Treatment Patterns Among Patients With Cystic Fibrosis Using Twice Daily Dornase Alfa Regimen

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BACKGROUND & OBJECTIVE

- Use of dornase alfa, a mucolytic agent, reduces risk of respiratory infection and helps pulmonary function in cystic fibrosis (CF) patients.
- Since FDA approval in 1993, dornase alfa has become one of the most commonly prescribed medications for patients with CF.[1]
- Recommended dosage of dornase alfa is once-daily (QD), although data from pivotal clinical trials suggest twice-daily (BID) use may be beneficial for patients ≥ 21 years who have a relatively small effect with QD use.[2]
- We set out to examine the extent of BID dornase alfa use among CF patients in a real-world setting, which is currently unknown.

METHODS

- Retrospective analysis of US insurance claims data that examined patients with CF (ICD-9-CM: 277.0x) who initiated BID dornase alfa regimens in the identification (ID) period (1/1/2009 – 10/31/2011).
- Index date defined as the first fill date of BID use in the ID period.
- Exclusion criteria: patients not continuously enrolled in the 3 months before or 1 year after index; patients who had a BID dispensing in the pre-index period.

Measures

- Baseline characteristics were measured in 3 months before the index date.
- BID treatment uptake, duration, and discontinuation in the year following index.
  - Treatment duration was calculated as time to discontinuation (gap in BID use of > 60 days after completion of previous BID fill) of the index BID regimen.
- For reference, respiratory exacerbations were also measured 3 months before and after the index date, defined as one of the following:
  - Hospitalization or ED visits with primary diagnosis of CF.
  - A medical claim with an ICD-9-CM code for: hemoptysis (786.3); pneumothorax (512.xx); acute asthma (493.01/02, 493.11/12, 493.21/22, 493.91/92); acute resp. infection (460.xx–466.xx); pneumonia and influenza (480.xx–488.xx); acute resp. failure or pulmonary insufficiency (518.81/82); or bronchospasm (519.11).
  - A pharmacy claim for any antibiotics: oral (except azithromycin) and IV.

Statistical Analysis

- We evaluated patterns of use by plotting medication dispensed over time. Each color represented a different regimen (BID, QD, QD & BID, and no use). Graphical results were reported in aggregate and for each patient.
- The analysis was repeated for patients ≥ 21 years old (n=89).
- All data transformations and analyses were performed using SAS® version 9.4.

RESULTS

Demographics and Patient Characteristics

- Among 6,815 CF patients, 170 (2.5%) patients were new BID users **(Figure 1)**.
- Mean (SD) age was 24 years (14.1), 47.6% were female, and geographic distribution was spread evenly across US regions **(Table 1)**.
- Patients had mean Charlson Comorbidity Index of 1.8 (1.8) **(Table 1)**.
- Comorbidities included: diabetes (17.1%), pancreatic insufficiency (71.2%), pseudomonas infection (55.3%), gastroesophageal reflux (14.1%), chronic sinusitis (32.4%), malnutrition (9.4%), osteoporosis (1.8%), and allergic bronchopulmonary aspergillosis (4.7%) **(Table 1)**.

