**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 conditionsNausea and vomiting symptomsDeathPainDecreased appetiteDyspneaRashDiarrheaWeight decreasedDizziness | 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 | DiarrheaNausea and vomiting symptomsPainAsthenic conditionsDyspneaCoughDecreased appetiteIdiopathic pulmonary fibrosisWeight decreasedDeath | 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 errorDyspneaNontherapeutic responsesCoughDrug dose omissionPainProduct packaging confusionCircumstance or information capable of leading to medical errorAsthenic conditionsWrong 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 | DyspneaDrug ineffectiveCoughDysphoniaPainDrug dose omissionDizzinessOff label useHeadachePneumonia | 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 | PainAsthenic conditionsHeadacheNontherapeutic responsesDyspneaDrug dose omissionAsthmaCoughRashPruritis | 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 | DiarrheaNausea and Vomiting SymptomsPainWeight decreasedInsomniaAsthenic conditionsDizzinessDyspneaHeadacheDecreased 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 | DyspneaDrug dose omissionCoughNontherapeutic responsesPainDrug dispensing errorWrong technique in product usage processAsthenic conditionsWrong technique in device usage processDysgeusia | 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 | DysgeusiaHeadacheEpistaxisNontherapeutic responsesPainAsthenic conditionsNausea and Vomiting symptomsDizzinessSomnolence | 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 discomfortNontherapeutic responsesHeadacheEpistaxisBurning sensationSneezingPainNasal congestionAsthenic conditionsCough | 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 | DyspneaIntentional product misuseOff label useDrug dose omissionAsthmaCoughDevice malfunctionDrug ineffectiveProduct quality issueMalaise | 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 | DyspneaDrug ineffectivePneumoniaPainCoughFatigueNauseaAsthmaDizzinessHeadache | 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) | 0.78781.2693 | [0.6428, 0.9656][1.0356, 1.5558] |
| Cough(n=380) | Female (n=265)Male (n=115) | 1.49580.6685 | [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) | 0.68781.4538 | [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) | 1.98790.5030 | [1.3350, 2.9602][0.3378, 0.7491] |
| Pain(n=99) | Female (n=66)Male (n=33) | 2.01700.4958 | [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