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Office of Surveillance and Epidemiology

Drug Use Review -- Brief

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Reviewer(s):	Shekhar H. Mehta, PharmD MS Drug Utilization Analyst *Division of Epidemiology II*
Team Leader	Rajdeep Gill, PharmD Drug Utilization Data Analysis Team Leader *Division of Epidemiology II*
Deputy Division Director	LCDR Grace P. Chai, PharmD Deputy Director of Drug Utilization *Division of Epidemiology II*
Drug Name(s):	Oralair, Grastek
Application Type/Number:	BLA 125471; BLA 125473
Submission Number:	multiple
Applicant/sponsor:	Stallergenes; Merck
OSE RCM #:	2017-570; 2017-572

****This document contains proprietary drug use data obtained by FDA under contract. The drug use data/information cannot be released to the public/non-FDA personnel without contractor approval obtained through the FDA/CDER Office of Surveillance and Epidemiology.****

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1 INTRODUCTION

The Division of Epidemiology in CBER's Office of Biostatistics and Epidemiology (OBE/DE) consulted the Office of Surveillance and Epidemiology of CDER for drug utilization information on Grastek and Oralair for the upcoming pediatric advisory committee (PAC) meeting scheduled for September 2017. Drug Utilization in CDER provides, via this review, a single consolidated review for both products GRASTEK (timothy grass pollen allergen extract, and ORALAIR (Sweet Vernal, Orchard, Perennial Rye, Timothy, and Kentucky Blue Grass Mixed Pollens Allergen Extract). OBE/DE requests available utilization and distribution data stratified by age groups (pediatric 0-17 and 18+).

1.1 PRODUCT INFORMATION

GRASTEK is indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirmed by positive skin test or in vitro testing for pollen-specific IgE antibodies for Timothy grass or cross-reactive grass pollens. GRASTEK is approved for use in person 5 through 65 years of age. It is provided as a once-daily oral sublingual tablet of 2800 bioequivalent allergy units (BAUs). Pediatric labeling was added to GRASTEK in April 11, 2014.

Oralair is an allergen extract indicated as immunotherapy for the treatment of grass pollen-induced allergic rhinitis with or without conjunctivitis confirm by positive skin test or in vitro testing for pollen-specific IgE antibodies for any of the five grass species contained in the product. It is approved for use in person 10 through 65 years of age. Pediatric labeling was added to Oralair in April 1, 2014.

Active ingredient	Proprietary Name	FDA approval date	BLA number	Sponsor
Sweet vernal, orchard, perennial rye, timothy, and Kentucky blue grass mixed pollens allergen extract	Oralair	April 1, 2014	125471	Stallergenes
Timothy grass pollen allergen extract	Grastek	April 11, 2014	125473	Merck Sharp & Dohme Corp.

2 METHODS AND MATERIALS

Proprietary drug utilization databases available to the Agency were used to conduct this analysis (See Appendix for full database descriptions).

2.1 DATA SOURCES USED

Confidential reports regarding post-marketing summaries of safety information submitted directly to the FDA for each product were used to identify approximate number of tablets distributed from manufacturers to all U.S. channels of distribution for marketing periods that were available.

Sales Distribution Data

The QuintilesIMS, National Sales Perspective (NSP) database was used to determine the settings of distribution based on the nationally estimated number of tablets sold for Oralair and Grastek from the manufacturers to all U.S. channels of distribution for April 2014 through December 2016. The sales distribution data captured in this database represent the amount of product sold from manufacturers to pharmacies and other settings of care; it does not reflect what is being sold to or administered to patients directly. Of note, based on the sales data provided by the Sponsor, only a fraction of sales from the manufacturer are captured in this database.

Outpatient Retail Settings

The Symphony Health Solutions' PHAST Patient Monthly database was used to provide the nationally projected patient counts for Oralair and Grastek dispensed from retail pharmacy and mail-order pharmacy settings, from March 2014 through February 2017.

2.2 DRUG UTILIZATION RESULTS

2.2.1 Sales Distribution Data

From April 2014 through December 2016, approximately 1.26 million tablets were sold for Grastek from manufacturers to all U.S. settings of distribution. Approximately 87% of Grastek tablets were distributed through outpatient retail pharmacies, 6% through non-retail settings, and 7% through mail-order in 2016. Of the estimated 137,610 tablets sold for Oralair, all sales were to mail order channels.[1]

Accordingly, U.S. outpatient retail pharmacy utilization patterns, including mail-order distribution channels were examined in this review.

2.2.2 Patient data

Table 1 displays the nationally estimated number of unique patients who received dispensed prescriptions for Oralair and Grastek from March 2014 and February 2017. During the examined time period approximately 2,500 patients received Oralair and of those 32% (526 patients) were 16 years or younger. Approximately 9,300 patients received Grastek and of those approximately 21% or 3,000 patients were 16 years or younger.