Figure 1. Patient Identification

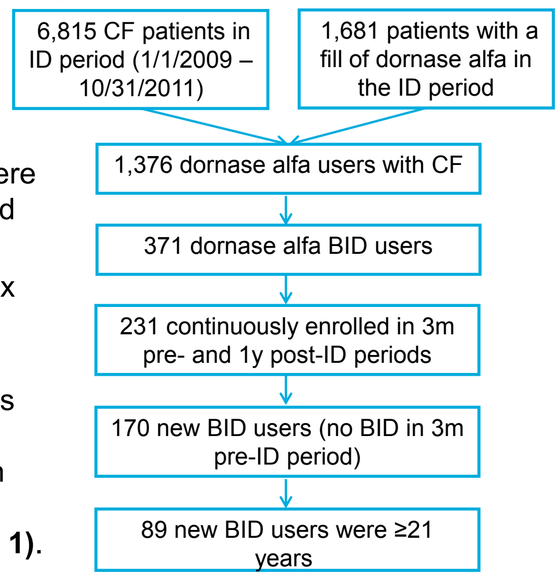


Table 1. Patient Demographics and Comorbidities

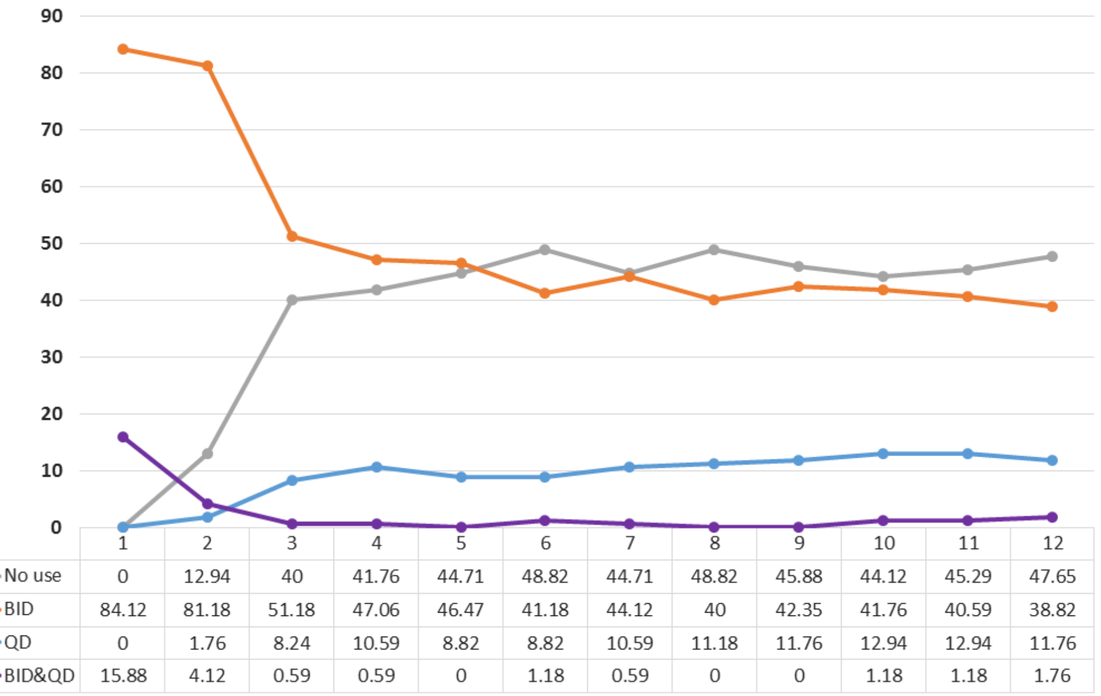
	BID New Users N = 170
Age, mean years (SD)	24.0 (14.1)
Age, year, n (%)	
<21	81 (47.6)
21+	89 (52.4)
Female	81 (47.6)
Charlson Comorbidity Index, mean (SD)	1.8 (1.8)
Comorbidities associated with CF, n (%)	159 (93.5)
Diabetes mellitus	29 (17.1)
Pancreatic insufficiency	121 (71.2)
Pseudomonas aeruginosa pulmonary infection	94 (55.3)
Gastroesophageal reflux	24 (14.1)
Chronic sinusitis	55 (32.4)
Malnutrition or failure to thrive	16 (9.4)
Osteoporosis	3 (1.8)
Allergic bronchopulmonary aspergillosis	8 (4.7)

RESULTS

BID Dornase Alfa Utilization

- Patients initiating BID use received on average 4.2 (3.1) BID fills, corresponding to mean days supply of 132.5 (109.9; results not shown).
- Under half of patients (41.2%) continued BID for 6 months with 38.8% on the regimen at 1 year **(Figures 2 & 3)**.

Figure 2: Monthly Dornase Alfa Use Following Initiation of BID Regimen (N = 170)



	1	2	3	4	5	6	7	8	9	10	11	12
No use	0	12.94	40	41.76	44.71	48.82	44.71	48.82	45.88	44.12	45.29	47.65
BID	84.12	81.18	51.18	47.06	46.47	41.18	44.12	40	42.35	41.76	40.59	38.82
QD	0	1.76	8.24	10.59	8.82	8.82	10.59	11.18	11.76	12.94	12.94	11.76
BID&QD	15.88	4.12	0.59	0.59	0	1.18	0.59	0	0	1.18	1.18	1.76

Respiratory Exacerbations

- Clinically, 3-month pre-index exacerbation rates were 69.4% for BID users, with a mean of 2.4 (3.5) exacerbations/patient. Exacerbation rates at 3 months post-index dropped 10.2% to 62.4%, with a mean of 2.2 (4.2) exacerbations/patient.
- Trend towards reduction in respiratory exacerbations in the post BID initiation period, however, observation period and sample size were small **(Table 2)**.

