**Appendix**

**Table 1e. Demographics and number of reports– Sex, Age, Reporter Occupation – in our data**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Sex** | **Age** | **Reporter Occupation** |
| Total observations  (n=63,613) | 61,490 (96.6%) | 36,805 (57.9%) | 62,726 (98.6%) |
| Mean Age | 70.28 ± 0.06 | 70.26 ± 0.06 | 70.45 ± 0.06 |
| Male Sex (%)  (n=61,490) | 50.9% | 50.2% | 49.3% |

**Table 2e. Ten Most Frequently Reported Adverse Events for Chronic Lower Respiratory Disease Medications Approved between Q1 2012 - Q1 2017 with Greater than 500 Reports**

|  |  |
| --- | --- |
| **ADR** | **Frequency** |
| Asthenic conditions | 3,129 (4.91%) |
| Nausea and vomiting symptoms | 2,967 (4.66%) |
| Pain | 2,744 (4.31%) |
| Dyspnea | 2,004 (3.15%) |
| Diarrhea | 1,806 (2.84%) |
| Nontherapeutic responses | 1,450 (2.28%) |
| Decreased appetite | 1,358 (2.13%) |
| Dizziness | 1,074 (1.69%) |
| Headache | 1,024 (1.61%) |
| Rash | 9,43 (1.48%) |
| Pneumonia | 6,95 (1.09%) |

ADR = Adverse Drug Reaction

**Table 3e. Ten Most Frequently Reported Adverse Events for Chronic Lower Respiratory Disease Medications Approved between Q1 2012 - Q1 2017 with Greater than 500 Reports**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Generic (Brand)** | **Total ADR reports (n)** | **ADR Outcome** | **Frequency n (%)** | **Category** |
| Pirfenidone (Esbriet®) | 24,746 | Asthenic conditions  Nausea and vomiting symptoms  Death  Pain  Decreased appetite  Dyspnea  Rash  Diarrhea  Weight decreased  Dizziness | 1908 (7.72)  1755 (7.10)  1465 (5.93)  1249 (5.05)  947 (3.83)  685 (2.77)  679 (2.75)  660 (2.67)  601 (2.43)  582 (2.35) | IPF |
| Nintedanib (OFEV®) | 11,479 | Diarrhea  Nausea and vomiting symptoms  Pain  Asthenic conditions  Dyspnea  Cough  Decreased appetite  Idiopathic pulmonary fibrosis  Weight decreased  Death | 1055 (9.21)  775 (6.77)  589 (5.14)  509 (4.45)  443 (3.87)  380 (3.32)  308 (2.69)  293 (2.56)  262 (2.29)  212 (1.85) | IPF |
| Umeclidinium/vilanterol (Anoro Ellipta®) | 8,533 | Drug dispensing error  Dyspnea  Nontherapeutic responses  Cough  Drug dose omission  Pain  Product packaging confusion  Circumstance or information capable of leading to medical error  Asthenic conditions  Wrong technique in product usage process | 469 (5.50)  390 (4.57)  324 (3.80)  303 (3.55)  284 (3.33)  197 (2.37)  183 (2.14)  133 (1.56)  126 (1.48)  126 (1.48) | COPD |
| Fluticasone/vilanterol  (Breo Ellipta®) | 7,154 | Dyspnea  Drug ineffective  Cough  Dysphonia  Pain  Drug dose omission  Dizziness  Off label use  Headache  Pneumonia | 424 (5.93)  381 (5.33)  276 (3.86)  222 (3.10)  196 (2.74)  134 (1.87)  97 (1.36)  79 (1.10)  75 (1.05)  74 (1.03) | COPD |
| Mepolizumab (Nucala®) | 3,924 | Pain  Asthenic conditions  Headache  Nontherapeutic responses  Dyspnea  Drug dose omission  Asthma  Cough  Rash  Pruritis | 234 (5.96)  168 (4.28)  119 (3.03)  117 (2.98)  107 (2.73)  104 (2.65)  98 (2.50)  72 (1.83)  69 (1.76)  63 (1.61) | Asthma |
| Roflumilast (Daliresp®) | 2,480 | Diarrhea  Nausea and Vomiting Symptoms  Pain  Weight decreased  Insomnia  Asthenic conditions  Dizziness  Dyspnea  Headache  Decreased appetite | 176 (7.09)  136 (5.48)  123 (4.95)  116 (4.67)  103 (4.15)  77 (3.10)  71 (2.86)  71 (2.86)  69 (2.78)  63 (2.54) | COPD |
| Umeclidinium  (Incruse Ellipta®) | 2,285 | Dyspnea  Drug dose omission  Cough  Nontherapeutic responses  Pain  Drug dispensing error  Wrong technique in product  usage process  Asthenic conditions  Wrong technique in device  usage process  Dysgeusia | 112 (4.90)  107 (4.68)  86 (3.76)  84 (3.68)  79 (3.46)  68 (2.98)  60 (2.63)  39 (1.71)  36 (1.58)  27 (1.18) | COPD |
| Fluticasone/azelastine  (Dymista®) | 1,652 | Dysgeusia  Headache  Epistaxis  Nontherapeutic responses  Pain  Asthenic conditions  Nausea and Vomiting symptoms  Dizziness  Somnolence | 74 (4.48)  71 (4.30)  64 (3.87)  60 (3.63)  47 (2.85)  46 (2.78)  39 (2.36)  37 (2.24)  35 (2.12) | SAR |
| Beclomethasone dipropionate  (QNASL®) | 1,425 | Nasal discomfort  Nontherapeutic responses  Headache  Epistaxis  Burning sensation  Sneezing  Pain  Nasal congestion  Asthenic conditions  Cough | 106 (7.44)  77 (5.40)  63 (4.42)  53 (3.72)  48 (3.37)  39 (2.74)  38 (2.67)  34 (2.39)  32 (2.25)  25 (1.75) | Asthma |

