ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

Drug Class Review: Long-acting muscarinic antagonists (LAMAs) for treatment of chronic obstructive pulmonary disease (COPD)

Comprehensive Research Plan: Pharmacoepidemiology Unit

April 10th, 2014

30 Bond Street, Toronto ON, M5B 1W8 www.odprn.ca info@odprn.ca

ODPRN Drug Class Review Proposal
Pharmacoepidemiology Unit

Study Title: Epidemiologic analyses of long-acting muscarinic antagonists (LAMA) in the management of patients with Chronic Obstructive Pulmonary Disease (COPD)

Objective:	To examine trends in LAMA use across Canada, and to describe characteristics of patients prescribed LAMA products (either as single, dual or triple therapy)

Objective 1a: National and provincial trends in COPD Therapies

Study Design:	Design: Time series analysis with quarterly time intervals Study period: • *National and provincial trends (IMS Compuscript):* October 2009 to December 2013 Population: All provinces Prescription Drug Data Source: • *IMS Compuscript:* aggregated data for all prescriptions dispensed at retail pharmacies across Canada
Study Population:	**Inclusion Criteria:** • All privately and publically-funded prescriptions dispensed in Canada for LAMAs • Note that the Pharmacepidemiology Report on ICS/LABA combination products will provide more details on trends in use of other products used in COPD
Outcome(s) of Interest:	Measured over entire study period (quarterly): • Number of prescriptions dispensed • Total cost of prescriptions Report: • Overall rates of use by province • Distribution of prescriptions by payer (public, private, cash, NIHB)
Limitations:	• Information for privately funded prescriptions is only available at the prescription and unit level.

Objective 1b: Trends in publically-funded LAMA utilization in Ontario

Study Design:	Design: Time series analysis with quarterly time intervals Study period: • October 2009 to March 2014 Population: Ontario Prescription Drug Data Source: • *Ontario Drug Benefit Database (ODB)*: individual level data for all publically funded prescriptions dispensed in Ontario.
Study Population:	**Inclusion Criteria:** • All publically-funded prescriptions for LAMA products dispensed in Ontario (tiotropium-Spiriva, glycopyrronium bromide-Seebri Breezhaler)
Outcome(s) of Interest:	Measured over entire study period (quarterly): • Number of prescriptions dispensed • Number of units (puffs) dispensed • Total cost of prescriptions • Number of users • Cost per user Report: • Overall rates of use • Distribution of prescriptions by LAMA (tiotropium, glycopyrronium bromide) • Distribution of prescriptions by age (<65, 65+)
Limitations:	• Aclidinium (Tudorza Genuair) is not listed on the Ontario public drug formulary; we are therefore unable to obtain utilization information on this drug
Objective 2: Trends in Indication of Use of LAMAs	
Study Design:	Design: Cross-sectional analysis with annual time intervals Study period: April 2000 to March 2013 Prescription Drug Data Source: • Ontario Drug Benefit Database (ODB)
Study Population:	**Inclusion Criteria:** • All publically-funded prescriptions for LAMA products (tiotropium) dispensed in Ontario • Adults aged 35+ at time of LAMA dispensing

Outcome(s) of Interest:	Measured over entire study period (quarterly)
	• Proportion of LAMA prescriptions dispensed to disease cohorts:
	  ○ COPD + Asthma
	  ○ COPD only
	  ○ Asthma only
	  ○ Neither asthma nor COPD
	
	Stratify all analyses by:
	• Age (<65, 65+)

Limitations:	• COPD and Asthma diagnosis defined via validated datasets developed at ICES. Although these datasets have 85% and 84% sensitivity and 78% and 76% specificity, respectively, there may be some misclassification. • COPD database is only created for those aged 35 and older. • Glycopyrronium bromide (Seebri Breezhaler) was added to the provincial formulary in August 2013; therefore, use of this drug will not be captured in this analysis. We cannot extend the study period to capture glycopyrronium use since the COPD and Asthma databases are only updated to March 2013. Aclidinium (Tudorza Genuair) is not listed on the provincial drug formulary.
Objective 3: Characteristics of COPD Patients treated with LAMA Products in Ontario	
Study Design:	Design: Cross-sectional analysis Study period: April 2012 to March 2013 Prescription Drug Data Sources: • Ontario Drug Benefit Database (ODB)
Study Population:	**Inclusion Criteria:** ○ All publically-funded beneficiaries of Ontario with a diagnosis of COPD who are prescribed a LAMA product (tiotropium) ○ Cohort #1: Adults aged 36+ at time of LAMA dispensing ○ Cohort #2: Adults aged 66+ at time of LAMA dispensing

