

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**201739Orig1s000**

**SUMMARY REVIEW**

## Division Memorandum Addendum

<b>Date</b>	July 31, 2012
<b>From</b>	Susan Limb, MD, Clinical Team Leader, Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
<b>Through</b>	Badrul Chowdhury, MD, PhD, Division Director, DPARP
<b>NDA/BLA #</b>	NDA 201739
<b>Applicant</b>	Intelliject
<b>Date of Submission</b>	May 7, 2012
<b>PDUFA Goal Date</b>	November 7, 2012
<b>Proprietary Name / Established (USAN) names</b>	Epinephrine
<b>Dosage forms / Strength</b>	Epinephrine auto-injector 0.15 mg and 0.3 mg (epinephrine injection USP 1:1000)
<b>Proposed Indication(s)</b>	1. Emergency treatment of allergic reactions including anaphylaxis
<b>Recommended:</b>	Approval

### 1. Executive Summary

Intelliject submitted a 505(b)(2) new drug application (NDA 201739) on September 9, 2010, for a new drug-device combination product, epinephrine auto-injector 0.15 mg and 0.3 mg (epinephrine injection USP 1:1000). The epinephrine auto-injector (EAI) is proposed for the emergency treatment of allergic reactions including anaphylaxis. The application received a Tentative Approval on July 29, 2011, contingent on resolution of a patent infringement suit. The Applicant subsequently submitted a Stipulated Order of Dismissal dated February 16, 2012, to address the patent issue and to support the final approval of the product. Therefore, the recommended action for this application is now Approval.

The Division Memorandum dated June 6, 2012, provided an interval update since the Tentative Approval and summarized the basis for the recommended regulatory action. The June 6, 2012, memorandum noted that the proposed tradename, "e-cue," had been found acceptable by the Division of Medication Error Prevention and Analysis (DMEPA). However, since that time, DMEPA has raised new concerns regarding the proposed tradename. DMEPA has cited a potential for confusion between e-cue and Preque, a prescription prenatal vitamin which is currently marketed unapproved. The Applicant submitted the alternative tradename, "Auvi-Q," which was found to be acceptable by DMEPA and the Division. The Applicant subsequently submitted revised labeling with the new tradename. No other issues are identified at this time, and the recommended regulatory action is Approval.

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/s/  
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SUSAN L LIMB  
08/06/2012

BADRUL A CHOWDHURY  
08/06/2012  
I concur

## Division Memorandum

<b>Date</b>	June 7, 2012
<b>From</b>	Susan Limb, MD, Clinical Team Leader, Division of Pulmonary, Allergy, and Rheumatology Products (DPARP)
<b>Through</b>	Badrul Chowdhury, MD, PhD, Division Director, DPARP
<b>NDA/BLA #</b>	NDA 201739
<b>Applicant</b>	Intelliject
<b>Date of Submission</b>	May 7, 2012
<b>PDUFA Goal Date</b>	November 7, 2012
<b>Proprietary Name / Established (USAN) names</b>	e-cue/epinephrine
<b>Dosage forms / Strength</b>	Epinephrine auto-injector 0.15 mg and 0.3 mg (epinephrine injection USP 1:1000)
<b>Proposed Indication(s)</b>	1. Emergency treatment of allergic reactions including anaphylaxis
<b>Recommended:</b>	Approval

### 1. Executive Summary

Intelliject submitted a 505(b)(2) new drug application (NDA 201739) on September 9, 2010, for a new drug-device combination product, epinephrine auto-injector 0.15 mg and 0.3 mg (epinephrine injection USP 1:1000). The epinephrine auto-injector (EAI) is proposed for the emergency treatment of allergic reactions including anaphylaxis. The proposed tradename is "e-cue," which has been found acceptable by the Division of Medication Error Prevention and Analysis (DMEPA). The application received a Tentative Approval on July 29, 2011, contingent on resolution of a patent infringement suit. The Applicant subsequently submitted a Stipulated Order of Dismissal dated February 16, 2012, to address the patent issue and to support the final approval of the product. Therefore, the recommended action for this application is now Approval.

