Common Drug Review
Pharmacoeconomic Review Report

January 2018

Drug	umeclidinium bromide (Incruse Ellipta)
Indication	Indicated for long-term, once daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.
Listing request	List in a similar manner to other LAMAs as a maintenance bronchodilator treatment for COPD.
Dosage form(s)	Dry powder for oral inhalation, 62.5 mcg per inhalation
Manufacturer	GlaxoSmithKline Canada Inc. (GSK)

This review report was prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH). In addition to CADTH staff, the review team included a clinical expert in respirology who provided input on the conduct of the review and the interpretation of findings.

Redactions: Confidential information in this document has been redacted at the request of the manufacturer in accordance with the *CADTH Common Drug Review Confidentiality Guidelines.*

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

TABLE OF CONTENTS

Tables

ABBREVIATIONS

CDR	CADTH Common Drug Review
COPD	chronic obstructive pulmonary disease
FEV_1	forced expiratory volume in one second
GOLD	Global Initiative for Chronic Obstructive Lung Disease
ICS	inhaled corticosteroid
ITC	indirect treatment comparison
LABA	long-acting beta2-agonist
LAMA	long-acting muscarinic antagonist
ODB	Ontario Drug Benefit
SGRQ	St. George's Respiratory Questionnaire
TDI	Transition Dyspnea Index

SUMMARY

Background

Umeclidinium bromide (Incruse Ellipta) is a long-acting muscarinic antagonist (LAMA) indicated for long-term, once-daily maintenance bronchodilator treatment of chronic obstructive pulmonary disease (COPD), including emphysema and chronic bronchitis.[1] The manufacturer is requesting for umeclidinium bromide (hereafter frequently referred as "umeclidinium") to be listed as per indication and in a manner similar to other LAMAs currently available for the treatment of COPD. The recommended dose is one inhalation of 62.5 mcg daily. The manufacturer submitted a confidential price of [redacted] per 30 inhaled doses for a daily cost of [redacted].

Umeclidinium was previously reviewed by the CADTH Common Drug Review (CDR) as part of its review of Anoro Ellipta, a fixed-dose combination product consisting of umeclidinium/vilanterol. Anoro Ellipta received a positive listing recommendation for patients with moderate to severe COPD who had an inadequate response to LAMA or long-acting beta2-agonist (LABA) monotherapy.[2]

Summary of the economic analysis submitted by the manufacturer

The manufacturer submitted a cost comparison of umeclidinium versus other LAMA monotherapies used in the treatment of COPD: tiotropium 18 mcg once daily (Spiriva HandiHaler); glycopyrronium bromide 50 mcg once daily (Seebri Breezhaler); and aclidinium bromide 400 mcg twice daily (Tudorza Genuair).[3] The analysis was undertaken from the public-payer perspective. Ontario Drug Benefit (ODB) formulary prices (November 2014) were used to calculate comparator costs. An 8% markup was applied to all drug costs. The assumption of similar treatment efficacy was based on a manufacturer-sponsored indirect treatment comparison (ITC), where umeclidinium and all other comparators were found to be similar in clinical efficacy in terms of lung function (as assessed by trough forced expiratory volume in one second [FEV_1] at 12 weeks) and for other outcomes, such as: trough FEV_1 at 24 weeks; St. George's Respiratory Questionnaire (SGRQ) score; Transition Dyspnea Index (TDI) score; and use of rescue medication.[4]

The manufacturer concluded that umeclidinium would lead to one-year savings of [redacted] per patient compared with tiotropium, and [redacted] compared with aclidinium and glycopyrronium.

Key limitations

CDR noted several limitations in the submitted economic analysis. A key limitation is the lack of comparative clinical information for umeclidinium compared with other LAMAs. As a result, the manufacturer conducted an ITC to provide information on the comparative clinical efficacy of umeclidinium. The exclusion of exacerbations and exercise capacity from the manufacturer's ITC is a major limitation. Exacerbations are responsible for the majority of costs related to COPD,[5] and are known to have an impact on patient quality of life and mortality.[6,7] While a recent network meta-analysis[8] indicates that tiotropium, aclidinium, and glycopyrronium have similar efficacy in preventing exacerbations, no such data are available for umeclidinium.

