

**Division Director Memo**  
**Division of Clinical Evaluation and Pharmacology/Toxicology**  
**Office of Tissues and Advanced Therapies**

<b>APPLICATION:</b>	BLA 125700	<b>TRADE NAME:</b>	ADSTILADRIN
<b>APPLICANT/SPONSOR:</b>	FKD Therapeutics Oy	<b>ESTABLISHED NAME:</b>	Nadofaragene firadenovec
<b>CBER RECEIVED DATE</b>	9/3/2019		
<b>PDUFA DATE</b>	4/3/20	<b>PRODUCT CLASS:</b>	
<b>REVIEW DATE:</b>	4/16/20	<b>ROUTE:</b>	Intravesical administration

**INDICATION:** Treatment of high grade, Bacillus Calmette-Guérin (BCG) unresponsive non-muscle invasive bladder cancer.

**Review Team**

**Clinical:** Drs. Laronna Colbert, Yuxia Jia, Daniel Suzman, Ke Liu, Paul Kluetz; **Statistical:** Dr. Jiang Hu  
**Pharm/Tox:** Dr. Ying Huang; **Clin Pharm:** Xiaofei Wang; **CMC:** Dr. Ramjay Vatsan

**REVIEW SUMMARY:**

FKD Therapeutics Oy submitted this original BLA to seek marketing approval for ADSTILADRIN for the treatment of high grade, Bacillus Calmette-Guérin (BCG) unresponsive non-muscle invasive bladder cancer. The clinical review was conducted in conjunction with Oncology Center of Excellence, with a recommendation of full approval. However, due to significant CMC concerns, a Complete Response Letter will be submitted to the Applicant.

Efficacy determination was based on a single-arm trial in subjects with high-grade, BCG-unresponsive non-muscle invasive bladder cancer (NMIBC). A total of 107 subjects were enrolled, of which 103 were considered BCG-unresponsive, the intended study population. The primary efficacy outcome measures were Complete Response (CR) and durability of CR. The CR rate of 53.4% (95% CI: 43, 63%) was associated with a median duration of response of 9.7 months (95% CI: 9.9, 13.9 months), which is considered to confer a meaningful clinical benefit in this patient population.

The most common adverse reactions ( $\geq 10\%$ ) in subjects who received ADSTILADRIN were instillation site discharge, bladder spasm, micturition urgency, dysuria, fatigue, fever and chills. There were no deaths in the study.

The benefit risk profile for ADSTILADRIN for the proposed indication is favorable; however, there were significant CMC issues that preclude approval.

Please see primary reviews from the clinical/OCE and statistical reviewers for details of the review. I concur with the OCE/clinical review team's recommendation of Approval and conclude that the Applicant has provided substantial evidence of effectiveness and safety from an adequate and well controlled study to support the proposed indication. However, due to CMC issues, a Complete CR will be sent to the sponsor. Please refer to CMC review memo for details.

**RECOMMENDED REGULATORY ACTION:**

**COMPLETE RESPONSE (FOR CMC ISSUES)**

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