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Proton Pump Inhibitors: A High Cost Employee Benefit with Over-the-Counter Alternatives

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EXECUTIVE SUMMARY

The healthcare affordability crisis combined with a difficult economic period means tough decisions for employers who sponsor health benefit plans. Certainly, one option is increasing employee costs through higher cost sharing or higher contributions. Other approaches use medical management, network restrictions, and benefit design to shift spending to get the most value. Prescription drugs account for about 15% of an employer's total medical spend and making decisions about which drugs to include on a formulary is a standard approach to managing cost. This paper is about one such decision, the potential to shift one costly class of prescription drugs – Proton Pump Inhibitors (PPIs) – out of the pharmacy benefit to greater over the counter (OTC) usage. Today three PPI OTC products are available, one of which has been available since 2003.

PPIs are a top spend prescription drug category for employers. Express Scripts 2009 Drug Trend Report (published April 2010) indicates that the *ulcer disease drug class*, of which PPIs contribute 91% of the utilization and 94% of the cost, is the 6th most costly therapeutic class. According to the report, 8.2% of members have one or more scripts for ulcer drugs, and this category contributes $45.75 PMPY to total PMPY spend.[1] Although spending on this category has moderated the past few years with some increased shift to generics and OTC options, a dramatic reduction has not occurred. Given the OTC availability of PPIs, many employers would benefit from a closer examination of PPI prescription drug spend and PPI prescription coverage policies.

We analyzed the PPI prescription drug spend for a typical PPO type commercially insured population using Medstat 2008 claim data. We found that:

- 6% of the total population (including children) had one or more prescription claims for a PPI
- 43% of those have 3 or fewer PPI prescriptions
- Annual PPI allowed spend per PPI user was $717 with 80% of that spend contributed by brand PPIs
- Per member per month (PMPM) allowed spend on PPIs was $3.72 PMPM which amounts to approximately 6.7% of prescription drug spend and 1.2% of total allowed spend (based on an average $305 total allowed PMPM)

Employers considering shifting PPI usage to OTC will probably want to examine the portion of their PPI prescription drug takers that could use OTC PPI therapy. OTC PPIs are indicated for frequent heartburn with recommendations for a 14 day course of therapy no more than once every 4 months unless otherwise directed by the prescriber. It is important to balance cost effectiveness of OTC PPIs with the needs of patients for whom an OTC PPI therapy is not an appropriate option. In considering coverage decisions for PPIs, each employer should consult with medical experts to determine which patients may use OTC products, as PPI's vary in dosage, duration of use, and indications.

OTC PPIs are not indicated for all GI conditions, so we classified each PPI user into a GI condition category. This allowed us to examine the opportunity to shift certain prescription PPI takers to OTC. Our analysis found a majority of PPI users are not diagnosed with any relevant GI condition in the same year or the year prior to the fill of a PPI prescription – we have grouped these PPI users into the "not coded" category. If a severe GI diagnosis were involved, we would expect to see one or more claims containing such diagnosis code during the year of the prescription or the year prior.

In addition to the heartburn category for which OTC PPIs is indicated, there is also likely opportunity in the *not coded* cohort as many of these patients may have milder GI conditions including heartburn. The majority of prescription PPI takers appear to be appropriate for shift to OTC (See Figure 1).

FIGURE 1: PREVALENCE OF GI CONDITIONS AMONG PRESCRIPTION PPI USERS (COMMERCIAL POPULATION)

CONDITION	PORTION OF PATIENTS	ALLOWED $$ PER 10,000 EMPLOYEES	PAID PPI PMPM
NOT CODED*	55.7%	$481,762	$1.61
GERD	32.2%	$329,022	$1.10
SEVERE DIAGNOSES**	3.6%	$36,709	$0.12
DYSPEPSIA	3.1%	$26,098	$0.09
HEARTBURN	1.7%	$17,595	$0.06
NON-EROSIVE ESOPHAGITIS	1.7%	$15,261	$0.05
HIATAL HERNIA	1.0%	$9,946	$0.03
PEPTIC ULCER	1.0%	$7,721	$0.03
TOTAL	100.0%	$916,393	$3.09

*Not Coded means the patient did not have claims coded with one of the GI conditions, as described in Appendix B.
**Severe Diagnoses are defined in Appendix B.
Milliman analysis of 2008 Medstat Marketscan database.

To successfully evaluate and implement a pharmacy benefit design change, employers should proceed through several steps including:

- Determine current spending on the PPI category
- Model potential savings with OTC shift (Milliman savings model available in August 2010 at: https://www.otcbenefitadvisor.com)
- Define medical considerations
- Review operational considerations
- Consider design incentives
- Communicate plan design change

This paper was commissioned by Procter & Gamble, which markets an OTC PPI. In writing this paper, the authors do not imply Milliman's endorsement of any product or policy. As with any economic study, the information contained in this report cannot consider all possible factors, and our information may not be suitable for use in certain situations. Particular employers or insurers may have results that differ significantly from the averages presented here. Employers should obtain advice from their own internal or external medical and benefits professionals when reviewing plan benefit designs.

I. HISTORICAL PERSPECTIVE ON OTC PRODUCT USAGE

Over-the-counter (OTC) medicines are considered safe, clinically effective and cost effective as well as convenient since they often do not require the assistance of a health care provider. Millions of Americans use these products daily to treat a wide variety of symptoms. There are many OTC products available that previously were only available by prescription. Surveys indicate that 92% of American consumers consider OTC drugs effective; 83% consider OTC drugs safe; and 73% report that they prefer to treat symptoms themselves with OTC drugs.[2]

When an ingredient is first introduced as an OTC medicine, in some instances it has been first marketed by a manufacturer as a prescription medicine. After a sufficient amount of time has passed to enable the manufacturer to gather appropriate scientific information on the product, the manufacturer may elect to submit a new drug application to the Food and Drug Administration (FDA) for consideration for OTC status. Drug manufacturers or citizen groups can petition the FDA to switch an approved prescription medication to OTC status. The main criteria considered by the FDA for a proposed switch are 1) whether the product has a high safety profile and 2) if labeling can be clear, accurate and understood by the lay person. Essentially the FDA weighs the risks and benefits of the proposed switch.[3]

Since 1976, over 90 ingredients, indications, or dosage strengths have been approved for OTC switch status.[4] The following OTC medicines were once prescription only and are now well known OTC brands[5] and also have generic versions:

- Pain - Advil®, Aleve®, Naproxen
- Allergy - Claritin®, Zyrtec®
- Heartburn H2 blockers- Zantac®, Tagamet®, Pepcid AC®
- Obesity - Xenical®
- Yeast Infections - Monistat®

Proton Pump Inhibitors (PPIs) were available by prescription only, until 2003, when the first PPI became available as OTC. Today, three PPIs are available as OTC products. The wide availability of OTC PPIs today, combined with the high use and cost of brand PPIs, raises the potential for cost reductions under certain circumstances for both employers and employees. Many employers have already seen the cost of the PPI category decline due to more wide spread generic use and the increased availability of OTC options but significant opportunity to further reduce spend in this prescription drug class still exists.