In addition to the limitations with the outcomes considered in the manufacturer's ITC, as noted in the CDR clinical review, several issues were identified with the ITC that limit the confidence that may be placed in the conclusions. The CDR clinical review noted insufficient detail on key patient and trial characteristics to allow assessment of heterogeneity between studies; heterogeneity in reported patient characteristics and treatment duration; and lack of data on patient withdrawal and severity of COPD.

These limitations introduce uncertainty into claims of similarity between umeclidinium and comparators for the selected clinical outcomes.

As per COPD treatment guidelines,[9,10] LABAs and combination inhaled corticosteroids/LABAs (ICSs/LABAs) are appropriate alternative treatments for some patients within the approved indication for umeclidinium. CDR compared the annual cost per patient of umeclidinium to that of the available LABA and ICS/LABA products (Table 5). At the submitted confidential price of [redacted] daily, umeclidinium is less expensive than all ICS/LABA fixed-dose combinations, but more expensive than most LABA-only products. Further, it is appropriate for some patients to be treated with a LAMA and a LABA or a LABA and ICS.[10] For patients requiring LAMA and LABA therapy, currently available LAMA/LABA fixed-dose combinations are less expensive than all possible combinations of umeclidinium plus a LABA (Table 6).

Results and conclusions

The lack of comparative studies or a well-conducted indirect comparison for umeclidinium limits the assessment of umeclidinium in comparison to other LAMAs.

At the submitted confidential daily cost of [redacted], umeclidinium is less expensive than the current list prices of all other available LAMAs ($1.77 daily for aclidinium or glycopyrronium; $2.17 daily for tiotropium). While umeclidinium is less expensive than available fixed-dose ICS/LABA combination products (range: $2.76 to $4.61 daily), it is more expensive than most individual LABA products (range: $1.55 to $1.87 daily). For patients requiring LAMA and LABA therapy, currently available LAMA/LABA fixed-dose combinations are less expensive than all possible combinations of umeclidinium plus a LABA.

Cost comparison table

Clinical experts have deemed the comparator treatments presented in Table 1 to be appropriate. Comparators may be recommended (appropriate) practice versus actual practice. Comparators are not restricted to drugs, but may be devices or procedures. Costs are manufacturer list prices, unless otherwise specified. Additional drugs to treat COPD can be found in Appendix 2: Additional Cost Comparators.

Table 1: Cost Comparison Table for LAMAs, LABAs, and Combinations for COPD

Drug/Comparator	Strength	Dosage Form	Price ($)	Price/ Dose ($)	Recommended Daily Use	Daily Drug Cost ($)	Average Annual Cost ($)
Umeclidinium bromide (Incruse Ellipta)	**62.5 mcg**	**Inhalant pwd (30 doses)**	[redacted][a]	[redacted]	**62.5 mcg once daily**	[redacted]	[redacted]
Other LAMAs							
Aclidinium bromide (Tudorza Genuair)	400 mcg	Inhalant pwd (60 doses)	53.1000	0.8850	400 mcg twice daily	1.77	646
Glycopyrronium bromide (Seebri)	50 mcg	Inhalant pwd capsule	1.7700	1.7700	50 mcg daily	1.77	646
Tiotropium (Spiriva	18 mcg	Inhalant pwd capsule	2.1667	2.1667	18 mcg daily	2.17	791
LABAs							
Formoterol (Foradil)	12 mcg	Inhalant pwd capsule	0.8181	0.8181	12 mcg to 24 mcg twice daily	1.64 to 3.27	597 to 1,194

