Common Drug Review

Pharmacoeconomic Review Report

May 2017

Drug	Propiverine hydrochloride (Mictoryl/Mictoryl Pediatric)
Indication	For symptomatic treatment of urinary incontinence and/or increased urinary frequency and urgency in patients with overactive bladder
Reimbursement Request	As per indication
Dosage form(s)	30 mg and 45 mg modified-release capsules and pediatric 5 mg tablet
NOC Date	January 5, 2017
Manufacturer	Duchesnay Inc.

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ABBREVIATIONS

CDR	CADTH Common Drug Review
ER	extended-release formulation
IR	immediate-release formulation
MR	modified-release formulation
OAB	overactive bladder
RCT	randomized controlled trial

EXECUTIVE SUMMARY

Background

Propiverine modified-release formulation (Mictoryl, MR) and propiverine pediatric (Mictoryl Pediatric) are detrusor relaxant drugs with antimuscarinic and calcium-modulating properties indicated for symptomatic treatment of urinary incontinence and/or increased urinary frequency and urgency in patients with overactive bladder (OAB).[1] Propiverine MR is available in 30 mg and 45 mg capsules, taken once daily, for adults with OAB. Propiverine pediatric is an immediate-release formulation (IR) available in 5 mg tablets for children, with body weight–adjusted dosage to be taken twice daily. The manufacturer has submitted a price of $1.39 per 30 mg or 45 mg MR capsule ($1.39 per day), and $0.37 per 5 mg IR tablet ($0.74 to $2.22 per day).[2] Propiverine IR 15 mg was never marketed in Canada.

Summary of the Economic Analysis Submitted by the Manufacturer

The manufacturer submitted a cost comparison of propiverine to oxybutynin IR, tolterodine IR and extended-release formulation (ER), solifenacin, mirabegron, fesoterodine, trospium, and darifenacin for both the adult and pediatric OAB populations in separate analyses over a one-year time horizon.[2] The manufacturer assumed clinical similarity to other anticholinergics in the adult OAB population on the basis of a randomized controlled trial (RCT) comparing 30 mg propiverine MR once daily to 15 mg propiverine IR twice daily and placebo,[3] and a noninferiority trial comparing 30 mg propiverine MR with 4 mg tolterodine ER.[4] Propiverine MR was noninferior to propiverine IR in terms of change from baseline for incontinence frequency, noninferior to tolterodine for change from baseline micturition frequency, and superior to tolterodine in terms of reducing incontinence frequency. No comparisons of propiverine MR to other OAB treatments were available.

For the pediatric population, the manufacturer assumed clinical similarity on the basis of a propiverine IR placebo-controlled RCT,[5,6] and a retrospective observational cohort study of children with urinary incontinence due to OAB taking propiverine IR or oxybutynin IR tablets.[7] Propiverine pediatric was superior to placebo in terms of reducing incontinence and micturition frequencies. The observational study found no significant differences in efficacy and improved tolerability with propiverine pediatric compared to oxybutynin, although the propiverine pediatric appeared to be underdosed and there appeared to be a larger number of patients receiving propiverine pediatric on unspecified concomitant therapy compared with placebo (14.2% versus 4.4%).[7]

Key Limitations

Substantial Uncertainty in Assumption of Clinical Similarity

The manufacturer made the assumption of clinical similarity necessary to support the use of a cost comparison analysis on the basis of the International Continence Society and the European Association of Urology guidelines, which state, from a clinical perspective, "There is no consistent evidence that one antimuscarinic drug is superior to an alternative antimuscarinic drug for cure or improvement of urinary incontinence."[2] While the manufacturer did provide some evidence that propiverine MR was at least noninferior to propiverine IR and tolterodine in terms of efficacy for the adult population,[3,4] no direct or indirect comparisons of propiverine MR to other OAB treatments were available. Evidence is even less certain in the pediatric population, where the basis for the assumption was an observational study that found no significant differences in efficacy and improved tolerability with propiverine pediatric compared to oxybutynin.[7] Given the lack of direct or indirect evidence comparing propiverine with other anticholinergics (aside from propiverine IR, which is not marketed in Canada), substantial uncertainty

exists in the assumption of clinically similar efficacy, safety and tolerability between propiverine and appropriate comparators in a Canadian setting.