PPI Indications

Proton pump inhibitors (PPIs) are a class of drugs that decrease acid production in the stomach by blocking an enzyme needed for acid production. Acid is produced by the stomach to assist with food break down making food easier to digest, but, in some circumstances, acid can irritate the lining of the stomach and duodenum causing indigestion and possibly ulcers.

PPIs are considered very effective and generally safe medicines. They are recommended to treat acid related disorders including but not limited to heartburn, gastroesophageal reflux disease (GERD), and gastric ulcers.

Heartburn is described as a burning sensation which begins behind the breastbone and radiates to the neck and throat. It is caused by temporary relaxation of the lower esophageal sphincter which permits abnormal reflux of gastric contents into the esophagus. Treatment includes lifestyle changes (i.e., weight loss, avoiding large meals, alcohol, spicy food, and smoking) and drug therapy including antacids, proton pump inhibitors and histamine$_2$ receptor antagonists H_2RAs.[6] 20% of adults are reported to experience heartburn or acid regurgitation weekly and 40% experience these symptoms at least once a month.[7] Occasional heartburn is not a cause for worry. However, if the symptom persists and does not respond to self-treatment with an acid reducing product and life style changes, a physician may need to be consulted. Persistent heartburn that is unresponsive to self-management with an OTC acid suppressant agent may be a symptom of a more serious problem.[8]

According to a Neilson survey, the majority of heartburn sufferers self treat and use OTC acid reducing products. The 2008 survey of 17,412 people who had experienced heartburn during the previous 12 months' reports that 55% of respondents used only OTC treatment for their symptoms and 61% had not discussed their heartburn with a physician. Of the 39% who did discuss their symptoms with their doctor, about 44% received a recommendation for an OTC product and 13% were given a prescription. Many were advised to change their diet, lose weight, quit smoking or modify their lifestyle. 94% of those who used OTC products reported they were satisfied.[9]

Gastroesophageal reflux disease (GERD) is defined as persistent heartburn or acid reflux that occurs more than twice a week. GERD is characterized by symptoms and/or tissue damage that results from repeated or prolonged exposure of the lining of the esophagus to acidic contents from the stomach and occurs when the lower esophageal sphincter (LES) does not seal off the esophagus from the stomach. The prevalence of GERD is estimated to be 10-26% of adults.[10]

Treatment for GERD includes lifestyle changes, acid suppression therapy with PPIs and promotility therapy in selected patients especially as an adjunct to acid suppression treatment.[11] Untreated GERD can cause serious complications (i.e., damage to and bleeding in the lining of the esophagus). About 64 million prescriptions for GERD were filled in 2004 for a retail cost of nearly $7.7 billion. Proton pump inhibitors comprised the majority of the volume and cost of these prescriptions.[12] The direct medical cost of GERD was estimated to be $12 billion in 2004, more than half of which was attributed to prescription drug costs.[13]

There are seven available PPIs on the market today. Three are available as both prescriptions and OTCs. One is available as a brand-name and generic drug. The remaining three are only available as prescription brand drugs.

II. PPI COSTS, PRICING, AND UTILIZATION MANAGEMENT

PPIs are a highly utilized class of medication and have long been a top volume prescription category. PPI's are categorized as an *ulcer drug* which is a Top 10 cost category with several large PBM's. *Express Scripts 2009 Drug Trend Report* (published April 2010) indicates that the *ulcer disease drug class*, of which PPIs contribute 91% of the utilization and 94% of the cost, is the 6th most costly therapeutic class with 5.7% of the spend. According to the report, 8.2% of members have one or more scripts for ulcer drugs, and this category contributes $45.75 PMPY to total PMPY spend.[14] CVS-Caremark reported in 2009 Ulcer Medications as the 2nd highest cost therapeutic class representing 7.3 % of the total Rx spending.[15] In *Walgreens Health Initiative 2009 Trend Report*, Ulcer Disease was ranked 4th in spend representing 6.3 % of total pharmacy spending.[16]

The PPI class, once comprised of blockbuster brand drugs, more recently includes a mix of major generic competitors as well as three available OTCs. PBMs have taken advantage of the advent of PPI generics and OTC drugs by changing brand PPIs from a preferred tier to a non-preferred tier – with a higher copayment.[17] Additionally, in an effort to mitigate PPI costs, many insurers are using medical management and other formulary restrictions to control PPI use. HMOs have imposed many common utilization management techniques to control costs the most common of which are prior authorization, step edits and limits on duration of therapy.[18]

Prices vary dramatically in the PPI class. For example, the Wholesale Acquisitions Cost (WAC) per dose for a PPI brand Rx ranges from $3.65 to $5.99; or up to $180/month.[19] Similarly, the WAC per dose for PPI generic Rx ranges from $0.38 cents to $3.27 (approximately $12-$90/month).[20] Branded and generic OTC PPI prices also vary widely, although the range of WAC per dose for brand and generic OTCs is similar (See Figure 2)

FIGURE 2: PPI CATEGORY WHOLESALE PRICE RANGES

RX CATEGORY	WAC/DOSE*
BRANDED RX PPIS	$3.65 - $5.99
GENERIC RX PPIS	$0.38 - $3.27
OTC CATEGORY	**WAC/DOSE***
BRANDED OTC PPIS	$0.57 - $0.72
GENERIC OTC PPIS	$0.40 - $0.76

* Wolters Kluwer – Price RX. April 1, 2010. Wholesale Acquisition Cost per dose can range based on product strength and/or manufacturer.