Drug/Comparator	Strength	Dosage Form	Price ($)	Price/ Dose ($)	Recommended Daily Use	Daily Drug Cost ($)	Average Annual Cost ($)
Indacaterol maleate (Onbrez)	75 mcg	Inhalant pwd capsule	1.5500	1.5500	75 mcg daily	1.55	566
Salmeterol (Serevent)	50 mcg	Inhalant pwd dose	0.9350	0.9350	50 mcg twice daily	1.87	683
LABA/LAMA Combinations							
Indacaterol/ glycopyrronium (Ultibro Breezhaler)	110 mcg/ 50 mcg	Inhalant pwd capsule	2.6800[b]	2.6800	110 mcg/ 50 mcg daily	2.68	978
Umeclidinium/ vilanterol (Anoro Ellipta)	62.5 mcg/ 25 mcg	Inhalant pwd (30 doses)	81.0000[c]	2.7000	62.5 mcg/ 25 mcg daily	2.70	985
Inhaled Corticosteroid/LABA Combinations							
Budesonide/ formoterol (Symbicort Turbuhaler)	100 mcg/ 6 mcg 200 mcg/ 6 mcg	Inhalant pwd (120 doses)	64.5600 83.8800	0.5380 0.6990	400 mcg/12 mcg twice daily	2.80	1,021
Fluticasone furoate/vilanterol trifenatate (Breo Ellipta)	100 mcg/ 25 mcg	Inhalant pwd (30 doses)	120.0000	4.0000	100 mcg/25 mcg once daily	4.00	1,460
Fluticasone propionate/ salmeterol (Advair Diskus)	100 mcg/ 50 mcg 250 mcg/ 50 mcg 500 mcg/ 50 mcg	Inhalant pwd (60 doses)	81.3900 97.4280 138.3120	1.3565 1.6238 2.3052	250 mcg/50 mcg or 500 mcg/ 50 mcg twice daily	3.25 to 4.61	1,186 to 1,684

COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; LABA = long-acting beta2-agonist; LAMA = long-acting muscarinic antagonist; pwd = powder.

[a] Source: Manufacturer's confidential submitted price.

[b] Source: Canadian Drug Expert Committee Final Recommendation for Ultibro Breezhaler: http://www.cadth.ca/media/cdr/complete/cdr_complete_SR0369_Ultibro%20Breezhaler_Jan30_2015.pdf.

[c] Source: Ontario Drug Benefit Formulary.[11]

Note: Alternatives currently under review by the CADTH Common Drug Review are aclidinium/formoterol (Duaklir Genuair) and tiotropium bromide (Spiriva Respimat). Source: Alberta Health Drug Benefit list (April 2015) unless otherwise stated.

APPENDIX 1: REVIEWER WORKSHEETS

TABLE 2: SUMMARY OF MANUFACTURER'S SUBMISSION

Drug Product	Umeclidinium Bromide (Incruse Ellipta)
Treatment	Umeclidinium 62.5 mg once daily
Comparators	Tiotropium 18 mcg once daily (Spiriva HandiHaler) Glycopyrronium 50 mg once daily (Seebri Breezhaler) Aclidinium bromide 400 mg twice daily (Tudorza Genuair)
Study Question	To estimate the relative cost of treatment with umeclidinium (Incruse Ellipta) compared with that of tiotropium bromide (Spiriva HandiHaler), aclidinium bromide (Tudorza Genuair) and glycopyrronium bromide (Seebri Breezhaler) in individuals with moderate to severe COPD. Using cost comparisons, the aim was to estimate the difference between the annual cost of umeclidinium and annual cost of comparators over a five-year horizon. A secondary objective was to estimate the annual cost difference between umeclidinium and the current mix of comparator interventions based on market share values for each of the three comparator therapies. A further aim was to assess how cost differences between umeclidinium and comparator interventions are predicted to change at different market share values for each of the three comparators.
Type of Economic Evaluation	Cost-minimization analysis
Target Population	Adult patients with COPD, including chronic bronchitis and emphysema, representing the umeclidinium clinical trials and the approved indication.
Perspective	Canadian public payer
Outcome Considered	Drug costs
Key Data Sources	
Cost	The price of umeclidinium was based on the manufacturer's confidential submitted price. The costs of comparators were based on ODB formulary list prices, including an 8% markup.
Clinical Efficacy	Comparable efficacy was established by a manufacturer-commissioned ITC. The primary outcome was 24-hour trough FEV_1 at 12 weeks in addition to several secondary outcomes (trough FEV_1 at 24 weeks, SGRQ score, TDI score, and use of rescue medication).
Harms	Not considered.
Market Share	IMS Brogan claims data
Time Horizon	Five years, with annual cost differences presented.
Results for Base Case	At the submitted daily cost of [redacted], the use of umeclidinium is less expensive per patient annually than the current list price (1- and 5-year savings of [redacted] and [redacted] compared with tiotropium, [redacted] and [redacted] compared with aclidinium and glycopyrronium, and [redacted] and [redacted] compared with the currently used product mix of LAMAs).