Patient Weight and Dose Distribution

While the dose distribution is not a consideration in drug costs in the adult population due to flat pricing for all treatments compared, the recommended dosing of propiverine pediatric is weight-based and ranges from $0.74 to $2.22 per day. The distribution the manufacturer assumed was based on unspecified German utilization data and was not considered appropriate in a Canadian context by the clinical experts consulted by CADTH Common Drug Review (CDR). It also was inconsistent with both the patient weights in the propiverine pediatric trial population and the doses used in the trial.[5,6] Reanalysis by CDR increased the weighted-average cost per day of propiverine pediatric from $1.30 to $1.48 per patient per day.

Actual Analysis Time Horizon

The manufacturer incorporated 365 days of therapy into their one-year time horizon for the adult population economic analysis but only included 180 days of therapy over one year in their pediatric population, citing expert opinion. The experts consulted by CDR did not agree that this was appropriate, and an observational study cited elsewhere by the manufacturer concluded that patients on their first anticholinergic remained on it for a mean of 429 days.[8] CDR's reanalysis for the pediatric population thus included 365 days of therapy.

Issues for Consideration

Dosage Form May Be of Limited Use in the Pediatric Population

The pediatric expert consulted by CDR raised concerns that the utility of propiverine pediatric may be limited as many pediatric patients are unable or reluctant to swallow tablets.

Publicly Available List Prices May Not Reflect Actual Costs to Public Plans

The actual costs paid by Canadian public drug plans for anticholinergics and other therapies for OAB are likely lower than those listed on publicly available formularies, which reduces the relative attractiveness of the submitted prices of propiverine MR and propiverine pediatric.

Results/Conclusions

CDR reviewers accepted the manufacturer's conclusion that at $507 per patient per year, the cost of propiverine MR for adults with OAB ranged from $400 more than oxybutynin IR ($107 per patient annually) and $87 less than trospium (per patient annually $595). CDR reanalyses of the pediatric population concluded that propiverine pediatric would cost a weighted average of approximately $540 per patient per year, which was $468 more than oxybutynin IR ($71 per patient annually) and $54 less than trospium ($595 per patient annually). The experts consulted by CDR believed the most relevant comparator for the pediatric population in Canada to be oxybutynin syrup, which was not considered by the manufacturer and costs $378 less per patient per annually than CDR's estimate for propiverine pediatric. The cost of propiverine MR would need to be reduced by 79% to be cost-neutral to oxybutynin IR in the adult population, and by 70% to be cost-neutral to oxybutynin syrup in the pediatric population. CDR noted substantial uncertainty in the assumption of clinical similarity between propiverine and its comparators, particularly in the pediatric population.

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. Existing product reimbursement agreements are not reflected in the table and as such may not represent the actual costs to public drug plans.