Variable(s) of Interest:	For each cohort, measure: • Number of patients • Number of new LAMA users • Age • Gender • History of asthma • COPD Severity • Residence in LTC • Drug plan coverage (Seniors, Ontario Disability Support Program, Ontario Works, Long-Term Care, Homes for Special Care, Trillium, Home Care, Special Drugs Program, Other) [based on first prescription dispensed over the study period) • Urban vs. rural residents • Socioeconomic status • Average annual cost of LAMA prescriptions per person • Past COPD maintenance therapy (1 year; ICS, LABA, ICS/LABA combination products, SABA, SAMA, theophylline) • Past treatment for COPD exacerbations (1 year) Stratify by: • Age (<65, 65+)
Limitations:	• COPD and Asthma diagnosis defined via validated datasets developed at ICES. Although these datasets have 85% and 84% sensitivity and 78% and 76% specificity, respectively, there may be some misclassification. • COPD database is only created for those aged 35 and older. • Glycopyrronium bromide (Seebri Breezhaler) was added to the provincial formulary in August 2013; therefore, use of this drug will not be captured in this analysis. We cannot extend the study period to capture glycopyrronium use since the COPD and Asthma databases are only updated to March 2013. Aclidinium (Tudorza Genuair) is not listed on the provincial drug formulary.
Objective 4: **a. Prevalence of single, dual and triple LAMA therapy**	
Study Design:	Design: Cross-sectional analysis Study period: April 2012 to March 2013 Prescription Drug Data Sources: • Ontario Drug Benefit Database (ODB)

Study Population:	**Inclusion Criteria:** ○ All publically-funded beneficiaries of Ontario with a diagnosis of COPD who are prescribed an LAMA product (tiotropium) ○ Adults aged 35+ at time of LAMA dispensing
Outcomes of interest:	Type of LAMA Therapy DEFINITION OF ONGOING USE Define ongoing use of LAMA therapy according to receipt of a subsequent prescription within 180 days of the prior prescription. For each individual, also define a period of continuous use of: ○ LABA ○ LAMA ○ ICS ○ ICS/LABA combination product Define individuals as single, dual or triple therapy based on whether they have overlapping periods of continuous use for more than 30 days as follows: ○ Single Therapy: LAMA with no overlapping use of other therapies ○ Dual Therapy: LAMA with overlapping use of LABA or ICS ○ Triple therapy: LAMA with overlapping use of either ICS/LABA combination product or overlapping use of both ICS and LABA products Note: if people have multiple different types of therapy over the study period, assign them to the highest category. ○ Report the following: ○ Number of individuals receiving each type of therapy ▪ Stratify by age (<65 vs. 65+) ▪ Stratify by COPD severity ▪ Stratify by dual therapy (LAMA+ICS, LAMA+LABA)
Objective 4: **b. Adherence to single, dual, and triple LAMA therapy**	
Study Design:	Design: Cross-sectional analysis Study period: April 2008 to March 2013 Prescription Drug Data Sources: • Ontario Drug Benefit Database (ODB)

Study Population:	**Inclusion Criteria:** ○ All publically-funded beneficiaries of Ontario with a diagnosis of COPD who are prescribed an LAMA product (tiotropium) ○ Adults aged 66+ at time of LAMA dispensing

Outcomes of interest:	Type of LAMA Therapy
	
	DEFINITION OF ADHERENCE
	Define ongoing use of LAMA therapy according to receipt of a subsequent prescription within 180 days of the prior prescription.
	
	For each individual, also define a period of continuous use of:
	○ LABA
	○ LAMA
	○ ICS
	○ ICS/LABA combination product
	
	Define individuals as single, dual or triple therapy based on whether they have overlapping periods of continuous use for more than 30 days as follows:
	
	○ Single Therapy: LAMA with no overlapping use of other therapies
	○ Dual Therapy: LAMA with overlapping use of LABA or ICS
	○ Triple therapy: LAMA with overlapping use of either ICS/LABA combination product or overlapping use of both ICS and LABA products
	
	Note: if people have multiple different types of therapy over the study period, assign them to the highest category.
	○ Report the following:
	  ○ Number of individuals receiving each type of therapy (single, dual, triple)
	  ▪ Stratify by COPD severity
	  ▪ Stratify by dual therapy (LAMA+ICS, LAMA+LABA)
	  ○ Median duration of therapy (days)
	  ▪ Stratify by therapy type (single, dual, triple)
	  ▪ Stratify by COPD severity
	  ▪ Stratify by dual therapy (LAMA+ICS, LAMA+LABA)
	  ○ Kaplan Meier curves of time to discontinuation of therapy
	  ▪ Stratify by therapy type (single, dual, triple)
	  ▪ Stratify by COPD severity
	  ▪ Stratify by type of dual therapy (LAMA+ICS vs. LAMA+LABA)

Objective 5:

a. Rapid Review of Relevant Literature

Objective:	Review of population-based studies on comparative effectiveness and safety of LAMA products among patients with COPD
Study Population	Adults with COPD
Study Design:	Observational studies • Comparative effectiveness studies • Safety studies
Study Inclusion Criteria	1. Canadian population 2. English Language 3. Published in last 10 years
Interventions	LAMA products (in single, dual or triple therapy)
Comparators	Any COPD therapy
Outcomes	Any reported outcomes

General Limitations

Two new LABA+LAMA combination products [indacaterol + glycopyrronium (Ultibro) and vilanterol + umeclidinium (Anoro Ellipta)] were approved for marketing in Canada in early 2014. There is therefore no utilization data available for these products during the study period; as a result, these products will not be captured in this analysis.