Figure 3. Dornase Alfa Use for Each Patient Initiating BID Regimen (N=170)

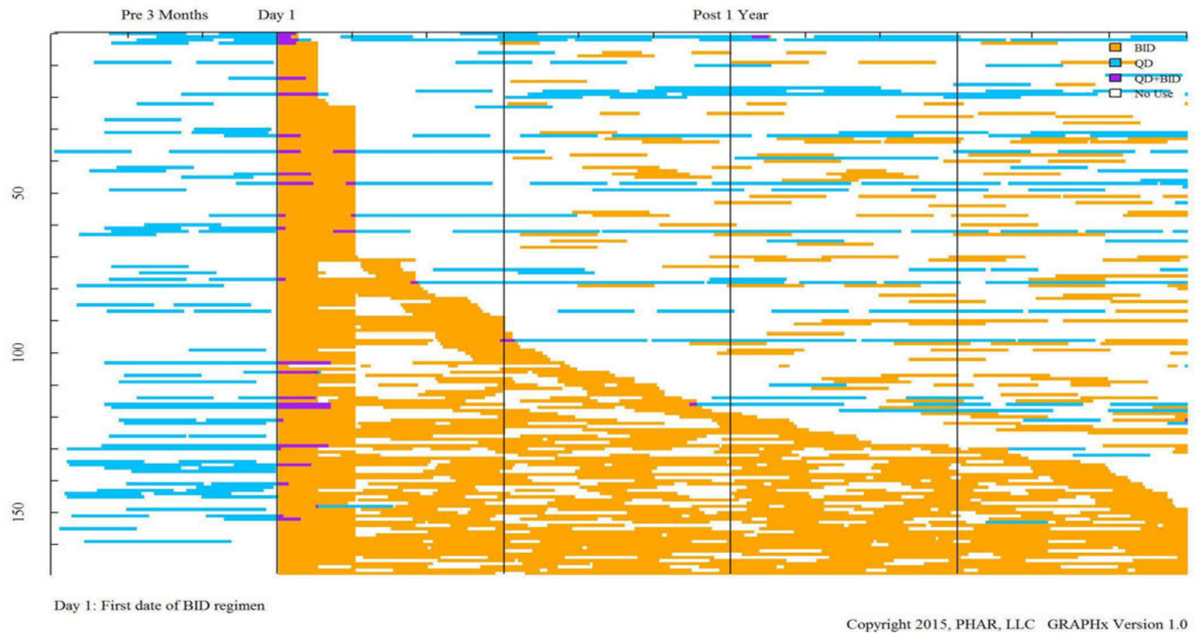


Table 2. Respiratory Exacerbations Before and After Initiating BID Regimen

	BID New Users N = 170
Before BID initiation (3-month pre-index)	
Any respiratory exacerbations, n (%)	118 (69.4)
No. of respiratory exacerbations, mean (SD)	2.4 (3.5)
After BID initiation (3-month post-index)	
Any respiratory exacerbations, n (%)	106 (62.4)
No. of respiratory exacerbations, mean (SD)	2.2 (4.2)

LIMITATIONS

- Our treatment patterns analysis was based on dispensing data as reported on pharmacy claims, which may not reflect how the medication was actually used.
- Results may not be generalizable to uninsured individuals or to those with other types of insurance not included in this database.

CONCLUSION

- On average, patients continued BID use for about 4 months before switching to QD or stopping. Most patients discontinued BID use by month 6, with a further drop over the remainder of the year.
- Some patients may benefit from BID dornase alfa use for a period of time.
- This study suggests that physicians and patients practice appropriate BID use, without need for health plan management to restrict access to higher doses of dornase alfa.

REFERENCES

1. Wagener JS. Curr Opin Pulm Med Nov 2012; 18(6):609-14.
2. Genentech, Inc., “Highlights of Prescribing Information for Pulmozyme® (dornase alfa).”

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