TABLE 1: COST COMPARISON TABLE FOR DRUGS USED FOR THE MANAGEMENT OF OAB IN ADULTS

Drug/Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Daily Drug Cost ($)	Annual Drug Cost ($)
Propiverine hydrochloride (Mictoryl)	**30 mg 45 mg**	**ER cap**	**1.3900**	**30 mg daily, increasing to 45 mg daily if needed**	**1.39**	**507**
Darifenacin (Enablex)	7.5 mg 15 mg	ER tab	1.6116	7.5 mg to 15 mg daily	1.61	588
Fesoterodine fumarate (Toviaz)	4 mg 8 mg	ER tab	1.5000	4 mg to 8 mg daily	1.50	548
Mirabegron (Myrbetriq)	25 mg 50 mg	ER tab	1.4600	25 mg to 50 mg once daily	1.46	533
Onabotulinum toxin A (Botox)	50 units 100 units 200 units	vial	178.5000 357.0000 714.0000	100 units/dose Every 3 months Every 4 months[b]	 3.91 2.93	 1,428 1,071
Oxybutynin chloride (generics)	5 mg	tab	0.0986	5 mg 2 to 3 times daily	0.20 to 0.30	72 to 108
Oxybutynin (Oxytrol)	36 mg	TD patch	6.4775[c]	One patch twice weekly	1.85	676
Oxybutynin chloride (Gelnique)	100 mg/g	topical gel	1.9763[d]	One 1 g sachet daily	1.98	721
Oxybutynin chloride ER (Ditropan XL)	5 mg 10 mg	ER tab	2.3292[c]	5 mg to 30 mg daily	2.33 to 6.99	850 to 2,550
Solifenacin succinate (generics)	5 mg 10 mg	tab	0.4223	5 mg to 10 mg daily	0.42	154
Tolterodine ER (generics)	2 mg 4 mg	ER cap	0.4911	4 mg daily	0.49	179
Tolterodine (generics)	1 mg 2 mg	tab	0.2455	2 mg twice daily	0.49	179
Trospium chloride (Trosec)	20 mg	tab	0.8144	20 mg twice daily	1.63	595

cap = capsule; ER = extended-release formulation; OAB = overactive bladder; tab = tablet; TD = transdermal.

[a] Manufacturer's submitted price.

[b] Onabotulinum toxin A is indicated for OAB up to every three months; however, some plans, including Ontario Drug Benefit, limit reimbursement to three times annually.

[c] Quebec Liste des medicaments (January 2017).

[d] Wholesale price nationwide as reported by QuintilesIMS Delta PA (accessed November 17, 2016).

Note: All prices are from the Ontario Drug Benefits Formulary (accessed January 2017) unless otherwise indicated and do not include mark-ups and dispensing fees.

TABLE 2: COST COMPARISON TABLE FOR DRUGS USED FOR THE MANAGEMENT OF OAB IN CHILDREN

Drug/Comparator	Strength	Dosage Form	Price ($)	Recommended Dose	Average Daily Drug Cost ($)	Annual Drug Cost ($)
Propiverine hydrochloride (Mictoryl Pediatric)	**5 mg**	**tab**	**0.3700[a]**	**10 mg to 30 mg daily in two doses based on weight as laid out in monograph table**	**0.74 to 2.22**	**270 to 810**
Oxybutynin chloride (generics)	5 mg	tab	0.0986	5 mg twice daily	0.20	72
	1 mg/mL	oral syrup	0.0444	5 mg twice daily	0.44	162
Comparators Without a Pediatric Indication						
Darifenacin (Enablex)	7.5 mg 15 mg	ER tab	1.6116	7.5 mg to 15 mg daily	1.61	588
Fesoterodine fumarate (Toviaz)	4 mg 8 mg	ER tab	1.5000	4 mg to 8 mg daily	1.50	548
Mirabegron (Myrbetriq)	25 mg 50 mg	ER tab	1.4600	25 mg to 50 mg once daily	1.46	533
Solifenacin succinate (generics)	5 mg 10 mg	tab	0.4223	5 mg to 10 mg daily	0.42	154
Tolterodine ER (generics)	2 mg 4 mg	ER cap	0.4911	4 mg daily	0.49	179
Tolterodine (generics)	1 mg 2 mg	tab	0.2455	2 mg twice daily	0.49	179
Trospium chloride (Trosec)	20 mg	tab	0.8144	20 mg twice daily	1.63	595

cap = capsule; ER = extended-release formulation; OAB = overactive bladder; tab = tablet.
[a] Manufacturer's submitted price.
Note: All prices are from the Ontario Drug Benefit Formulary (accessed January 2017) unless otherwise indicated and do not include mark-ups and dispensing fees.