COPD = chronic obstructive pulmonary disease; FEV_1 = forced expiratory volume in one second; ITC = indirect treatment comparison; LAMA = long-acting muscarinic antagonist; ODB = Ontario Drug Benefit; SGRQ = St. George's Respiratory Questionnaire; TDI = Transition Dyspnea Index.

Manufacturer's results

The manufacturer submitted a cost comparison of drug costs for umeclidinium compared with other long-acting muscarinic antagonist (LAMA) monotherapies used in the treatment of chronic obstructive pulmonary disease (COPD): tiotropium dry powder inhaler 18 mcg once daily (Spiriva HandiHaler); glycopyrronium bromide 50 mcg once daily (Seebri Breezhaler); and aclidinium bromide 400 mcg twice daily (Tudorza Genuair).[3] The analysis was undertaken from the public-payer perspective with a time horizon of five years.

Ontario Drug Benefit (ODB) formulary prices were used to calculate comparator costs. An 8% markup was applied to all drug costs. The assumption of similar treatment efficacy was based on a manufacturer-commissioned indirect treatment comparison (ITC), which found umeclidinium and all other comparators to be similarly efficacious with regard to lung function and several secondary outcomes of interest.[4] The manufacturer concluded that umeclidinium is cost-saving compared with tiotropium, and modestly cost-saving compared with aclidinium and glycopyrronium (Table 3).

TABLE 3: MANUFACTURER'S BASE-CASE RESULTS

Comparator	Incremental cost compared with UMEC — Year 1 ($)	Incremental cost compared with UMEC — Year 5 ($)
Umeclidinium, 62.5 mcg once daily (Incruse Ellipta)	-	-
Tiotropium, 18 mcg once daily (Spiriva HandiHaler)	[redacted]	[redacted]
Glycopyrronium, 50 mcg once daily (Seebri Breezhaler)	[redacted]	[redacted]
Aclidinium bromide, 400 mcg twice daily (Tudorza Genuair)	[redacted]	[redacted]
Current LAMA product mix (IMS Brogan data)	[redacted]	[redacted]

LAMA = long-acting muscarinic antagonist; UMEC = umeclidinium bromide.
Source: Manufacturer's pharmacoeconomic submission, Tables 4 and 5.[3]

A scenario analysis considered the cost savings expected under different market shares of umeclidinium when compared with the current product mix of LAMAs based on market share data from IMS Brogan. Analyses considering umeclidinium capturing 0.5%, 1%, and 2% of the LAMA market were assessed (all other comparators were modelled as having a decrease in proportion with their current market share). Under all market share scenarios, the use of umeclidinium is associated with cost savings (Table 4).

TABLE 4: MANUFACTURER'S SCENARIO ANALYSIS RESULTS

Umeclidinium Market Share	Incremental Cost Compared with Current Product Mix — Year 1 ($)	Incremental Cost Compared with Current Product Mix — Year 5 ($)
0.5%	–$0.79	–$3.46
1%	–$1.58	–$6.91
2%	–$3.16	–$13.83

Source: Manufacturer's pharmacoeconomic submission, Tables 4 and 5.[3]

CADTH Common Drug Review results

While the other LAMA products are the most direct comparators to umeclidinium, current COPD guidelines[9,10] also recommend long-acting beta2-agonists (LABAs) or combination inhaled corticosteroids/LABAs (ICSs/LABAs) as appropriate alternatives to LAMA therapy for some portions of the patient population within umeclidinium's approved indication. For example, the 2015 Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend a LAMA *or* a LABA for patients with significant symptoms at low risk of exacerbations (Group B), a LAMA *or* an ICS/LABA for patients with few symptoms at high risk of exacerbation (Group C), and a LAMA *and/or* an ICS/LABA for patients with many symptoms and a high risk of exacerbation (Group D).

The CADTH Common Drug Review (CDR) compared the annual cost per patient of umeclidinium with that of the available LABA and ICS/LABA products. Alberta Health list prices (without markup or fees) were used for the comparators rather than ODB formulary prices, as Alberta Health reimburses more LABA-containing products for patients with COPD; LAMA list pricing was identical between ODB and Alberta Health in April 2015. At the submitted price, umeclidinium is less expensive than all ICS/LABA fixed-dose combinations, but more expensive than most LABA-only products (Table 5). Price reductions of [redacted] and [redacted] are necessary for umeclidinium to be cost neutral compared with formoterol and indacaterol, respectively.