The purpose of this memorandum is to provide an interval update since the Tentative Approval and to summarize the basis for the recommended regulatory action. Details of the e-cue product and development program can be found in the Division Director memorandum dated July 29, 2011, the CDTL review dated July 8, 2011, and the primary reviews from the CMC, clinical pharmacology, nonclinical pharmacology/toxicology, and clinical review teams, respectively.

The NDA references NDA 19-430 for EpiPen® Auto-injector 0.3 mg and EpiPen Jr® Auto-injector 0.15 mg. In contrast to the reference product and other approved epinephrine auto-injector products, e-cue has a different shape and design, highlighted by an electronic auditory prompt system that provides real-time, verbal and visual cues to guide the user through the

administration steps of the product. The proposed EAI is not currently marketed anywhere. The clinical development program for e-cue was comprised of a comparative pharmacokinetics trial and three human factor studies. No efficacy and safety trials were conducted for the application. The PK trial, which was not a requirement for the application, demonstrated bioequivalence (BE) between e-cue 0.3 mg and the reference 0.3 mg product using a scaled BE approach, which is an analytic approach that may be applied in situations of high intra- and inter-individual variability. Satisfactory review of the drug constituent and device components, in conjunction with the Agency's prior findings of efficacy and safety for epinephrine in the proposed indication, form the basis of the Approval recommendation for e-cue. Supplementary information from the pharmacokinetic trial provides added support for the recommendation of approval.

As mentioned above, the Applicant was placed on a 30-month-stay during the original review cycle due to a patent infringement suit initiated by Meridian Medical Technologies, claiming infringement of US Patent No. 7,794,432 B2. Section 505(c)(3)(C) of the Act provides that approval of a new drug application submitted pursuant to section 505(b)(2) of the Act shall be made effective immediately, unless an action is brought for infringement of one or more of the patents that were the subject of the Paragraph IV certifications. Therefore, a Tentative Approval was issued on July 29, 2011, noting that final approval could not be granted until expiration of the 30-month period or other court action and assurance that there was no new information that would affect whether final approval should be granted.

The Applicant submitted a Stipulated Order of Dismissal dated February 16, 2012, which provided the required evidence of the resolution of the patent infringement suit. The Applicant also submitted a Complete Response on May 7, 2012, that referenced the Stipulated Order of Dismissal (b) (4)

 No other information was submitted that altered the prior conclusions made regarding the safety and efficacy of the product for the proposed indication.

## 2. Labeling

Unlike the reference product, the labeling for e-cue 0.3 and 0.15 mg is in the PLR format. The Division, in conjunction with consultants from the Office of Surveillance and Epidemiology and CDRH, reviewed labeling during the original review cycle. No new information has been submitted that would impact the previously agreed-upon labeling that was included in the Tentative Approval Letter dated July 29, 2011.

## 3. Recommendations/Risk Benefit Assessment

- Recommended Regulatory Action

The recommended regulatory action is Approval.

- Risk Benefit Assessment

The efficacy and safety e-cue rely on the Agency's previous findings of efficacy and safety for epinephrine in the treatment of allergic reactions and anaphylaxis. The information provided in the application does not alter the known risk benefit profile of epinephrine for the proposed indication, thereby supporting approval of e-cue.

- Recommendation for Postmarketing Risk Evaluation and Management Strategies

No postmarketing risk evaluation and management strategies (REMS) are recommended.

- Recommendation for other Postmarketing Requirements and Commitments

No postmarketing requirements (PMR) and commitments (PMC) are recommended at this time.

- Recommended Comments to Applicant

None.

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/s/  
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SUSAN L LIMB  
06/19/2012

BADRUL A CHOWDHURY  
06/19/2012  
I concur