APPENDIX 1: REVIEWER WORKSHEETS

TABLE 3: SUMMARY OF MANUFACTURER'S SUBMISSION

Drug Product	Propiverine hydrochloride (Mictoryl, Mictoryl Pediatric)
Treatment	Adults: 30 mg to 45 mg daily Children: 0.8 mg per kg in 2 doses, per monograph chart
Comparators	Oxybutynin IR Tolterodine ER Tolterodine ER Solifenacin Mirabegron Fesoterodine Trospium Darifenacin
Study Question	From the Ministry of Health perspective, what is the cost of propiverine and propiverine pediatric relative to alternative pharmacotherapies for OAB in both adult and pediatric populations?
Type of Economic Evaluation	Cost comparison
Target Population	Per the clinical trials, primarily adult and pediatric patients with OAB.
Perspective	Public drug plan
Outcome(s) Considered	Costs, incremental costs
Key Data Sources	
Cost	ODB Formulary, manufacturer's submitted price for propiverine
Clinical Efficacy	Adults: Junemann et al. (2006), Leng et al. (2016) Pediatric: Marschall-Kehrel et al. (2009)
Harms	Adults: Junemann et al. (2006), Leng et al. (2016) Pediatric: Marschall-Kehrel et al. (2009), Alloussi et al. (2010) observational study
Time Horizon	Adult 1 year, pediatric 180 days of use
Results for Base Case	Adults: At $507 per patient, the annual cost of propiverine ranged from $87 less to $400 more than its comparators. Pediatric: At a weighted-average cost of $233 per patient, 180 days of use with propiverine pediatric ranged from $60 less to $198 more than the included comparators.

ER = extended-release formulation; IR = immediate-release formulation; OAB = overactive bladder; ODB = Ontario Drug Benefit.

The manufacturer submitted a cost comparison of propiverine to oxybutynin immediate-release formulation (IR), tolterodine IR and extended-release formulation (ER), solifenacin, mirabegron, fesoterodine, trospium, and darifenacin for both the adult and pediatric overactive bladder (OAB) populations in separate analyses over a one-year time horizon.

The manufacturer assumed clinical similarity to other anticholinergics in the adult OAB population on the basis of Junemann et al. (2006),[3] a randomized controlled trial (RCT) comparing 30 mg propiverine MR once daily to 15 mg propiverine IR twice daily and placebo, and Leng et al. (2016),[4] a noninferiority

trial comparing 30 mg propiverine modified-release formulation (MR) with 4 mg tolterodine ER. Propiverine MR was noninferior to propiverine IR in terms of change from baseline for incontinence frequency, noninferior to tolterodine for change from baseline micturition frequency, and superior to tolterodine in terms of reducing incontinence frequency. No comparisons of propiverine MR to other OAB treatments were available.

For the pediatric population, the manufacturer assumed clinical similarity on the basis of Marschall-Kehrel et al. (2009),[5,6] a propiverine IR placebo-controlled RCT, and Alloussi et al. (2010),[7] a retrospective observational cohort study of children with urinary incontinence due to OAB taking propiverine IR or oxybutynin IR tablets. Propiverine pediatric was superior to placebo in terms of reducing incontinence and micturition frequencies. The observational study found no significant differences in efficacy and improved tolerability with propiverine pediatric compared with oxybutynin, although the propiverine appeared to be underdosed and there appeared to be a larger number of propiverine patients (14.2%) on unspecified concomitant therapy compared with oxybutynin (4.4%), though the study reported that "concomitant treatment did not confound the primary outcome variable."[7]

No indirect comparisons were submitted by the manufacturer and CADTH Common Drug Review (CDR) clinical reviewers did not identify relevant indirect comparisons of propiverine MR to other OAB treatments.

Manufacturer's Results

The manufacturer found that for adults with OAB, the use of propiverine MR ($507 per patient per year) would cost between $80 less and $400 more per patient per year than its comparators (see Table 4).

TABLE 4: MANUFACTURER'S RESULTS FOR THE USE OF PROPIVERINE VERSUS COMPARATORS FOR THE TREATMENT OF OVERACTIVE BLADDER IN ADULTS