TABLE 5: CADTH COMMON DRUG REVIEW COMPARISON OF ANNUAL COST OF UMECLIDINIUM VERSUS LABA AND ICS/LABA ANNUAL COSTS

Comparator	Daily Cost ($)	Cost per Year ($)	Incremental Cost Compared With UMEC ($)	Price Reduction for UMEC for Cost Neutrality
Umeclidinium, 62.5 mg once daily	[redacted]	[redacted]	Reference	-
LABAs				
Formoterol	1.64 to 3.27	599 to 1,194	[redacted]	[redacted]
Indacaterol maleate	1.55	566	[redacted]	[redacted]
Salmeterol	1.87	683	[redacted]	-
ICS/LABAs				
Budesonide/formoterol (Symbicort Turbuhaler)	2.76	1,007	[redacted]	-
Fluticasone furoate/vilanterol trifenatate (Breo Ellipta)	4.00	1,460	[redacted]	-
Fluticasone propionate/salmeterol (Advair Diskus)	3.25 to 4.61	1,186 to 1,683	[redacted]	-

ICS = inhaled corticosteroid; LABA = long-acting beta2-agonist; UMEC = umeclidinium bromide.
Note: Markups and dispensing fees not included. Prices are based on the Alberta Health Drug Benefit list (March 2015), with the exception of UMEC (manufacturer's submitted price).

Further, according to current guidelines for the management of COPD, it is appropriate for some patients to be treated with a LAMA plus a LABA or a LABA and an ICS (e.g., alternate therapy choices for patients defined as Group B, C, or D by the 2015 GOLD guidelines).

As shown in Table 6, the cost (without markup or fees) of umeclidinium in combination with the available LABA products ranges from [redacted] to [redacted] per patient per year, while the annual per-patient cost of the indacaterol/glycopyrronium and umeclidinium/vilanterol fixed-dose combination inhalers is $978 and $985, respectively. Thus, for patients requiring combination therapy with a LAMA plus a LABA, the available LABA/LAMA fixed-dose combinations are less expensive than all possible combinations that include umeclidinium. While not included in Table 6, the use of a LABA/LAMA fixed-dose combination rather than umeclidinium plus an individual LABA would also save a dispensing fee every 30 to 90 days, depending on refill interval.

TABLE 6: COST OF UMECLIDINIUM PLUS A LABA COMPARED WITH COSTS OF AVAILABLE LABA/LAMA FIXED-DOSE COMBINATIONS

Available Individual LABAs	LABA Cost/Day	LABA + UMEC ([redacted]) Cost/Day	LABA + UMEC Cost/Year	Relative Cost vs. IND/GLYCO per Year ($978)	Relative Cost vs. UMEC/VIL per Year ($985)
Indacaterol 75 mcg q.d.	$1.55	[redacted]	[redacted]	[redacted]	[redacted]
Formoterol 12 mcg b.i.d.	$1.64	[redacted]	[redacted]	[redacted]	[redacted]
Salmeterol 50 mcg b.i.d.	$1.87	[redacted]	[redacted]	[redacted]	[redacted]
Formoterol 24 mcg b.i.d.	$3.27	[redacted]	[redacted]	[redacted]	[redacted]

b.i.d. = twice daily; IND/GLYCO = indacaterol/glycopyrronium 110/50 mcg daily (Ultibro Breezhaler); LABA = long-acting beta2-agonist; LAMA = long-acting anti-muscarinic antagonist; q.d. = once daily; UMEC = umeclidinium 62.5 mcg daily (Incruse Ellipta); UMEC/VIL= umeclidinium/vilanterol 625/25 mcg daily (Anoro Ellipta); vs. = versus.
Note: This table is not intended to imply the clinical appropriateness or equivalence of any included combination. Markups and dispensing fees not included.