III. CLAIMS ANALYSIS: PPI UTILIZATION AND COST FINDINGS

2008 MedStat Marketscan – PPI Data

We analyzed the PPI prescription drug claims in the 2008 MedStat Marketscan database, as well as the medical claims for the PPI drug users. The Medstat Marketscan database is a comprehensive database containing both medical and drug claims for individuals that are insured by large employers and health plans. Approximately 18 million lives generated the data used in the analysis.

Defining Disease Conditions

For PPI users, gastrointestinal (GI) disease conditions were assigned using ICD-9 diagnosis codes. We examined inpatient, emergency room (ER), outpatient, and physician visit claims for presence of select GI condition ICD-9 codes in any position on the claim (primary position not required). We applied a hierarchy to assign patients to mutually exclusive disease conditions. The *Severe Diagnosis* category was the top disease condition in the hierarchy followed by *Heartburn*. (See Appendix B) We show the portion of patients assigned to each disease condition below. The *not coded* means the individual did not have a diagnosis code in the claims data in the prescription year (or prior year) for any of the listed conditions (i.e., GERD, severe diagnoses, dyspepsia, heartburn, peptic ulcer, non-erosive esophagitis or hiatal hernia).

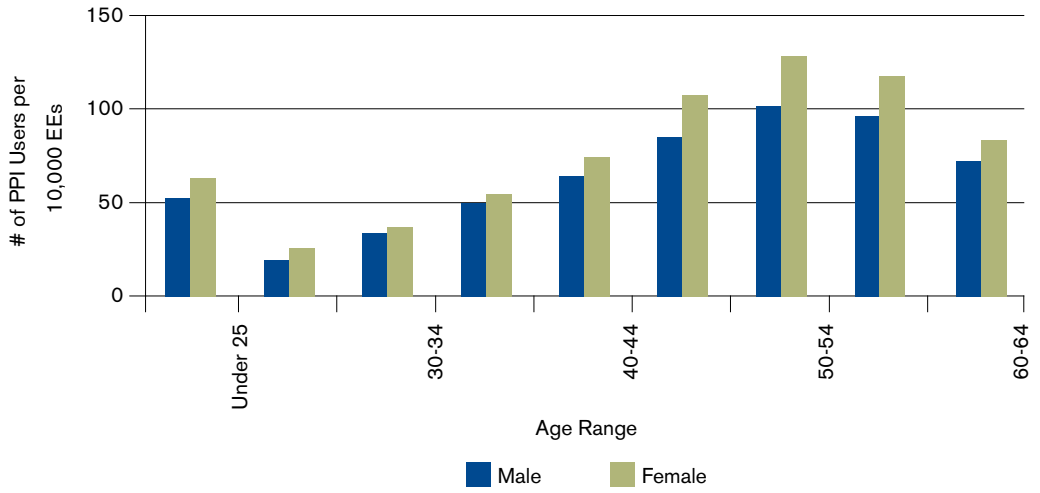
FIGURE 3: DISTRIBUTION OF GI CONDITIONS AMONG PRESCRIPTION PPI USERS (COMMERCIAL POPULATION)

CONDITION	PORTION OF PATIENTS
NOT CODED	55.7%
GERD	32.2%
SEVERE DIAGNOSES	3.6%
DYSPEPSIA	3.1%
HEARTBURN	1.7%
NON-EROSIVE ESOPHAGITIS	1.7%
HIATAL HERNIA	1.0%
PEPTIC ULCER	1.0%
TOTAL	100.0%

Key Findings from Data Analysis

Of the 18 million Medstat lives we examined, we identified more than 1 million unique PPI users, or approximately 6% of the total population, and more than 4.2 million PPI scripts. Figure 4 provides the demographic distribution of the PPI users for an illustrative population of 10,000 employees and their dependents (spouse and children=12,700 additional lives). PPI prescription use peaks in the 50-54 year old age group and is higher in woman than men.

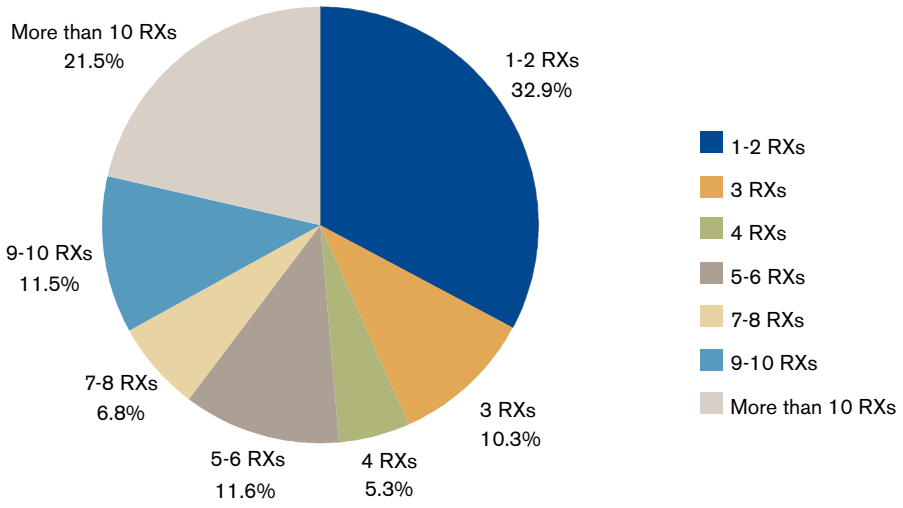
FIGURE 4: PPI USERS BY AGE AND SEX



Milliman analysis of Medstat Marketscan 2008.

The frequency of PPI use varies across the PPI users. Figure 5 shows that about 43% of PPI users had three or fewer scripts annually (on a 30 day basis). This cohort could be considered candidates for switching to OTC as OTC PPI's are indicated for frequent heartburn for 14 days of treatment, up to three times per year.