Comparator	Unit Strength	Units Per Day	Cost Per Unit ($)	Weighted Utilization	Annual Cost ($)	Incremental Cost (Savings) With Propiverine
Propiverine	30 mg 45 mg	1 1	1.3900	75% 25%	507.35	Reference
Oxybutynin IR	5 mg	3	0.0980	100%	107.31	400.04
Tolterodine ER	2 mg 4 mg	1 1	0.4911	75% 25%	179.25	328.10
Tolterodine IR	1 mg 2 mg	2 2	0.2455	50% 50%	179.22	328.14
Solifenacin	5 mg 10 mg	1 1	0.4223	75% 25%	154.14	353.21
Mirabegron	25 mg 50 mg	1 1	1.4600	75% 25%	532.90	(25.55)
Fesoterodine	4 mg 8 mg	1 1	1.5000	75% 25%	547.50	(40.15)
Trospium	20 mg	2	0.8144	100%	597.51	(87.16)
Darifenacin	7.5 mg 15 mg	1 1	1.6116	75% 25%	588.23	(80.88)

ER = extended-release formulation; IR = immediate- release formulation.
Note: Derived from Table 2 and Table 4 in the manufacturer's economic submission.[2]

In the pediatric population, assuming that all children using propiverine take three or four 5 mg tablets daily and that patients would receive an average of 180 days of medication per year, this leads to a cost of $233 per patient, which ranges from $60 less to $198 more than the cost of 180 days of the comparators (see Table 5).

TABLE 5: MANUFACTURER'S RESULTS FOR THE USE OF PROPIVERINE PEDIATRIC VERSUS COMPARATORS FOR THE TREATMENT OF OVERACTIVE BLADDER IN CHILDREN

Comparator	Unit Strength	Units Per Day	Cost Per Unit ($)	Weighted Utilization	Cost for 180 Days of Use ($)	Incremental Cost (Savings) With Propiverine
Propiverine pediatric	5 mg	2 3 4 5 6	0.3700	0% 50% 50% 0% 0%	233.10	Reference
Oxybutynin IR	5 mg	2	0.0980	100%	35.28	197.82
Tolterodine ER	2 mg 4 mg	1 1	0.4911	100% 0%	88.40	144.70
Tolterodine IR	1 mg 2 mg	2 2	0.2455	100% 0%	88.38	144.72
Solifenacin	5 mg 10 mg	1 1	0.4223	100% 0%	76.01	157.09
Mirabegron	25 mg 50 mg	1 1	1.4600	100% 0%	262.80	(29.70)
Fesoterodine	4 mg 8 mg	1 1	1.5000	100% 0%	270	(36.90)
Trospium	20 mg	2	0.8144	100%	293.18	(60.08)
Darifenacin	7.5 mg 15 mg	1 1	1.6116	100% 0%	290.09	(56.99)

ER = extended-release formulation; IR = immediate- release formulation.
Note: Derived from Table 3 and Table 5 in the manufacturer's economic submission.[2]

The manufacturer also presented an average overall incremental cost of propiverine versus its comparators when equally weighted (base case), and using market share distributions based on Ontario Drug Policy Research Network user and forecasted data. CDR did not consider these average incremental cost estimates to be helpful as:

- They assume propiverine will displace its comparators in either equal proportions or in the same proportions as their current or forecasted market shares, which is unlikely given differing dosing regimens and the availability of the non-antimuscarinic mirabegron.
- Market shares are fluctuating with the introduction of newer antimuscarinics and mirabegron and vary by jurisdiction. For example, in the third quarter of 2016, oxybutynin IR made up 95% of all public claims for the included comparators in British Columbia, but only 56% and 20% in Saskatchewan and Ontario, respectively (derived from IMS Quintiles Pharmastat public claims data).
- The manufacturer's method of forecasting from Ontario Drug Policy Research Network data is unclear.

Other sensitivity analyses included the reduction of adherence from 100% to 80%, which changed the magnitude but not the direction of incremental costs or savings associated with propiverine, as well as

the inclusion of pharmacy fees and mark-ups, which had no impact on incremental costs due to identical dispensing patterns across comparators.

CADTH Common Drug Review Results

The manufacturer did not include all available treatments for OAB available in Canada, leaving out oxybutynin ER, the gel and patch formulations, as well as onabotulinum toxin A (Botox). However, CDR did not consider this a significant limitation given that alternate formulations of oxybutynin are rarely covered by CDR-participating drug plans and are more expensive than the manufacturer's submitted price for propiverine and propiverine pediatric. Additionally, onabotulinum toxin A use is unlikely to be replaced by another entry into the anticholinergic market.