\* Data are number, n, of reports in FAERS unless otherwise specified

ADR = Adverse Drug Reaction

IPF = Idiopathic Pulmonary Fibrosis

COPD = Chronic Obstructive Pulmonary Disease

SAR = Seasonal Allergic Rhinitis

**Table 4e. Ten Most Frequently Reported Adverse Events for Chronic Lower Respiratory Disease Medications used as Comparators with Greater than 500 Reports**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Generic (Brand)** | **Total ADR reports (n)** | **ADR Outcome** | **Frequency n (%)** | **Category** |
| Budesonide/formoterol  (Symbicort®) | 47,947 | Dyspnea  Intentional product misuse  Off label use  Drug dose omission  Asthma  Cough  Device malfunction  Drug ineffective  Product quality issue  Malaise | 2699 95.63)  2400 (5.01)  2174 (4.53)  1731 (3.61)  890 (1.86)  887 (1.85)  885 (1.85)  762 (1.59)  745 (1.55)  690 (1.44) | COPD |
| Fluticasone/salmeterol  (Advair®) | 30,468 | Dyspnea  Drug ineffective  Pneumonia  Pain  Cough  Fatigue  Nausea  Asthma  Dizziness  Headache | 1056 (9.20)  777 (6.77)  589 (5.13)  510 (4.44)  443 (3.86)  381 (3.32)  309 (2.69)  295 (2.57)  263 (2.29)  214 (1.86) | IPF |

\* Data are number, n, of reports in FAERS unless otherwise specified

*Chronic Obstructive Pulmonary Disease*

**Table 5e. Reporting Odds Ratios of each Sex reporting ADRs of UMEC/VI and UMEC**

|  |  |  |  |
| --- | --- | --- | --- |
| **ADR (n=17,945)** | **Sex** | **ROR** | **95% CI** |
| Nontherapeutic responses  (n=393) | Female (n=218)  Male (n=175) | 0.7878  1.2693 | [0.6428, 0.9656]  [1.0356, 1.5558] |
| Cough  (n=380) | Female (n=265)  Male (n=115) | 1.4958  0.6685 | [1.1969, 1.8695]  [0.5349, 0.8355] |

\* Data are number, n, of reports in FAERS unless otherwise specified

ADR = Adverse Drug Reaction

ROR = Reporting Odds Ratio

CI = Confidence Interval

**Table 6e. Reporting Odds Ratios of Age Group for ADRs of UMEC/VI and UMEC**

|  |  |  |  |
| --- | --- | --- | --- |
| **ADR (n=17,945)** | **Sex** | **ROR** | **95% CI** |
| Nontherapeutic responses  (n=393) | Younger adults (n=34)  Older adults (n=359) | 0.6878  1.4538 | [0.4811, 0.9834]  [1.0169, 2.0785] |

\* Data are number, n, of reports in FAERS unless otherwise specified

ADR = Adverse Drug Reaction

ROR = Reporting Odds Ratio

CI = Confidence Interval

**Table 7e. Reporting Odds Ratio of each Sex for ADRs of Roflumilast**

|  |  |  |  |
| --- | --- | --- | --- |
| **ADR**† | **Sex** | **ROR** | **95% CI** |
| Nausea and Vomiting  (n=125) | Female (n=89)  Male (n=35) | 1.9879  0.5030 | [1.3350, 2.9602]  [0.3378, 0.7491] |
| Pain  (n=99) | Female (n=66)  Male (n=33) | 2.0170  0.4958 | [1.3189, 3.0850]  [0.3242, 0.7583] |

\* Data are number, n, of reports in FAERS unless otherwise specified

† 2,064 ADR reports analyzed, only 224 reports included in table that do not show overlapping confidence interval

ADR = Adverse Drug Reaction

ROR = Reporting Odds Ratio

CI = Confidence Interval