

## Supplementary tables

Supplementary Table 1 Population with diagnosed and treated COPD for each country

	Belgium	Germany	Sweden	United States
<b>Population</b>	11,492,641 <sup>1</sup>	73,009,237 <sup>2</sup>	10,319,473 <sup>3</sup>	256,416,340 <sup>4</sup>
<b>COPD prevalence</b>	4.4% <sup>5</sup>	7.6% <sup>6</sup>	4.0% <sup>7</sup>	6.7% <sup>8,9</sup>
<b>Proportion inhaled use</b>	68.4% <sup>10</sup>	87.9% <sup>11</sup>	80.0% <sup>7</sup>	52.0% <sup>12</sup>
<b>Population with diagnosed and treated COPD</b>	346,051	4,863,367	330,223	8,986,880

**Abbreviations:** COPD, chronic obstructive pulmonary disease.

**Supplementary Table 2 Population with diagnosed and treated COPD for each country**

	<b>Belgium</b>	<b>Germany</b>	<b>Sweden</b>	<b>United States</b>
<b>Low exacerbations/low symptoms, % (proportion of those with high EOS)</b>	19.0 <sup>13</sup> (19.5) <sup>14</sup>	6.4 <sup>11</sup> (14) <sup>15</sup>	29 <sup>7</sup> (27) <sup>16,17</sup>	43.1 <sup>12</sup> (27) <sup>18</sup>
LAMA, %	28.0 <sup>a</sup>	48 <sup>11</sup>	29 <sup>7</sup>	26 <sup>b</sup>
LABA, %	21.1 <sup>a</sup>	6 <sup>11</sup>	4 <sup>7</sup>	NA
LAMA/LABA, %	3.4 <sup>a</sup>	15 <sup>11</sup>	24 <sup>7</sup>	12 <sup>b</sup>
LABA/ICS, %	47.6 <sup>a</sup> (19.5) <sup>14</sup>	8 <sup>11</sup> (4) <sup>15</sup>	13 <sup>7</sup> (3) <sup>16,17</sup>	52 <sup>b</sup> (14) <sup>b</sup>
LAMA/LABA/ICS, %	0.0 <sup>a</sup>	23 <sup>11</sup> (10) <sup>15</sup>	29 <sup>7</sup> (8) <sup>16,17</sup>	FDC: 3 <sup>b</sup> (1) <sup>b</sup> ; free dose: 7 <sup>b</sup> (2) <sup>b</sup>
<b>Low exacerbations/high symptoms, % (proportion of those with high EOS)</b>	39.0 <sup>13</sup> (20.7) <sup>14</sup>	44.4 <sup>11</sup> (14) <sup>15</sup>	57 <sup>7</sup> (27) <sup>16,17</sup>	42.4 <sup>12</sup> (27) <sup>18</sup>
LAMA, %	22.0 <sup>a</sup>	47 <sup>11</sup>	20 <sup>7</sup>	26 <sup>b</sup>
LABA, %	11.0 <sup>a</sup>	4 <sup>11</sup>	3 <sup>7</sup>	NA
LAMA/LABA, %	10.3 <sup>a</sup>	17 <sup>11</sup>	28 <sup>7</sup>	12 <sup>b</sup>
LABA/ICS, %	56.5 <sup>a</sup> (20.6) <sup>14</sup>	5 <sup>11</sup> (2) <sup>15</sup>	3 <sup>7</sup> (1) <sup>16,17</sup>	52 <sup>b</sup> (14)
LAMA/LABA/ICS, %	0.3 <sup>a</sup> (0.1) <sup>14</sup>	27 <sup>11</sup> (12) <sup>15</sup>	46 <sup>7</sup> (13) <sup>16,17</sup>	FDC: 3 <sup>b</sup> (1) <sup>b</sup> ; free dose: 7 <sup>b</sup> (2) <sup>b</sup>

	Belgium	Germany	Sweden	United States
<b>High exacerbations/low symptoms, % (proportion of those with high EOS)</b>	18.0 <sup>13</sup> (20.3) <sup>14</sup>	3.2 <sup>11</sup> (14) <sup>15</sup>	2 <sup>7</sup> (27) <sup>16,17</sup>	4.2 <sup>12</sup> (27) <sup>18</sup>
LAMA, %	12.1 <sup>a</sup>	37 <sup>11</sup>	15 <sup>7</sup>	21 <sup>b</sup>
LABA, %	1.7 <sup>a</sup>	4 <sup>11</sup>	4 <sup>7</sup>	NA
LAMA/LABA, %	9.4 <sup>a</sup>	19 <sup>11</sup>	22 <sup>7</sup>	9 <sup>b</sup>
LABA/ICS, %	75.7 <sup>a</sup> (20.0) <sup>14</sup>	4 <sup>11</sup> (1) <sup>15</sup>	4 <sup>7</sup> (1) <sup>16,17</sup>	51 <sup>b</sup> (14) <sup>b</sup>
LAMA/LABA/ICS, %	1.11 <sup>a</sup> (0.3) <sup>14</sup>	36 <sup>11</sup> (13) <sup>15</sup>	55 <sup>7</sup> (15) <sup>16,17</sup>	FDC: 6 <sup>b</sup> (1) <sup>b</sup> ; free dose: 13 <sup>b</sup> (3) <sup>b</sup>
<b>High exacerbations/high symptoms, % (proportion of those with high EOS)<sup>c</sup></b>	24.0 <sup>13</sup> (19.2) <sup>14</sup>	46.0 <sup>11</sup> (14) <sup>15</sup>	12 <sup>7</sup> (27) <sup>16,17</sup>	10.4 <sup>12</sup> (27) <sup>18</sup>
LAMA, %	2.3	38	7	21
LABA, %	0.9	3	2	NA
LAMA/LABA, %	13.9	18	16	9
LABA/ICS, %	78.4 (18.1)	3 (1)	2 (0)	51 (14)
LAMA/LABA/ICS, %	4.6 (1.1)	38 (13)	74 (20)	FDC: 6 (1); free dose: 13 (3)