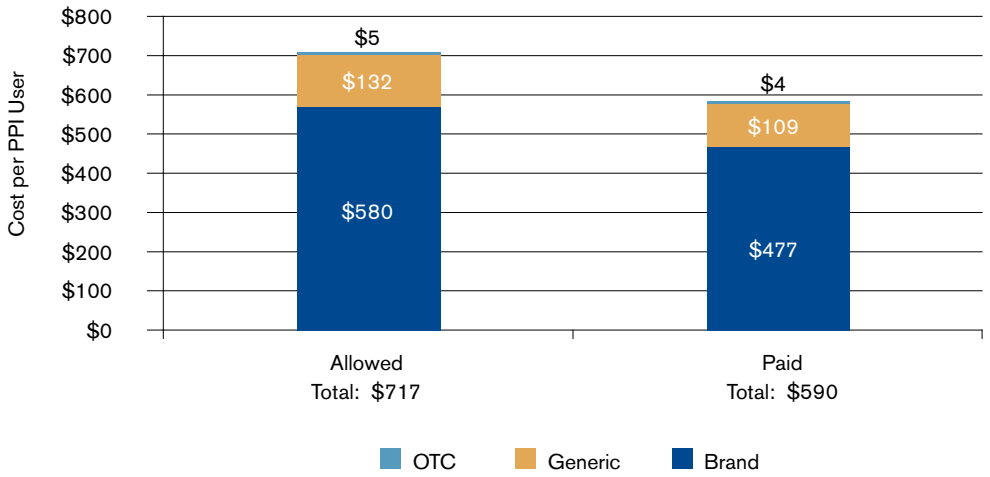
FIGURE 5: Rx FREQUENCY FOR PPI USERS PER YEAR



Milliman analysis of 4.2 million PPI scripts in 2008 Medstat Marketscan database,

We calculated the average annual allowed and paid cost per PPI user which reflects the average annual number of PPI scripts per user (4.2) and the average allowed cost per script ($172.75). Figure 6 shows PPIs cost a typical employer about $717 allowed (or $590 paid) per patient per year. Brand PPIs account for 80% of the *allowed* costs. Allowed can be considered the gross cost before any cost sharing is applied while Paid is net of cost sharing (i.e., co-pays, co-insurance etc.) and can be considered the plan/employer liability. OTC PPIs were covered by some benefit plans in the database and included in the cost calculation.

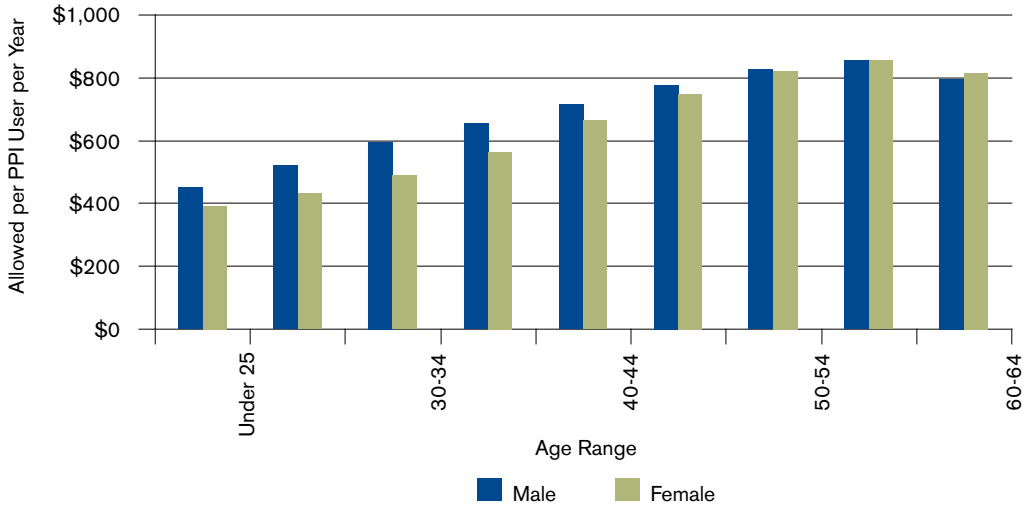
FIGURE 6: ANNUAL PPI COSTS PER PPI USER (ALLOWED AND PAID) BRAND, GENERIC, OTC CONTRIBUTION



Milliman analysis of Medstat Marketscan 2008.

Figure 7 shows the demographic distribution of annual cost per PPI user. Cost increases with age and is driven by both an increase in scripts per PPI user and cost per script for PPI users in the older age groups. The average number of scripts per PPI user is 4.2 and the average allowed cost per script is about $173.

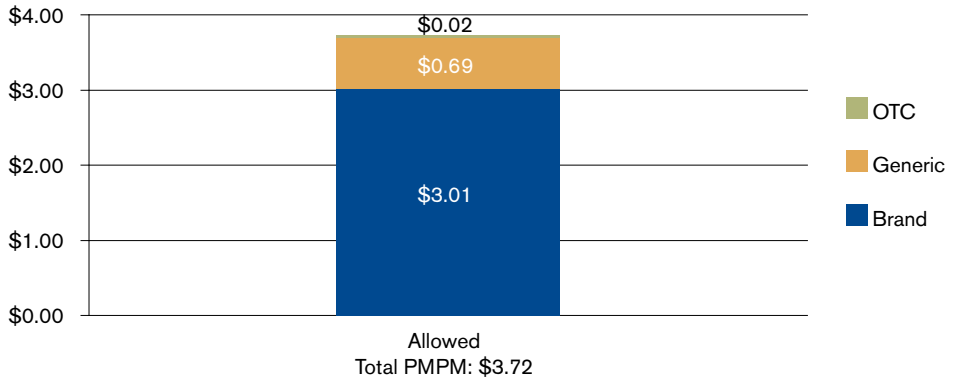
FIGURE 7: ALLOWED $ PER PPI USER BY AGE AND SEX



Milliman analysis of Medstat Marketscan 2008.

We calculated the Per Member per Month (PMPM) cost contributed by PPIs to total $3.72, or 1.2% of the total allowed spend (based on an average $305 total allowed PMPM). Rx brands contribute 80% of the total Rx spend. Some benefit plans in the database also cover OTC PPIs but the contribution to the total PMPM represented only $0.02 of the $3.72 Allowed PPI PMPM.

