Lists as a therapeutic alternative given that transition to cryoprecipitate-PR at the country level may take some time. The Committee acknowledged that solvent and detergent virus inactivation technologies and medical devices used in the plasma fractionation

industry are gaining momentum and are being adopted by an increasing number of blood establishments and national blood service centres. For this reason, the Committee considered that removal of non-pathogen-reduced cryoprecipitate from the Model Lists as a therapeutic alternative to cryoprecipitate-PR should be considered at the earliest opportunity (i.e. 2025) unless an application is received to support its retention.

The Committee emphasized the requirement that all blood, blood components and plasma derivates used as essential medicines should comply with WHO requirements developed by the WHO Expert Committee on Biological Standardization. The Committee also emphasized that blood donor and donation screening for infections before use of blood products should always be implemented."

(WHO Technical Report Series No. 1049. Report of the WHO Expert Committee on Selection and Use of Essential Medicines, 2023)

EML Secretariat advice for the 2025 Expert Committee:

The 2025 Expert Committee is respectfully advised that the recommendation of the 2023 Expert Committee relating to the removal of non-pathogen-reduced cryoprecipitate from the Model Lists should not be ratified without discussion because of submissions received relating to this matter, specifically:

- C.1 Cryoprecipitate – plasma-derived Factor VIII concentrates – plasma-derived Factor IX complex – changes to listings (submitted by the World Federation of Hemophilia)
- M.1a Non-pathogen-reduced cryoprecipitate – retention (submitted by the International Society of Blood Transfusion)

The attention of the Expert Committee is also drawn to any comments received regarding this matter during the public consultation period.

The 2025 Expert Committee is therefore advised that a recommendation in relation to the current listing of non-pathogen-reduced cryoprecipitate should be made following full consideration and discussion of the above-mentioned submissions and any additional comments received.