Human Factors Validation Study for a Wearable, Single-Use Injector

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CONTEXT

- Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, acquired hematologic condition characterized by life-threatening complement-mediated hemolysis (often leading to anemia) and thrombosis[1]
  - Patients with PNH can subsequently develop myeloid malignancies such as myelodysplastic disorders/acute myeloid leukemia2
- Pegcetacoplan is the first targeted complement protein 3 (C3) therapy approved for adults with PNH (US; EMPAVELI®) and adults with PNH plus anemia despite receiving complement protein 5 (C5)-targeted therapy for ≥3 months (EU; ASPAVELI™)[3–5]
  - After proper training in subcutaneous (SC) infusion, a patient or patient's caregiver may self-administer pegcetacoplan (1080 mg twice weekly) with an at-home infusion pump if a health care provider (HCP) determines that it is appropriate[3,4]
- A new, more convenient, wearable, single-use automatic injector with a hidden needle is being evaluated to deliver the approved dose of EMPAVELI® in the abdominal area
- A human factors usability study was completed to validate the safety and effectiveness of the EMPAVELI® injector for the intended users, utilizations, and usage environments

OBJECTIVE

- To validate the safety and effectiveness of the EMPAVELI® wearable, single-use automatic injector device for the intended use in the expected settings

CONCLUSIONS

- This study validated that the EMPAVELI® wearable injector can be used safely and effectively by intended users, including patients, caregivers, and HCPs, for prespecified utilizations in the expected settings
- Any residual risk observed in this study was determined to be acceptable with no additional mitigations required

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Disclosures

Michael Yeh, Hanaa Shahin, Scott Baver, Lawton Laurence, Jessica Savage, and **Dana Korkuch** are employees of Apellis Pharmaceuticals, Inc., and hold stock or stock options.

Abbreviations

C3/5, complement protein 3/5; FDA, US Food and Drug Administration; HCP, health care provider; IFU, instructions for use; KBA, knowledge-based assessment; PNH, paroxysmal nocturnal hemoglobinuria; SC, subcutaneous.

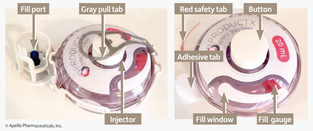
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METHODS

Figure 1. EMPAVELI® wearable, single-use injector device



Participants

- Participants included the intended users of the EMPAVELI® injector: patients, adult caregivers, and HCPs
  - Given the limited number of patients with PNH, patients with anemia (from all causes) were substituted in place of patients with PNH

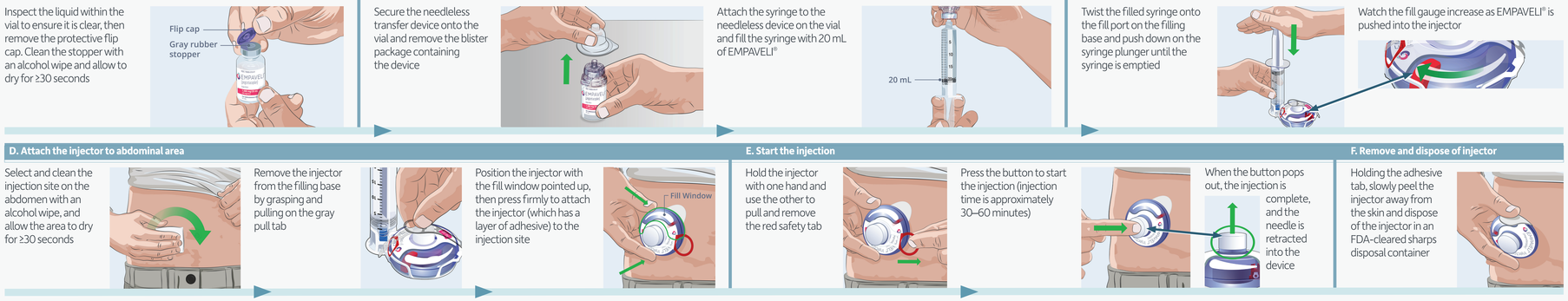
Materials

- Participants were provided an injector device (**Figure 1**), a drug mimic that simulated the appearance of EMPAVELI®, and the necessary ancillary supplies (alcohol wipes, needleless transfer device, sterile 20-mL syringe, and sharps container)

Training and Testing

- Patients and caregivers attended a 2-hour training session from an HCP trainer on the use of the injector and reviewed the instructions for use (IFU; **Figure 2**). A 1-hour learning decay period followed
  - HCPs were not trained but received the IFU
- Participants completed a simulated-use scenario and device placement activity (use test), which tested the participant's ability to correctly place the device, use the ancillary supplies, and deliver the drug mimic into an injection pad (i.e., the intended use of the EMPAVELI® injector)
  - Patients placed the injection pad and device on themselves, whereas caregivers and HCPs placed the device on an injection pad mounted onto a mannequin
  - Critical tasks were defined as tasks that if performed incorrectly or not at all could cause harm including compromising medical care
- Following the use test, participants underwent a critical knowledge-based assessment (KBA) in which they were asked knowledge and comprehension questions
- Observations from the use test and KBA, along with the potential severity of harm associated with use errors or incorrect answers on these assessments, respectively, were recorded
- Following the use test and KBA, participants were interviewed, and a root cause analysis was performed on critical use errors using prespecified root cause categories
- Training and testing were conducted at a testing facility designed to mimic the intended use environments for the EMPAVELI® injector (primarily the home setting, but may also be in a clinical setting)

