

MEMORANDUM



Department of Health and Human Services
Public Health Service
United States Food and Drug Administration
Center for Biologics Evaluation and Research



Pharmacology / Toxicology Review

To: File (STN 125351/0)

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Through: Susan Abbondanzo, M.D., Deputy Director, Hematology/OBRR

Subject: Filing of STN 125351/0 for Nycomed’s BLA for Fibrin Sealant Patch (TachoSil™)

This memorandum summarizes the preliminary review of BLA for TachoSil, Fibrin Sealant Patch, indicated as an adjunct for surgery (cardiovascular -----(b)(4)-----) indicated to improve haemostasis. Based on the pharmacological and toxicological data presented, the BLA 125351 TachoSil would be fileable based on preliminary review of pre-clinical data and completeness of previously recommended pre-clinical studies in conjunction with current on-going clinical studies and experience.

I. Background

Nycomed, Denmark has created a equine-derived collagen fibrin sealant patch (proposed trade name TachoSil) containing thrombin and fibrinogen proposed for indication as 1) -----(b)(4)----- 2) adjunct to hemostasis in cardiovascular surgery. TachoSil, or TachoComb S, is a modified third generation fibrin sealant adjunct is being processed for improvement of hemostasis -----(b)(4)----- with local application to wounds surfaces following ineffective control of bleeding after conventional surgical techniques. TachoSil was derived for elimination of bovine aprotinin, a protease inhibitor to prevent transmissible bovine diseases to humans and theoretical possibility of immunogenic reactions. Predecessors of TachoSil have been in use for several years in Europe including TachoComb H, Tachotop and TachoComb with the similar indications for treatment.

II. Proposed Use and Doses

TachoSil will be administered as an adjunct postoperative as prescribed by clinician in three sizes: mini, standard and midi.

III. Key Findings and Conclusion

There may be safety concerns regarding this product that will have to be addressed:

- An immunogenicity strategy following administration with product
- Safety concerns following repeat administration and multiple dosing with product prior to complete absorption of product.
- Sufficiency of pre-clinical pharmacokinetic studies to address absorption of product (single and repeat use)