Table1. **Nationally estimated number of patients who received prescriptions for Oralair and Grastek from U.S. outpatient retail and mail-order pharmacies, March 2014 through February 2017, aggregate**

[1] Source: IMS Health, IMS National Sales Perspectives™. April 2014-December 2016. Extracted May 2017.

		March 2014 - February 2017	
		Patients(N)	Share(%)
Oralair		**2,479**	***100%***
	0-16 years	**526**	***21%***
	17-64 years	**1,816**	***73%***
	65 years and older	**137**	***6%***
Grastek		**9,274**	***100%***
	0-16 years	**2,979**	***32%***
	17-64 years	**5,958**	***64%***
	65 years and older	**337**	**4%**

Symphony Health Solutions' PHAST Patient Monthly. Years 2014 - 2017.
Extracted April 2017. File: PHAST 2017-570 oralair grastek 4-27-2017.xls

2.2.3 Manufacturer Information

Permission was received by the manufacturers of Oralair and Grastek, Stallergenes and Merck, respectively to disclose information from FDA agency requests for information regarding post-marketing summaries of safety analysis including distribution data in the U.S. of these products during the marketing period from April 2014 through December 2016[2]. Estimates from Stallergenes on the distribution of Oralair indicate that 2,377,173 tablets were distributed in the U.S. from April 2014 through December 2016. Estimates from Merck on the distribution of Grastek indicate that 2,426,873 tablets were distributed in the U.S. from April through November 2016. Of note, these are estimates of tablets distributed from manufacturers to wholesalers and distributors and may not align with actual patient consumption.

3 LIMITATIONS

Findings from this review should be interpreted in the context of the known limitations of the databases used. We estimated that selected products Oralair and Grastek were distributed primarily to the outpatient setting based on the IMS Health, IMS National Sales Perspectives™ (NSP). However, based on the sales distribution obtained from the Sponsor, the NSP database only captures a fraction of total sales. In addition, these data do not provide a direct estimate of use but do provide an estimate of tablets sold from the manufacturer into the various channels of distribution. The amount of product purchased by these channels of distribution may be a possible surrogate for use, if we assume the facilities purchase drugs in quantities reflective of actual patient use, however it should be noted that this is only based on what is captured in the database. Manufacturers' estimation of tablets distributed to wholesalers and distributors may not align with actual patient consumption. In comparison to the data submitted by the Sponsor, the proprietary drug utilization databases currently available to the Agency are not a comprehensive capture of total utilization.

[2] BLA 125473 Grastek product correspondence STN, 125573/303 April 14, 2017; BLA 125471 Oralair product correspondence STN 125471/189 April 14, 2017

4 CONCLUSIONS

This drug utilization review focused on the U.S. outpatient retail setting where the majority of Oralair and Grastek were distributed according to information from proprietary databases available to the FDA. Approximately 21% of the 2,500 patients prescribed Oralair were 16 or younger over the examined time period from March 2014 through February 2017. Similarly approximately 32% of the 9,300 patients prescribed Grastek were 16 or younger.

APPENDICES

APPENDIX 1: DATABASE DESCRIPTIONS

IMS Health, IMS National Sales Perspectives™: Retail and Non-Retail

The IMS Health, IMS National Sales Perspectives™ measures the volume of drug products, both prescription and over-the-counter, and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Volume is expressed in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings.

Symphony Health Solutions' PHAST™ Patient Monthly

The Symphony Health Solutions' PHAST Patient Monthly is a syndicated view of U.S. retail and mail order pharmacy patient prescription activity, updated on a monthly basis at a projected national level. PHAST Patient monthly is based on the Symphony Health Solutions' longitudinal patient data source which captures adjudicated prescription claims across the United States across all payment types, including commercial plans, Medicare Part D, cash, assistance programs, and Medicaid. The database contains approximately 10 billion prescriptions claims linked to over 220 million unique prescription patients with an average of 4.2 years of prescription drug history, of which approximately 140 million patients are linked to a diagnosis.

Reviewer: Shekhar H. Mehta, PharmD MS
Drug Utilization Analyst
Division of Epidemiology II

Shekhar H. Mehta -S
Digitally signed by Shekhar H. Mehta -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2001955646, cn=Shekhar H. Mehta -S
Date: 2017.08.01 14:12:04 -04'00'

Team Leader: Rajdeep Gill, PharmD
Drug Utilization Data Analysis Team Leader
Division of Epidemiology II

Rajdeep K. Gill -A
Digitally signed by Rajdeep K. Gill -A
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2000420634, cn=Rajdeep K. Gill -A
Date: 2017.08.01 15:17:01 -04'00'

Deputy Division Director: LCDR Grace P. Chai, PharmD
Deputy Director of Drug Utilization
Division of Epidemiology II

Grace Chai -S
Digitally signed by Grace Chai -S
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