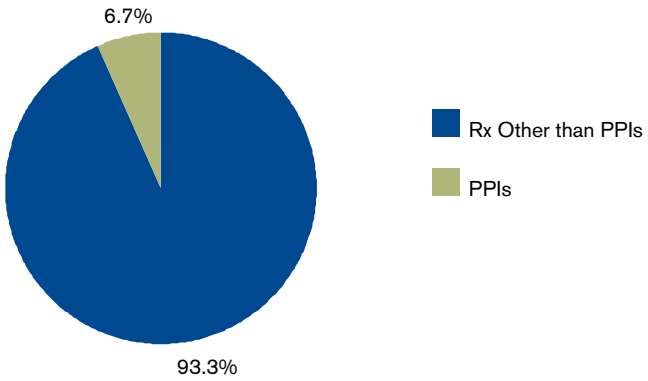
FIGURE 8: PORTION OF ALLOWED PPI PMPM BY BRAND, GENERIC AND OTC BRAND



Milliman analysis of Medstat Marketscan 2008.A typical employer prescription benefit costs about $55 PMPM on an allowed basis before rebates

The spend on PPIs represents 6.7 % of allowed drug spend This is slightly lower than, but consistent with, the three PBM drug trend reports cited earlier where PPIs were 5.7%, 7.3% and 6.3 % of drug spend respectively.[21]

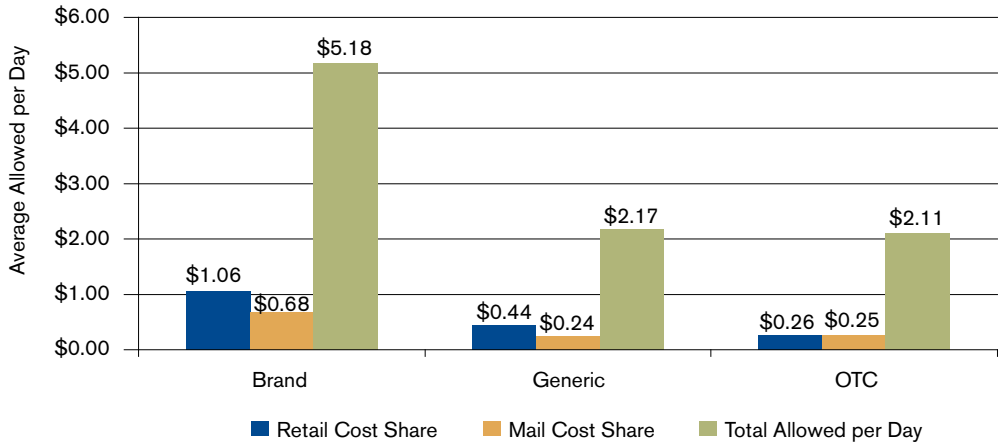
FIGURE 9: ALLOWED PPI PMPM AS PORTION OF TOTAL Rx



Milliman analysis of Medstat Marketscan 2008

Average member cost share per day for brand, generic, and OTC PPIs separately for retail and mail order are shown in Figure 10. We also show in Figure 10, alongside member cost share per day, the overall total allowed cost per day. This shows the relativity of the member out-of-pocket cost sharing to the total allowed per day. For example, retail brand and generic co-pays are approximately 20% of allowed costs. Co-pays are shown as cost per day and converts to about $32 per script for the average brand (e.g., $1.06 × 30). The average generic co-pay is over $13. *Shelf* or retail OTC PPI co-pays are less than generic co-pays and are much lower than the brand co-pays.

FIGURE 10: AVERAGE MEMBER COST SHARE PER DAY AND AVERAGE ALLOWED PER DAY BRAND, GENERIC, AND OTC



Milliman analysis of 2008 Medstat Marketscan database.

Determining the employer cost saving opportunity for OTC PPIs will typically begin with an analysis of GI disease conditions for patients using PPIs, as OTC PPIs are not indicated for all GI conditions. Figure 11 identifies the disease condition categories we used in our analysis based on diagnosis coding in the claims data; 55.7% of the patients could not be linked to any GI disease conditions and are referred to as *not coded; GERD* was the second most common category, with 32.2% of the patients. *Severe Diagnoses*, which is dominated by cancer, accounted for approximately 4% of the PPI users, or about $0.15 allowed PMPM ($0.12 paid PMPM).

FIGURE 11: PREVALENCE OF GI CONDITIONS AMONG PRESCRIPTION PPI USERS (COMMERCIAL POPULATION)

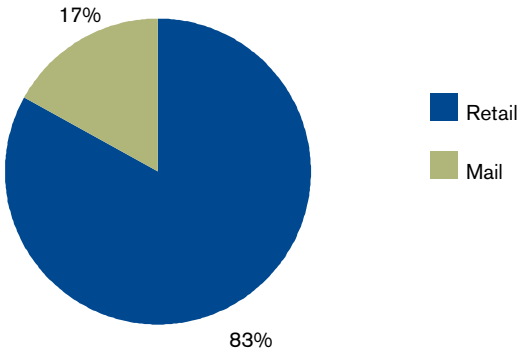
CONDITION	PORTION OF PATIENTS	ALLOWED $$ PER 10,000 EMPLOYEES	PAID PPI PMPM	PORTION OF PAID PMPM
NOT CODED	55.7%	$481,762	$1.61	52.6%
GERD	32.2%	$329,022	$1.10	35.9%
SEVERE DIAGNOSES	3.6%	$36,709	$0.12	4.0%
DYSPEPSIA	3.1%	$26,098	$0.09	2.8%
HEARTBURN	1.7%	$17,595	$0.06	1.9%
NON-EROSIVE ESOPHAGITIS	1.7%	$15,261	$0.05	1.7%
HIATAL HERNIA	1.0%	$9,946	$0.03	1.1%
PEPTIC ULCER	1.0%	$7,721	$0.03	0.8%
TOTAL	100.0%	$916,393	$3.09	100.0%

Milliman analysis of 2008 Medstat Marketscan database.

Figure 11 above includes all patients who filled one or more PPI prescription in 2008. We queried Medstat to identify all individuals with the above GI conditions and identified that 45% of all patients with these GI diagnoses did not fill any PPI Rx. There could be a number of reasons for this, but self-treatment with OTC's is certainly one possibility. Other possibilities include, physicians providing patient with PPI samples, prescriptions provided but never filled, fills that are not processed through the prescription benefit, treatment with other drug therapies or lifestyle changes.

Figure 12 shows that the vast majority of PPI Rxs are filled at retail (83%) rather than by mail (17%). The high portion of PPI RXs filled at retail suggests that an OTC switch will not require a significant shift in purchasing behavior (i.e. site of service) for most members.