CDR noted that, according to the manufacturer's results, the cost of propiverine would need to be reduced by 79% to be cost-neutral to oxybutynin IR in the adult population, 70% to be cost-neutral to solifenacin, and 65% to be cost-neutral to either form of tolterodine.

While CDR reviewers found the manufacturer's cost comparison for the adult population to be otherwise well conducted given that dose distribution has no impact on the cost of any comparator, the analysis for the pediatric population had more significant limitations. The manufacturer assumed that children would receive six 30-day claims in the year-long time horizon on the basis of expert opinion; however, neither expert consulted by CDR agreed with this assessment. While they believed that pediatric patients using anticholinergics would have high discontinuation rates due to side effects such as dry mouth and constipation similar to those in the adult population, they believed adherence to therapy would be higher for the duration of treatment due to parental administration. The observational study used by the manufacturer to inform their pediatric market share estimates found that the mean time a child spent on their initial anticholinergic therapy was 429 days, or over one year.[8] This substantially reduces the reported cost per year for all comparators, and thus also reduces incremental costs or savings between comparators.

The manufacturer did not consider oxybutynin oral syrup as a comparator in the pediatric population; this formulation is indicated in the pediatric population[9] and experts consulted by CDR specified that the majority of children receiving anticholinergics would be prescribed oxybutynin syrup due to the difficulty in teaching children to swallow tablets. While not specified in the propiverine pediatric product monograph,[1] the manufacturer clarified that the propiverine 5 mg IR tablets are small and sugar-coated, making it possible to crush and administer them with a spoon of preferred food when required. This technique is commonly used by pediatricians for children, but not considered by marketing authorities. Given the number of daily propiverine IR tablets some children would need to take, this extra step may reduce its utility relative to a pre-formulated syrup.

The manufacturer also assumed that 50% of children would use 15 mg of propiverine pediatric per day, and 50% 20 mg per day, and used this distribution to calculate an average cost per day of $1.30 per person. However, according to the recommended dose table in the product monograph, this suggests that all children using propiverine pediatric would weigh between 17 kg and 29 kg (see Table 6).

TABLE 6: MANUFACTURER'S ASSUMED PROPIVERINE PEDIATRIC DOSE DISTRIBUTION WITH MONOGRAPH RECOMMENDED DOSING AND RESULTANT DAILY COST

Body Weight (kg)	Number of 5 mg Tablets Per Day	Daily Cost ($)	Dose Distribution in Manufacturer's Econ Model[2]	Weighted-Average Daily Cost ($)
12 to 16	1-1	0.74	0%	1.30
17 to 22	1-2	1.11	50%	
23 to 28	2-2	1.48	50%	
29 to 34	2-3	1.85	0%	
≥ 35	3-3	2.22	0%	

Econ = economic.

While the experts consulted by CDR agreed that very few children less than 17 kg would receive an anticholinergic for OAB as many would still be toilet training and unable to swallow tablets, they did not agree that no children more than 28 kg would receive propiverine pediatric. According to World Health Organization growth charts, 25% of both boys and girls weigh 29 kg or more by the time they are eight years and four months old, while 50% weigh 29 kg or more by the time they are nine years and four months.[10,11] The experts consulted by CDR estimated that at least 10% of children receiving anticholinergics would be more than nine years old and thus weigh more than 29 kg. Additionally, the description of the manufacturer's own trial population reported a minimum weight of 18 kg, a lower quartile of 21.5 kg, a median of 24.3 kg, an upper quartile of 30 kg, and a maximum of 43 kg.[6] Using these data to estimate a dose distribution leads to a daily propiverine pediatric cost of $1.48 per person (see Table 7).