TABLE 7: KEY LIMITATIONS

Identified limitation	Description	Implication
Lack of evidence of comparative efficacy on exacerbations and exercise	The manufacturer's ITC demonstrated equivalence between umeclidinium and other LAMAs in several dimensions (trough FEV_1 at 12 and 24 weeks, SGRQ score, TDI score, and use of rescue medications); however, efficacy in reducing the occurrence of exacerbations was not established. Exacerbations account for the majority of costs of COPD treatment,[5] and contribute significantly to patient quality of life and mortality. While a recent network meta-analysis[8] indicates that tiotropium, aclidinium, and glycopyrronium have similar efficacy in preventing exacerbations, no such data are available for umeclidinium. Further, exercise capacity is moderately to strongly correlated with functional activity and health-related quality of life.[12] Notably, FEV_1 has been known to be a poor predictor of exercise capacity.[13]	If umeclidinium has a different effect on exacerbations, this could affect whether a cost-minimization analysis is appropriate, as it would be unclear whether umeclidinium is, in fact, cost saving, and whether it could be considered clinically equivalent.
Exclusion of some relevant comparators	According to COPD treatment guidelines,[9,10] it is appropriate to treat some patients in the approved indication with either a LAMA or LABA or a LAMA or LABA plus ICS. Thus, LABAs and LABA/ICS combination products are comparators of interest for some portions of the indicated population. Additionally, patients with severe COPD are often treated with a LAMA and a LABA; thus, considering umeclidinium as part of double therapy and considering available LAMA/LABA combinations is appropriate.	While umeclidinium is less expensive than other LAMA monotherapies, it is more expensive than some LABAs. Use of umeclidinium + LABA is more expensive than all available fixed-dose combinations of LABA/LAMA. Umeclidinium is less expensive than LABA/ICS combinations.

COPD = chronic obstructive pulmonary disease; FEV1 = forced expiratory volume in one second; ICS = inhaled corticosteroid; ITC = indirect treatment comparison; LABA = long-acting beta2-agonist; LAMA = long-acting muscarinic antagonist; SGRQ = St. George's Respiratory Questionnaire; TDI = Transition Dyspnea Index.

APPENDIX 2: ADDITIONAL COST COMPARATORS

TABLE 8: COSTS OF ADDITIONAL COMPARATORS FOR THE TREATMENT OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Drug/Comparator	Strength	Dosage Form	Price ($)	Price/ Dose ($)	Recommended Daily Use	Daily Drug Cost ($)	Average Annual Drug Cost ($)
ICSs							
Budesonide (Pulmicort Turbuhaler)	100 mcg 200 mcg 400 mcg	Inhalant pwd (200 doses)	31.1600 63.7200 93.0000	0.16 0.32 0.46	200 mcg to 400 mcg twice daily	0.64 to 0.93	233 to 339
Ciclesonide (Alvesco)	100 mcg 200 mcg	Solution aerosol (120 doses)	45.2160 74.7600	0.38 0.62	100 mcg to 800 mcg once daily	0.38 to 2.49	138 to 910
Fluticasone propionate (Flovent Diskus, Flovent)	50 mcg 100 mcg 250 mcg 500 mcg	Inhalant pwd (60 doses)	15.1300[a] 23.9300[a] 41.2800 82.5400	0.25 0.40 0.69 1.38	100 mcg to 500 mcg twice daily	0.80 to 2.75	291 to 1,004
	50 mcg 125 mcg 250 mcg	Aerosol MDI (120 doses)	23.9300 41.2800 82.5400	0.20 0.34 0.69		0.80 2.75	291 to 1,004
Short-Acting Anticholinergic							
Ipratropium bromide	20 mcg	MDI (200 doses)	18.9200	0.09	2 x 20 mcg, 3 to 4 times daily	0.57 to 0.76	207 to 276
Short-Acting Beta2-Agonist							
Salbutamol (Airomir)	100 mcg	Inhalant pwd (200 doses)	5.0000	0.02	100 mcg to 200 mcg up to 4 times daily	0.10 to 0.20	36 to 73
Salbutamol (Ventolin, generics)	100 mcg	Inhalant pwd (200 doses)	5.0000	0.02	100 mcg to 200 mcg up to 4 times daily	0.10 to 0.20	36 to 73
Terbutaline (Bricanyl Turbuhaler)	0.5 mg	Inhalant pwd (200 doses)	15.2800	0.08	0.5 mg up to 6 times daily	0.08 to 0.46	28 to 167
Xanthine Bronchodilator							
Theophylline (Uniphyl, generic)	100 mg 200 mg 300 mg 400 mg 600 mg	SR tab SR tab SR tab SR tab SR tab	0.1300 0.1350 0.1750 0.5030 0.6090	0.13 0.14 0.18 0.50 0.61	Once daily, generally 400 mg to 800 mg (varies with patient's lean muscle mass)	0.50 to 1.00	184 to 367

ICS = inhaled corticosteroid; MDI = metered dose inhaler; pwd = powder; SR = sustained-release.
Source: Alberta Health Formulary (February 2015) unless otherwise stated.
[a] Saskatchewan Drug Plan (April 2015).

