

OBSERVATIONAL STUDY OF THE APPROPRIATE USE OF THE MAPO004 INHALER AND COMPREHENSION OF THE ACCOMPANYING INSTRUCTIONS FOR USE

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INTRODUCTION

MAP Pharmaceuticals, Inc. is developing MAPO004, an orally inhaled, self-administered therapy intended for the treatment of migraines. MAPO004 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), MAPO004 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 MAPO004 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 MAPO004 Instructions for Use (IFU, Figure 2), 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 arm and the confirmatory arm. The preliminary 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 confirmatory arm was conducted with 25 subjects to confirm understanding of the final IFU design developed using inputs from the preliminary arm.

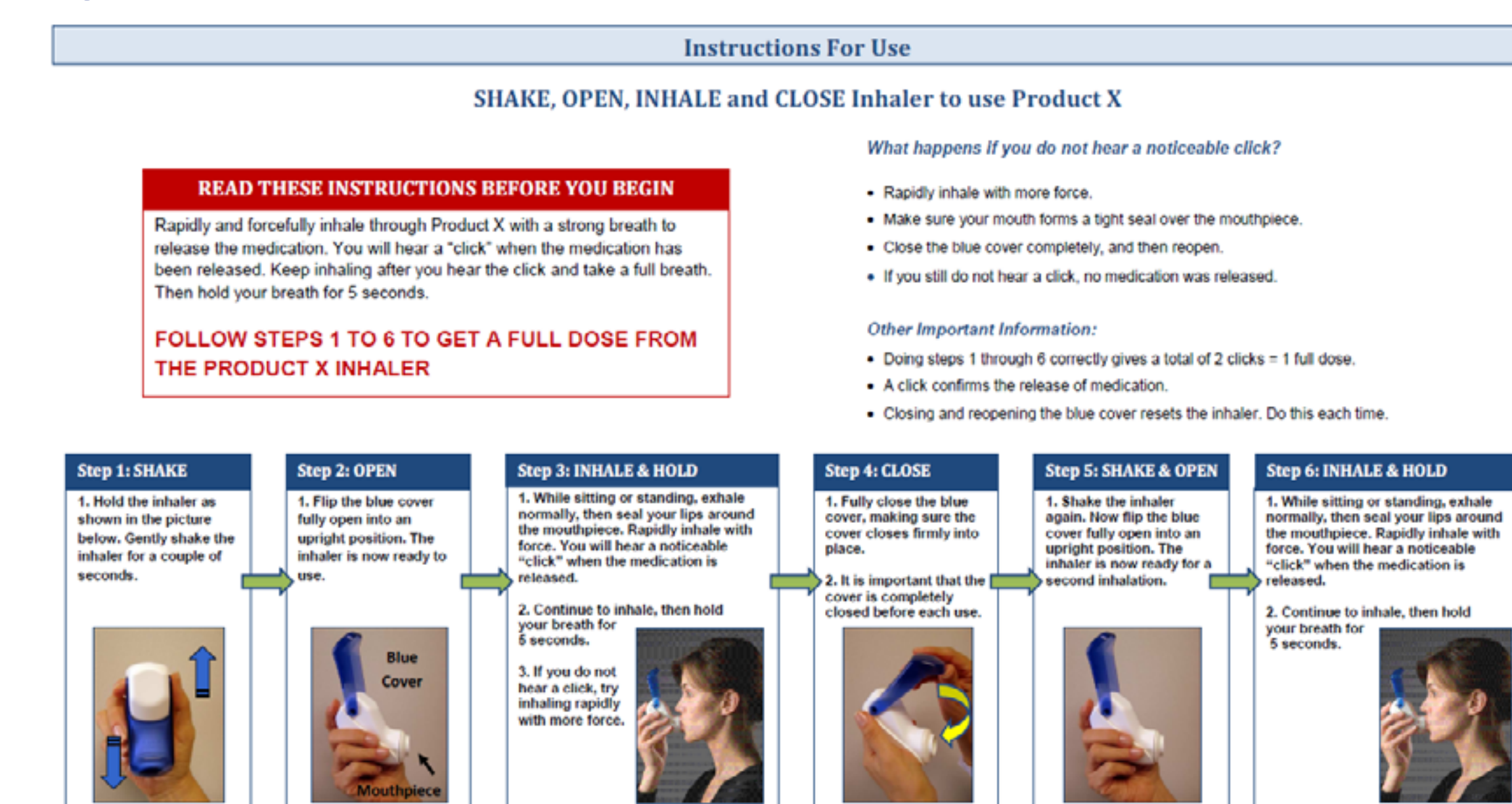
Study Procedure: The study was conducted at multiple geographical locations and was monitored by a Research Study Monitor (RSM). All subjects were given an Instruction Card (IC), the IFU and an unused TEMPO inhaler which contained no active drug or placebo. Subjects were instructed to read the IC and 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.

Figure 1: Tempo Inhaler



Figure 2: IFU



RESULTS AND DISCUSSION

The preliminary and confirmatory arms had similar demography 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 MAPO004 users. No specific guidance for enrollment was given as to previous inhalation product use.

Table 1: Study Demography

DEMOGRAPHY		Preliminary Arm (N=60)	Confirmatory 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 preliminary and confirmatory (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 (preliminary arm) and the final IFU (confirmatory arm) were clear and easy to follow. Similarly high ratings were given from subjects in the confirmatory 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?	Preliminary	52%	28%	15%	5%	0%
	Confirmatory	56%	32%	12%	0%	0%
Were instructions easy to follow?	Preliminary	63%	27%	8%	2%	0%
	Confirmatory	68%	12%	20%	0%	0%
How easy was it to get the inhaler to click?	Preliminary	47%	22%	12%	5%	15%
	Confirmatory	84%	16%	0%	0%	0%

Based on the observations during the preliminary 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 (Figure 2) were:

1. Inclusion of all 6 steps in picture form
2. Modification of font color (to blue) and use of upper case in the text regarding performance of Steps 1-6
3. Rewording of the subtitle to “SHAKE, OPEN, INHALE, CLOSE to Use MAPO004” from “To use MAPO004 follow these 4 steps: Shake, Open, Inhale, Close”
4. Modification of the font color (to red) of the box “READ THESE INSTRUCTIONS BEFORE YOU BEGIN”

RESULTS AND DISCUSSION

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 preliminary arm to 96% (24/ 25) in confirmatory arm. A single subject in the confirmatory arm who initially failed to actuate the inhaler was able to actuate it successfully after receiving verbal instruction. In the confirmatory 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	1 st Inhalation	2 nd Inhalation	Full dose
Preliminary	75%	88%	70%
Confirmatory	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 MAPO004. 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 MAPO004 correctly the first time without any external aid, and 100% of subjects were able to use MAPO004 correctly after simple verbal instruction from a healthcare professional.

REFERENCES

1. Efficacy and tolerability of MAPO004, a novel inhaled therapy, in treating acute migraine. As presented at the 14th Congress of the International Headache Society, September 2009