FIGURE 12: UTILIZATION DISTRIBUTION - RETAIL VS. MAIL



Milliman analysis of Medstat Marketscan 2008.

Actuarial Model for Individual Employers

Each employer has their own circumstances with covered benefits, covered population, and provider networks. To accommodate a customized analysis for each employer, we built an actuarial model that estimates the employer cost impact of shifting some PPI Rx utilization to member-paid OTC PPIs. Beginning in September 2010, the model will be available for employers at www.otcbenefitadvisor.com.

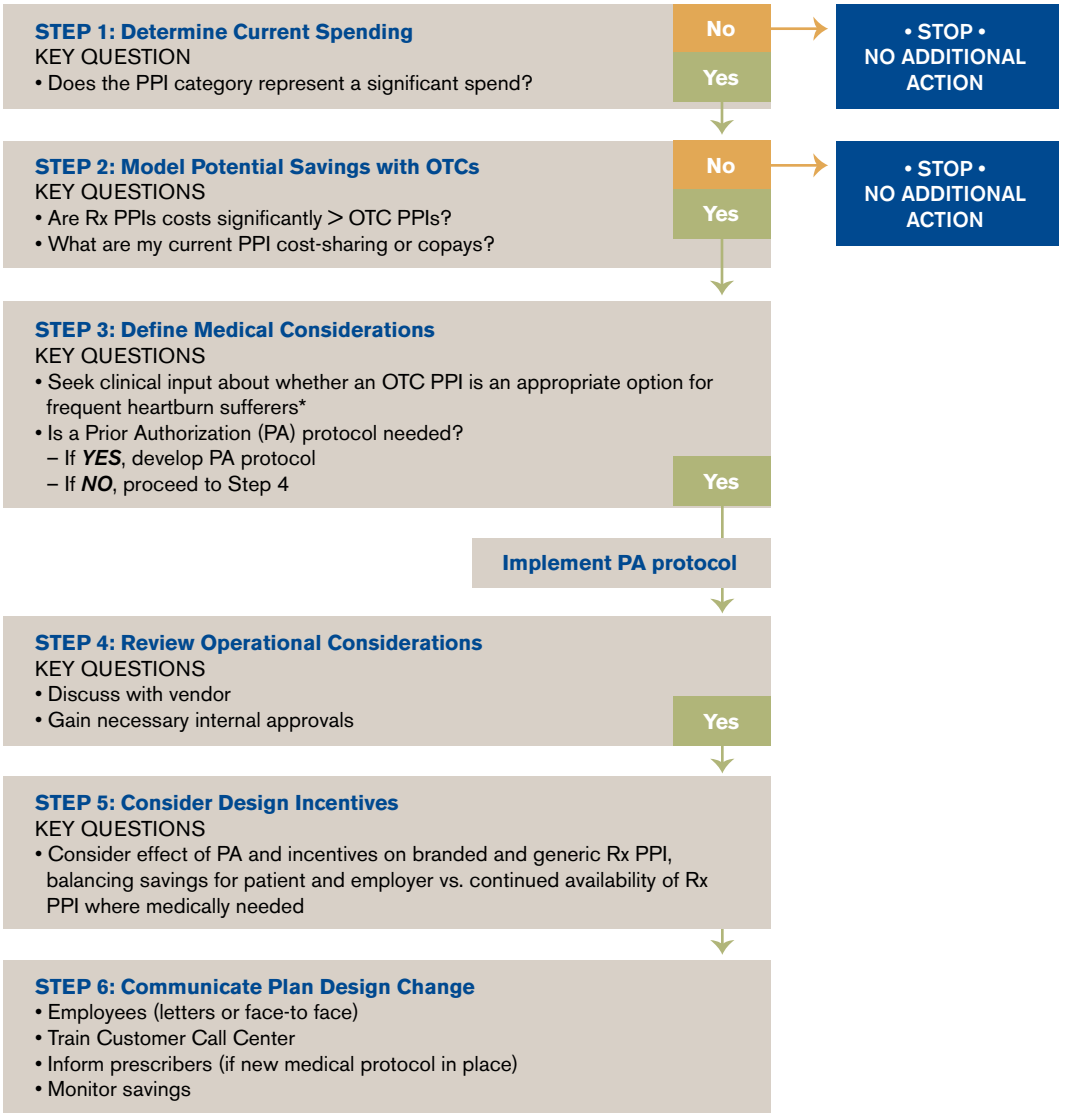
The model includes key inputs (i.e., number of covered members and benefit designs).

The outputs are the potential employer annual savings that could be realized by dropping/changing PPI coverage and encouraging employees to appropriately use OTC PPIs for the treatment of frequent heartburn. Actual employer PPI utilization and cost will vary from that estimated in the model. Each employer must balance the medical considerations of an OTC option for medically appropriate employees and the need for Rx PPIs when an OTC PPI is not an option.

IV. IMPLEMENTING AN OTC PHARMACY BENEFIT DESIGN CHANGE

If considering coverage decisions for PPIs, employers may want to review the following process outline.[22]

FIGURE 13: IMPLEMENTING AN OTC PHARMACY BENEFIT DESIGN CHANGE



* **PPIs are not interchangeable. PPIs may differ in dose,indication, efficacy, and directions for use. All patients should talk with their doctor before stopping or starting any medication therapy and to ask whether an OTC PPI is right for them and, if so, which one or ones.**

Step 1 – Determine current spending.

Brand PPIs often bring large rebates, so net cost spending should consider the rebates collected.

A PBM without full transparency will keep a portion of rebates. Although increasing OTC PPI use may significantly reduce rebate dollars, the total cost may be lower with a shift to OTC PPIs. A simple analysis of current net cost paid per day can indicate the savings opportunity. If the current net cost is not significant, there is little advantage to shifting to OTC PPIs.

Step 2 – Model Potential Savings

Benefits consultants or the model at www.otcbenefitadvisor.com will provide insight into potential cost savings. However, actuarial models are no substitute for insight from Medical or Pharmacy Directors (or clinical consultants) on the differences among each PPI (dosing, indications, duration of therapy, etc). The clinical input can be used to better estimate how many members could benefit from OTC PPIs.

Examining PBM contracts are an important step to understanding contractual restrictions, including the potential loss of rebates. For example, increasing cost sharing may maintain rebates, while imposing prior authorization requirements may lose rebates. Set realistic savings targets.