REFERENCES

1. [Pr]Incruse™ Ellipta™ (umeclidinium): 62.5 mcg umeclidinium per oral inhalation [product monograph]. Mississauga (ON): GlaxoSmithKline Inc; 2015 Jan 2. Submission Control No. 178543.
2. CDEC final recommendation: umeclidinium bromide/vilanterol trifenatate (Anoro Ellipta - GlaxoSmithKline). Indication: chronic obstructive pulmonary disease [Internet]. Ottawa: CADTH; 2015 Jan 15. [cited 2015 Apr 22]. (Common drug review). Available from: https://www.cadth.ca/sites/default/files/cdr/complete/cdr_complete_SR0371_Anoro_Ellipta_Jan-23-15.pdf
3. Pharmacoeconomic evaluation. In: CDR submission: Incruse™ Ellipta®, umeclidinium (as bromide), 62.5 mcg umeclidinium per oral inhalation. Company: GlaxoSmithKline [**CONFIDENTIAL** manufacturer's submission]. Mississauga (ON): GlaxoSmithKline. Mississauga (ON): GlaxoSmithKline; 2015 Mar 1.
4. Indirect treatment comparison of umeclidinium 62.5µg versus tiotropium 18µg, aclidinium 400µg and glycopyrronium 50µg in chronic obstructive pulmonary disease. In: CDR submission: Incruse™ Ellipta®, umeclidinium (as bromide), 62.5 mcg umeclidinium per oral inhalation. Company: GlaxoSmithKline [**CONFIDENTIAL** manufacturer's submission]. Mississauga (ON): GlaxoSmithKline; 2015 Feb 19.
5. Mittmann N, Kuramoto L, Seung SJ, Haddon JM, Bradley-Kennedy C, Fitzgerald JM. The cost of moderate and severe COPD exacerbations to the Canadian healthcare system. Respir Med. 2008 Mar;102(3):413-21.
6. Cazzola M, MacNee W, Martinez FJ, Rabe KF, Franciosi LG, Barnes PJ, et al. Outcomes for COPD pharmacological trials: from lung function to biomarkers. Eur Respir J [Internet]. 2008 Feb [cited 2015 May 10];31(2):416-69. Available from: http://erj.ersjournals.com/content/31/2/416.long
7. Seemungal TA, Donaldson GC, Paul EA, Bestall JC, Jeffries DJ, Wedzicha JA. Effect of exacerbation on quality of life in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 1998 May;157(5 Pt 1):1418-22.
8. Oba Y, Lone NA. Comparative efficacy of long-acting muscarinic antagonists in preventing COPD exacerbations: a network meta-analysis and meta-regression. Ther Adv Respir Dis. 2015 Feb;9(1):3-15.
9. O'Donnell DE, Aaron S, Bourbeau J, Hernandez P, Marciniuk DD, Balter M, et al. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease - 2007 update. Can Respir J [Internet]. 2007 Sep [cited 2015 Apr 1];14 Suppl B:5B-32B. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2806792/pdf/crj14005b.pdf
10. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: updated 2015. London (UK): GOLD; 2015.
11. Ontario drug benefit formulary/comparative drug index. Toronto: Ontario Ministry of Health and Long-Term Care; 2015 Jun 29.
12. Alison JA, McKeough ZI. Exercise and quality of life in COPD. In: Preedy VR, Watson RR, editors. Handbook of disease burdens and quality of life measures. New York: Springer; 2010. Chapter Volume 5 Part 3.9. p. 4119-31.
13. Carlson DJ, Ries AL, Kaplan RM. Prediction of maximum exercise tolerance in patients with COPD. Chest. 1991 Aug;100(2):307-11.