TABLE 7: TRIAL-WEIGHT-DERIVED PROPIVERINE PEDIATRIC DOSE DISTRIBUTION WITH MONOGRAPH RECOMMENDED DOSING AND RESULTANT DAILY COST

Body Weight (kg)	Number of 5 mg Tablets Per Day	Daily Cost ($)	Weight Distribution Estimated from Trial Population[6]	Weighted-Average Daily Cost ($)
12 to 16	1-1	0.74	0%	1.48
17 to 22	1-2	1.11	25%	
23 to 28	2-2	1.48	50%	
29 to 34	2-3	1.85	25%	
≥ 35	3-3	2.22	0%	

Finally, children in the Marschall-Kehrel 2009[6] double-blind, placebo-controlled trial were actually dosed at 20 mg per day if they weighed under 28 kg, and 30 mg per day if they weighed 28 kg or more. Thirty-four of 108 children (31%) weighed 28 kg or more; if these data are used to estimate the dose distribution, the cost of propiverine pediatric increases to $1.71 mg per day (see Table 8). However, CDR reviewers did consider this distribution to overestimate the likely dosing in clinical practice due to a number of the children receiving more than 0.9 mg per kg, as well as older children likely being switched to the MR 30 mg adult tablet when considered appropriate in clinical practice.

TABLE 8: TRIAL-DOSE-DERIVED PROPIVERINE PEDIATRIC DOSE DISTRIBUTION WITH MONOGRAPH RECOMMENDED DOSING AND RESULTANT DAILY COST

Body Weight (kg)	Number of 5 mg Tablets Per Day	Daily Cost ($)	Dose Distribution Used in Trial Population[6]	Weighted-Average Daily Cost ($)
12 to 16	1-1	0.74	0%	1.71
17 to 22	1-2	1.11	0%	
23 to 28	2-2	1.48	69%	
29 to 34	2-3	1.85	0%	
≥ 35	3-3	2.22	31%	

CDR thus included oxybutynin syrup as a main comparator for the pediatric population, incorporated 365 days of treatment into the year-long time horizon, and estimated the assumed patient weight and thus dose distribution from the Marschall-Kehrel trial population (Table 9) in its final analysis.[6]

TABLE 9: CDR'S RESULTS FOR THE USE OF PROPIVERINE PEDIATRIC VERSUS COMPARATORS FOR THE TREATMENT OF OVERACTIVE BLADDER IN CHILDREN

Comparator	Unit Strength	Units Per Day	Cost Per Unit ($)	Weighted Utilization	Annual Cost ($)	Incremental Cost (Savings) With Propiverine	Price Reduction for Propiverine to be Cost-Neutral
Propiverine pediatric	5 mg	2 3 4 5 6	0.3700	0% 25% 50% 25% 0%	540.35	Reference	Reference
Oxybutynin IR	5 mg	2	0.0980	100%	71.56	468.79	87%
Oxybutynin syrup	1 mg/mL	10	0.0444	100%	162.10	378.24	70%
Tolterodine LA	2 mg 4 mg	1 1	0.4911	100% 0%	179.30	361.05	67%
Tolterodine IR	1 mg 2 mg	2 2	0.2455	100% 0%	179.26	361.08	67%
Solifenacin	5 mg 10 mg	1 1	0.4223	100% 0%	154.18	386.17	71%
Mirabegron	25 mg 50 mg	1 1	1.4600	100% 0%	533.05	7.30	1%
Fesoterodine	4 mg 8 mg	1 1	1.5000	100% 0%	547.65	(7.30)	None
Trospium	20 mg	2	0.8144	100%	594.67	(54.33)	None
Darifenacin	7.5 mg 15 mg	1 1	1.6116	100% 0%	588.40	(48.05)	None

ER = extended-release; IR = immediate-release formulation; LA = long-acting formulation.

In conclusion, on average, propiverine pediatric is $378 to $469 more expensive per patient per year than oxybutynin, the only other anticholinergic indicated for use in children in Canada. It is also more expensive than tolterodine IR, tolterodine long-acting formulation, and solifenacin, the anticholinergics that appear most likely to be used off-label in Canada for pediatric patients with OAB.[8] It is roughly equivalent in price to mirabegron, which is not indicated in the pediatric population but may begin to be used in clinical practice as clinicians become more familiar with it due to its alternate mechanism of action and side-effect profile.

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