Step 3 – Resolve Medical Considerations

Employee benefit managers should use their in-house or independent clinical experts to determine medical appropriateness of covering Rx PPI's as well as the use of tools such as Prior Authorization (PA) for brand PPIs. In addition to decisions based on sound medical standards, the administrative costs of programs such as PA need to be considered.

The national average data presented above supports that *Severe Diagnosis* represents only a small fraction of the total, and that most PPI users fall into the *not coded* category. The high portion in *not coded* may suggest that some of these patients could be frequent heartburn sufferers for whom an OTC PPI is an appropriate option.

Step 4 – Review Operational Considerations

Any change in benefit design, including a shift to OTC PPIs, will raise operational issues. Third Party Administrators or PBMs need to be notified early so they can define and address operational barriers and contract limitations. For internal use, combining the clinical and financial rationale can help management and the benefits committees appreciate the value of resolving any operational challenges.

Step 5 – Consider Design Incentives

The shift to OTC PPIs may be difficult if the preferred brand cost sharing is too low. A review of cost sharing structures may be appropriate.

Step 6 – Communicate Plan Design Change

As with any benefit change, regular and consistent communications with stakeholders can be critical to program success. Components of communication could include the medical rationale, the emergence of OTC options, and how structures such as PA will work.

APPENDIX A:

DESCRIPTION OF KEY DATA SOURCES AND THEIR APPLICATION

Medstat 2008 claims data. This dataset contains all paid claims generated by approximately 28 million commercially insured lives. The Medstat database represents the inpatient and outpatient healthcare service use of individuals nationwide who are covered by the benefit plans of large employers, health plans, and government and public organizations. The MarketScan database links paid claims and encounter data to detailed patient information across sites and types of providers, and over time. The annual medical database includes private sector health data from approximately 100 payers. This data represent the medical experience of insured employees and their dependents for active employees, early retirees, COBRA continues, and Medicare-eligible retirees with employer-provided Medicare supplemental plans. No Medicaid or Workers Compensation data are included.

Member identification codes are consistent from year to year and allow for multiyear longitudinal studies. Information includes diagnosis codes, procedure codes, DRG codes, NDC codes along with site-of-service information, and the amounts paid by commercial insurers. For this study, we used MedStat 2008.

Milliman's 2009 Health Cost Guidelines. The Guidelines provide a flexible but consistent basis for the determination of health claim costs and premium rates for a wide variety of health plans. The Guidelines were developed as a result of Milliman's continuing research on health care costs. First developed in 1954, the Guidelines have been updated and expanded annually since that time. The Guidelines are continually monitored as they are used in measuring the experience or evaluating the rates of health plans, and as they are compared with other data sources. The standard demographics in the Guidelines were developed to be representative of the age and sex distribution of a typical large insured group. The standard demographics were developed using data from large insurers combined with Department of Labor sources. We used the Guidelines to demographically adjust our target population to a typical working-age population.

APPENDIX B: METHODOLOGY

Disease Condition Categories

Disease conditions were assigned based on ICD9 diagnosis codes in any position on the claim and by applying the following hierarchy (if more than one diagnosis coded for a given patient):

1. Severe Diagnosis: If a severe diagnosis was coded, the patient and all of its claim history were grouped in this category. We identified severe gastrointestinal disease conditions with at least 1 inpatient claim or two physician claims for:
   - Erosive Esophagitis (ICD9 Codes: 530.2, 530.20, 530.21, 530.82)
   - Barrett's Esophagus (ICD9 Code: 530.85)
   - Esophageal Cancer (ICD9 Codes: 150-150.99, 151.10)
   - Other Cancers (ICD9 Codes: 140-140.99, 151, 151.01-172.99, 174-198.1, 198.3-208.99)
2. Heartburn (ICD9 Code: 787.1)
3. Dyspepsia (ICD9 Code: 536.8)
4. GERD (ICD9 Codes: 530.11, 530.81)
5. Non-erosive Esophagitis (ICD9 Codes: 530.1, 530.10, 530.12, 530.19)
6. Hiatal Hernia (ICD9 Codes: 552.3, 553.3)
7. Peptic Ulcer (ICD9 Codes: 531-531.99, 532-532.99, 533-533.99, 534-534.99)

The disease condition categories are mutually exclusive – a patient is assigned to only one condition with the above hierarchy.

We note that OTC PPIs are intended to treat frequent heartburn for a 14 day duration of treatment with; no more than one 14-day course every 4 months unless otherwise directed by a prescriber. OTC PPIs are not indicated for any other condition. They should be used only as directed. Full labeling, including contraindications should be reviewed as part of any benefit design change to ensure appropriate use. The prevalence of Zollinger-Ellison Syndrome in MedStat data was determined to be immaterial for defining PPI user disease condition categories.

Proton Pump Inhibitors

We identified a member as a PPI User if he or she had at least one claim for a PPI NDC. The complete list of PPI NDCs used is available upon request to the authors.

A summary of unique PPI patients identified in our study are shown in Figure 14 below:

FIGURE 14

USER GROUP	UNIQUE USERS
NOT CODED*	563,977
GERD	326,269
SEVERE DIAGNOSES	36,388
DYSPEPSIA	31,440
HEARTBURN	17,469
NON-EROSIVE ESOPHAGITIS	16,912
HIATAL HERNIA	10,254
PEPTIC ULCER	10,546
TOTAL UNIQUE PPI USERS	1,013,255
COMMERCIAL POPULATION ANALYZED	19,201,460

Milliman analysis of 2008 Medstat Marketscan database.

* Not Coded means the individual did not have a code for any of the listed GI conditions: GERD, severe diagnoses, dyspepsia, heartburn, peptic ulcer or hiatal hernia. This could be the result of coding errors or omissions, absence of a specific condition or other reasons.

We limited our analysis of Marketscan to members in plans that were:

- Not in an HMO, a POS, a consumer-driven health plan, or a high-deductible plan
- Commercial plans only
- Had prescription drug benefits
- Less than 65 years of age with active full-time or unknown employee status

We excluded claims with a zero allowed amount as we assumed these claims were not covered by the member's benefit.

Our results are trended from 2008 MedStat to 2010 using an annual PMPM cost trend of negative 5.2%. This downward trend reflects the impact of generic PPIs since 2008 as well as increased use of generic and OTC PPIs.

