Observational Study of the Appropriate Use of the MAP0004 Inhaler and Comprehension of the Accompanying Instructions for Use

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INTRODUCTION

MAP Pharmaceuticals, Inc. is developing MAP0004, an orally inhaled, self-administered therapy intended for the treatment of migraines. MAP0004 utilizes a breath-actuated metered dose inhaler (TEMPO® inhaler, Figure 1) to deliver a novel, preservative-free formulation of dihydroergotamine mesylate. Based on the clinical study results (1), MAP0004 has the potential to provide both fast onset of action and sustained pain relief as well as relief of other migraine symptoms in an easy-to-use and non-invasive at-home therapy. A MAP0004 dose is two inhalations providing a 1.0 mg nominal dose (0.6 mg emitted) with an audible click for each inhalation.

The purpose of this study was to qualitatively and quantitatively assess subject comprehension of the MAP0004 instructions for use (IFU), ease-of-use of the inhaler and ability to successfully execute the steps necessary to deliver a full dose.

METHODS

Study Design

This was an observational study conducted in 85 subjects. The study was divided into 2 sequential arms: the Preliminary (P) arm and the Confirmatory (C) arm. The P arm was conducted with 60 subjects divided into 6 cohorts to improve a draft version of the IFU by assessing the readability and clarity and ease-of-use of the inhaler. The C arm was conducted with 25 subjects to confirm understanding of the final IFU design developed using inputs from the P arm.

Figure 1. Tempo inhaler.

Study Procedure

The study was conducted at multiple geographical locations and was monitored by a Research Study Monitor (RSM). All subjects were given an instruction card (IC), the IFU and an unused TEMPO inhaler which contained no active drug or placebo. Subjects were instructed to read the IC and IFU, and then perform the steps to administer a simulated dose consisting of two successive inhalations. If the subject failed to actuate the inhaler, the RSM would provide the subject verbal assistance or demonstration and assess if the subject could then successfully actuate the inhaler. Study results were recorded on an observation checklist. When it was determined that the subject had finished the task, the RSM proceeded to complete the study questionnaire with the subject verbally. The subjects were asked to provide feedback on the IFU and ease-of-use of the inhaler.

Study Analysis

The preferred method for measuring IFU comprehension and successful outcome is a binomial result, such as pass/fail or yes/no for reporting domains and correct/incorrect or yes/no for individual measures.

RESULTS AND DISCUSSION

The P and C arms had similar demographic distributions (Table 1). A specific effort was made to enroll subjects with a distribution of education and literacy levels, as it was hypothesized that literacy would impact IFU understanding and execution. Both arms had approximately 20% of subjects who had a high school level of education or below. In addition, the recruitment plan was focused on enrollment of subjects with a history of migraine to mirror the typical MAP0004 users. No specific guidance for enrollment was given as to previous inhalation product use.

Table 1.

Study demographics.

Demography		P Arm (N=60)	C Arm (N=25)
Gender	Female	73%	68%
	Male	27%	32%
Education	High School or below	20%	16%
	Some College or Graduate	73%	64%
	Post Graduate	7%	20%
Age	18-29	27%	16%
	30-39	23%	28%
	40-49	47%	52%
	50-59	3%	4%
Race/Ethnicity	Caucasian	60%	72%
	Asian	10%	8%
	African American	12%	12%
	Hispanic	15%	8%
	Other	3%	0%
Migraine History	YES	63%	100%

No apparent difference in the Opinion Rating of the IFU and inhaler was observed between P and C (Table 2) arms. Overall, more than 80% of the subjects agreed or strongly agreed (ratings ≥4 on a 5 point scale) that both instructions in the draft IFU (P arm) and the final IFU (C arm) were clear and easy to follow. Similarly, high ratings were given from subjects in the C arm using the final IFU for the ease of actuating the inhaler (reflected by the subjects obtaining an inhaler "click").

Table 2.

Opinion ratings of the IFU and TEMPO inhaler use (Rating 5=Very, 1=Not at all).

Questionnaire	Arm	5	4	3	2	1
Were instructions clear?	P	52%	28%	15%	5%	0%
	C	56%	32%	12%	0%	0%
Were instructions easy to follow?	P	63%	27%	8%	2%	0%
	C	68%	12%	20%	0%	0%
How easy was it to get the inhaler to click?	P	47%	22%	12%	5%	15%
	C	84%	16%	0%	0%	0%

Based on the observations during the P arm, a revised IFU was developed with modifications made to address the observed instructional limitations with each cohort of subjects. The major changes made from the first draft to the final draft IFU were:

- Inclusion of all 6 steps in picture form
- Modification of font color (to blue) and use of upper case in the text regarding performance of Steps 1-6
- Rewording of the subtitle to "SHAKE, OPEN, INHALE, CLOSE to Use MAP0004" from "To use MAP0004 follow these 4 steps: Shake, Open, Inhale, Close"
- Modification of the font color (to red) of the box "READ THESE INSTRUCTIONS BEFORE YOU BEGIN"

After implementing the above modifications, the rate of subjects successfully actuating the inhaler on the first attempt without any external input increased from 70% (42/ 60) in the P arm to 96% (24/ 25) in the C arm. A single subject in the C arm who initially failed to actuate the inhaler was able to actuate it successfully after receiving verbal instruction. In the C arm, 96% of subjects correctly delivered a full simulated dose (2 clicks) from the TEMPO inhaler (Table 3).

Table 3.

Success rate of subjects administering a dose from the inhaler.

Study Arms	1st Inhalation	2nd Inhalation	Full dose
P	75%	88%	70%
C	96%	100%	96%

CONCLUSION

An iterative process incorporating subject observations and feedback is a critical step in the development of effective instructions for the proper use of metered dose inhalers. Incorporation of subjects' feedback proved useful in improving unaided appropriate use results with MAP0004. This study affirmed the utility of pretesting instructions for use with drug-delivery platform medications intended for self-administration by patients in order to ensure the highest probability of safe and appropriate use. The study has shown that when using an appropriate IFU, 96% of subjects were able to use MAP0004 correctly the first time without any external aid, and 100% of subjects were able to use MAP0004 correctly after simple verbal instruction from a healthcare professional.

REFERENCE

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