Figure 2. Brief overview of the EMPAVELI® injector IFU



RESULTS

Table 1. Observed critical use step errors in the use test

Critical use step with use error (involves injector or ancillary supplies)	Highest potential severity of harm	Participant with error	Root cause*				
			Study limitation: participant's behavior was influenced by the nature of the simulated use step versus actual use	Device use is inconsistent with the user's expectations or intuition about device operation†	Lapse: participant forgot to perform or misinterpreted an instruction†	Intentional misuse: participant's behavior was based on personal preference with intentional disregard for instructions provided	IFU organization was not intuitive or clear†
Clean rubber stopper on vial with an alcohol wipe (ancillary supplies)	Infection	HCP (n=1)	X	X			
Remove top cover of the vial adapter package/Do not remove the vial adapter (ancillary supplies)	Infection	HCP (n=1)	X	X			
Remove blister packaging from vial adapter (ancillary supplies)	Infection	HCP (n=2)	X	X			
Remove air from syringe by pushing plunger gently (ancillary supplies)	Air injected (SC emphysema)	Patient (n=1)		X			
Clean site with alcohol wipe (ancillary supplies)	Infection	Caregiver (n=2)	X		X		
		HCP (n=1)	X	X			
Let site dry (ancillary supplies)	Infection	HCP (n=1)			X		
		Patient (n=2)			X		
		Caregiver (n=2)	X			X	
Remove injector from filling base (injector)	Insignificant delay in therapy	HCP (n=1)	X	X			
Remove safety tab (injector)	Insignificant delay in therapy	HCP (n=1)	X	X			
Push button (injector)	Infection	HCP (n=1)	X	X			
Wait for button to pop up (injector)	Infection	HCP (n=1)	X	X			

Errors listed in order of event within the IFU. *More than one root cause could be selected. †Verbiage from FDA Guidance "Applying Human Factors and Usability Engineering to Medical Devices™ was applied to modify this root cause category. Abbreviations: FDA, US Food and Drug Administration; HCP, health care provider; IFU, instructions for use; SC, subcutaneous.

Participants and Use Test Performance

- Overall, 45 participants were included in the study: 15 adults with anemia, 15 caregivers, and 15 HCPs
- Almost all participants (44 of 45; 97.8%) passed the use test (i.e., they were able to correctly place the device and deliver the medication on the first use)
  - One participant, an HCP who did not review the IFU, failed the use test but placed the device correctly after reviewing the IFU
- A total of 17 critical use errors were committed by 9 of 45 (20%) participants, including 3 patients, 4 caregivers, and 2 HCPs, during the use test (**Table 1**)
  - Infection was the most common highest potential severity of harm
- Most critical use errors involved the use of ancillary supplies
  - The one HCP who failed the use test committed 6 of 10 possible critical use errors, including errors with the injector. The root causes reported for these errors were "Study limitation" and "Device use is inconsistent with the user's expectations or intuition about device operation"
- Among patients and caregivers, "Study limitation" and "Lapse" were the most common root causes reported

KBA Performance

- Overall, 6 of 28 critical KBA errors were identified, of which the most common root cause was "IFU organization was not intuitive or clear" (**Table 2**)
- The residual risks posed by the potential use errors were deemed acceptable (i.e., the severity of harm was below the threshold for additional mitigations, and the benefits of the injector outweighed the risk)

Table 2. Observed errors in the KBA

KBA questions with incorrect answers	Highest potential severity of harm with incorrect answers	Participant with error	Root cause
What should you do if the EMPAVELI® injector is exposed to direct sunlight?	Device falls off, needle exposed to third party	HCP (n=1), Caregivers (n=3), and Patients (n=5)	IFU organization was not intuitive or clear
Is it OK to sweat while wearing the EMPAVELI® injector?*		HCPs (n=3) and Caregivers (n=2)	IFU organization was not intuitive or clear
What should you do if the device falls off while it is injecting?		Patients (n=2) and Caregiver (n=1)	IFU organization was not intuitive or clear
Is it ok to sleep while wearing the EMPAVELI® injector?		HCP (n=1)	Lapse; IFU organization was not intuitive or clear
What should you do if the EMPAVELI® injector has been dropped?	Non-sterility	Patients (n=2)	IFU organization was not intuitive or clear
Should the device be stored after filling?	Medical product exposure	Caregiver (n=1)	IFU organization was not intuitive or clear

*Question was flawed and could not be answered as asked. Abbreviations: HCP, health care provider; IFU, instructions for use; KBA, knowledge-based assessment.