Regression Analysis

A regression model analyzes relationships between independent variables and a (predicted) outcome. In this case, the independent variables are benefit design, demographic groups, and PPI benefit attributes and the predicted outcome is the PMPM cost of PPIs.

The regression model estimates PPI PMPMs separately for demographic groups (5-year age bands and gender) and for each drug tier (brand, generic, and OTC). The models are based on Milliman analysis of PPI drug claims data from the 2008 MedStat Marketscan database. For this analysis, we excluded claims for members who could not be associated with a particular plan. We also excluded from the analysis demographic groups with less than 12,000 member months.

The PMPM estimates produced by this model rely primarily on a regression model of plans which cover OTC PPIs. PMPMs of plans that do not cover OTC PPIs are calculated using the broader regression model:

$$y_i^{\text{OTC Uncovered}} = \delta_i \times y_i^{\text{OTC Covered}} \qquad i = 1, 2$$

$$y_3^{\text{OTC Uncovered}} = 0$$

where

y_1: Brand PPI PMPM

y_2: Generic PPI PMPM

y_3: OTC PPI PMPM

and δ is determined by demographics as

$$\delta_1 = \begin{cases} 1.219 + Age \times (-0.010) & Male \\ 0.997 + Age \times (-0.005) & Female \end{cases}$$

$$\delta_2 = \begin{cases} 0.871 + Age \times 0.010 & Male \\ 1.088 + Age \times 0.006 & Female \end{cases}$$

Regression model for the OTC-Covered Plans

The regression model for plans that cover over-the-counter PPIs consists of a multiple linear regression for each drug tier, and the significant variables included in the individual regressions vary by tier. In its most general form, the regression describes the relationship between the logarithm of y_i and x_j, where

y_i: Per Member Per Month Paid Claim Cost for Drug Tier

x_1: % Coinsurance Brand

x_2: % Coinsurance Generic

x_3: % Coinsurance OTC (Milliman default of 17% coinsurance, not a user input)

x_4: % Mail Order Brand

x_5: % Mail Order Generic

x_6: % Coinsurance Office Visit

The form of the model is:

$$\ln(y_i^{\text{OTC Uncovered}}) = \beta_i + \sum_{j=1}^{6} \alpha_{i,j} \times x_j \qquad i=1, 2, 3$$

The coefficients β_i and $\alpha_{i,j}$ are allowed to vary by demographic group. Each regression model consists of an intercept term (dependent on age and gender) and interaction terms involving the x_j's described above (dependent on benefit design, mail order, age and gender). Not all variables were determined to be significant in all three regressions. All six variables are included in the model for Brand PPIs, with the coefficients shown here:

$$\beta_i = \begin{cases} -7.058 + \ln(Age) \times 2.472 & Male \\ -5.193 + \ln(Age) \times 2.009 & Female \end{cases}$$

$$\alpha_{1,1} = \begin{cases} -8.514 + \max(30, Age) \times 0.109 & Male \\ -6.272 + \max(30, Age) \times 0.065 & Female \end{cases}$$

$$\alpha_{1,2} = \begin{cases} 5.339 + Age \times -0.123 & Male \\ -0.015 + Age \times -0.033 & Female \end{cases}$$

$$\alpha_{1,3} = \begin{cases} 11.054 + \max(42, \min(57, Age) \times -0.218 & Male \\ 2.67 + \max(42, \min(57, Age) \times -0.034 & Female \end{cases}$$

$$\alpha_{1,4} = \begin{cases} -1.061 + Age \times 0.011 & Male \\ 0.467 + Age \times -0.034 & Female \end{cases}$$

$$\alpha_{1,5} = \begin{cases} 1.350 + Age \times -0.021 & Male \\ -2.019 + Age \times 0.060 & Female \end{cases}$$

$$\alpha_{1,6} = \begin{cases} 1.919 + \max(30, Age) \times -0.044 & Male \\ 1.469 + \max(30, Age) \times -0.032 & Female \end{cases}$$

The Percent Coinsurance of Brand and Percent Coinsurance of Office Visit were determined not to be statistically significant predictors of Generic PPI PMPMs, and so these variables (x_1 and x_6) were excluded from that model. The remaining significant coefficients for the Generic PPI regression are:

$$\beta_2 = \begin{cases} -15.595 + \ln(Age) \times 4.273 & Male \\ -8.828 + \ln(Age) \times 2.549 & Female \end{cases}$$

$$\alpha_{2'2} = \begin{cases} 1.597 + \max(15, Age) \times -0.098 & Male \\ -10.220 + \max(15, Age) \times 0.098 & Female \end{cases}$$

$$\alpha_{2'3} = \begin{cases} 4.851 + \max(42, \min(62, Age)) \times -0.078 & Male \\ -6.821 + \max(42, \min(62, Age)) \times 0.169 & Female \end{cases}$$

$$\alpha_{2'4} = \begin{cases} -0.320 + \max(25, Age) \times -0.014 & Male \\ -2.525 + \max(25, Age) \times 0.023 & Female \end{cases}$$

$$\alpha_{2'5} = \begin{cases} 0.928 + Age \times -0.006 & Male \\ 1.558 + Age \times -0.017 & Female \end{cases}$$

No variable is a significant predictor of OTC PPI PMPM, so the OTC regression model consists only of the intercept term:

$$\beta_3 = \begin{cases} -9.247 + \ln(Age) \times 1.537 & Male \\ -8.479 + \ln(Age) \times 1.347 & Female \end{cases}$$

Limitations

The cost results presented in this study are averages, using specific methodologies and assumptions, and are based on data from 2008. This analysis uses diagnosis codes in medical claims data that may not accurately reflect patient status due to coding practices or errors and omissions. Revisions to the assumptions, methodologies, or more current data may change the results and related conclusions. Additionally, individual patient experiences may differ from the averages presented here. This analysis, and the data sources used, met HIPAA privacy and security rules.

This paper was commissioned by Procter & Gamble, a pharmaceutical manufacturer that markets an OTC PPI. While the authors followed applicable Actuarial Standards of Practice this report does not form a prescribed statement of actuarial opinion. Milliman does not intend to endorse any product or to benefit any third party through this report; the report reflects the findings of the authors. As with any financial forecast, our work is based on many assumptions and cannot capture all influences. Actual experience will likely vary from that presented here.

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