**Notes:** <sup>a</sup>IM Associates: Patient Data for 2018. Belgium. <sup>b</sup>Personal communication with the authors of Palli et al 2020.<sup>19</sup> <sup>c</sup>EOS figures were applied in Germany for the GOLD guideline setting only.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; EOS, eosinophils; FDC, fixed-dose combination; ICS, inhaled corticosteroids; LABA, long-acting  $\beta_2$  agonist; LAMA, long-acting muscarinic antagonist.

**Supplementary Table 3 Exacerbation and pneumonia rates**

<b>Exacerbation rates (annual)</b>		
Absolute risk with no prior exacerbations for LAMA/LABA (%)		
Moderate	7.13 <sup>20</sup>	
Severe	2.41 <sup>20</sup>	
Relative risk		
	No prior exacerbations <sup>20-22</sup>	Prior exacerbations <sup>23</sup>
LAMA	1.11	4.63
LABA	1.28	5.34
LAMA/LABA	1.00	4.17
LABA/ICS	1.15	4.79
LAMA/LABA/ICS	0.87	3.62
<b>Pneumonia rates (annual)</b>		
Absolute risk for LAMA/LABA (%)		
Mild to moderate	1.67 <sup>24</sup>	
Severe	3.08 <sup>24</sup>	
Relative risk for all therapies		
	Mild to moderate <sup>24</sup>	Severe <sup>24</sup>
LAMA	1.00	1.00
LABA	1.00	1.00
LAMA/LABA	1.00	1.00
LABA/ICS	1.31	1.70
LAMA/LABA/ICS	1.31	1.70

**Abbreviations:** COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids; LABA, long-acting  $\beta_2$  agonist; LAMA, long-acting muscarinic antagonist.

**Supplementary Table 4 Cost estimate for treatment, exacerbations and pneumonia**

	Belgium (€)	Germany (€)	Sweden (Kroner)	United States (\$)
<b>Treatment</b>				
LAMA	306.46 <sup>25</sup>	596.63 <sup>a</sup>	3778.49 <sup>26</sup>	3906.52 <sup>b</sup>
LABA	251.91 <sup>25</sup>	280.63 <sup>a</sup>	3900.03 <sup>26</sup>	NA
LAMA/LABA	437.54 <sup>25</sup>	722.32 <sup>a</sup>	5376.11 <sup>26</sup>	4086.62 <sup>b</sup>
LABA/ICS	379.16 <sup>25</sup>	669.52 <sup>a</sup>	5972.22 <sup>26</sup>	3796.28 <sup>b</sup>
LAMA/LABA/ICS	589.35 <sup>25</sup>	886.22 <sup>a</sup>	7278.13 <sup>26</sup>	FDC: 7208.57 <sup>b,c</sup> ; free dose: 7716.26 <sup>b</sup>
<b>Exacerbations</b>				
Moderate	48.26 <sup>25,27</sup>	60.85 <sup>28</sup>	2556.04 <sup>27</sup>	192.70 <sup>d</sup>
Severe	6352.5 <sup>25,27</sup>	3334.50 <sup>11,29,30</sup>	53,137.00 <sup>27</sup>	15,721.23 <sup>d</sup>
<b>Pneumonia events</b>				
Mild to moderate	61.36 <sup>31</sup>	66.01 <sup>11,28–30,32–34</sup>	5024.60 <sup>31</sup>	254.39 <sup>e</sup>
Severe	6055.7 <sup>31</sup>	3779.14 <sup>34–36</sup>	60,200.00 <sup>31</sup>	18,677.44 <sup>e</sup>

**Notes:** <sup>a</sup>Calculated based on drug cost data from Lauer-Taxe<sup>® 37</sup> and market shares from the IQVIA PharmaScope<sup>®</sup> National database.<sup>38</sup> Basis: Boehringer Ingelheim, own calculation. <sup>b</sup>Personal communication with the authors of Palli et al 2020.<sup>19</sup> <sup>c</sup>US: FDC: Weighted average based on assumed market share 90:10 Trelegy: Breztri Trelegy Ellipta;<sup>39</sup> Breztri Aerosphere.<sup>39</sup> <sup>d</sup>Moderate exacerbation cost: Weighted average of mean ambulatory visit cost (90%) and mean emergency department visit cost (10%). Defined as claims with a diagnosis of COPD in the primary position. Severe exacerbation cost: Mean cost per acute inpatient stay with a primary diagnosis of COPD. <sup>e</sup>Mild-to-moderate pneumonia events: Weighted average of mean ambulatory visit cost (83%) and emergency department visit cost (17%). Claims with a diagnosis for pneumonia or acute bronchitis/bronchiolitis in any position. Severe pneumonia events: Mean cost per acute inpatient stay with a diagnosis for pneumonia or acute bronchitis/bronchiolitis in any position.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; FDC, fixed-dose combination; ICS, inhaled corticosteroids; LABA, long-acting  $\beta_2$  agonist; LAMA, long-acting muscarinic antagonist.

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