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Identifying the association between health care resource utilization and switching of biologics in rheumatoid arthritis

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Identifying the association between health care resource utilization and switching of biologics in rheumatoid arthritis

by

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Abstract

Identifying the association between health care resource utilization and switching of biologics in rheumatoid arthritis

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The University of Texas at Austin, 2014

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Objectives: To identify the predictors of switching from the first biologic to a second biologic in rheumatoid arthritis (RA) patients newly initiated on biologic treatments.

Methods: Adult RA patients (18-64 years old) initiated on adalimumab, etanercept, infliximab, certolizumab, golimumab, abatacept, rituximab, tocilizumab, or anakinra between 2009 and 2011 were identified using a commercial claims database. Switching patterns were examined within one year after biologic initiation using descriptive statistics. Health care resource utilization (HCRU) variables (the number of 30-day supplies for steroid and DMARDs, and the claim counts for RA-related outpatient visits, radiographic, laboratory, intra-articular injections, rehabilitation, and surgical procedures) were assessed within one year prior to the switch date for switchers or the end of the study period for non-switchers. Pairwise comparisons of patient characteristics and HCRU variables were conducted using t-tests, Mann-Whitney U tests, and Chi-squared tests. Multiple logistic regressions were used to identify HCRU predictors of switching.

Results: A total of 12,370 patients were included in the analysis. The switch rate within one year after biologic initiation was 18.4%, and the median time to switch was 181 days.

More females switched compared to males (19.2% vs. 15.9%, $p<.001$). Switch rates were also higher in patients started on anti-TNFs compared to non-anti-TNFs (19.2% vs. 12.0%, $p<.001$). Furthermore, switch rates were highest in patients started on golimumab (21.0%) and were lowest in patients started on rituximab (4.8%). Overall, switchers had significantly higher rates and quantities of RA-related HCRU than non-switchers, except in the use of surgical procedures. Logistic regression models revealed that all the HCRU variables were significant predictors of switching, and patients on infliximab, abatacept, tocilizumab, and rituximab had significantly lower odds of switching than patients on etanercept. Combination therapy with DMARDs was also significantly associated with lower odds of switching.

Conclusion: Switching of biologics is common in RA patients initiated on biologic therapy. There are marked differences in demographic characteristics and HCRU patterns between switchers and non-switchers. This study demonstrates that patterns of RA-related HCRU can be used to predict switching and thus can potentially serve as useful measures of treatment ineffectiveness.

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Chapter 1: Introduction & Literature Review

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disease with unknown etiology. It is characterized by chronic inflammation of the joints, which leads to swelling, tenderness, stiffness, and pain of the joints. As a progressive illness, chronic inflammation of the cartilage, bone, and ligaments can lead to permanent joint destruction and deformity.

RA impacts about 1.3 million adults in the United States (US)[1] and is associated with physical and social impairments as it leads to physical disability and negatively impacts health-related quality of life. The societal impact can be high as RA and other arthritic diseases are the leading cause of disability in the US, which contributes to loss of work productivity. [2]

Although little is known about the trigger of RA, certain risk factors have been identified. Women are at higher risk for developing RA. The incidence of RA is two to three times higher in women than men.[3] In addition, RA is also more prevalent in the Native American population. The disease can impact people of all ages but the typical onset of RA is between 40 to 60 years old.[3] Other risk factors of RA include genetics, infectious agents, oral contraceptive agents, smoking, and education.[4] Estimated prevalence of familial RA is 9.8%. Patients with genetic disposition for RA usually experience disease onset before the age of 40 and it is more common in males.[5]

BURDEN OF RHEUMATOID ARTHRITIS

RA is associated with many comorbid conditions and a reduction in health-related quality of life (HRQoL), and can bring about significant economic burden to patients, the health care system, and the society as a whole.

Although the joints of the hands and feet are the primary target of RA, the autoimmune nature of the disease can lead to systemic inflammation impacting other organs such as the skin, heart, lung, and eye. Consequently, RA has been shown to correlate with other comorbidities such as cardiovascular diseases.

Although RA affects less than 1% of the general population, it can have a tremendous impact on individual patients, the health care system, and society. A systematic review by Cooper et al. found that the mean annual direct medical cost associated with RA is $5,720 per patient. Inpatient costs are the largest components of the total direct costs. Absenteeism due to RA ranges from 2.7 days to 30 days per year, which is associated with annual indirect costs of $5,822.[6] Compared to people without arthritis, the incremental direct medical cost for RA patients is almost four times higher and the incremental indirect costs are more than twice that of the arthritis-free population.[7,8]

TREATMENT FOR RHEUMATOID ARTHRITIS

There is no cure for RA. Treatment for RA focuses on symptomatic relief, inflammation reduction, and disease progression prevention. Numerous studies have shown that cytokines such as tumor necrosis factor alpha (TNF-α), interleukin-1 (IL-1),

interleukin-2 (IL-2), interleukin-6 (IL-6), and interleukin-23 (IL-23) play an important role in mediating the inflammatory pathways.[9] Many newer drugs have been developed to target these cytokines.

The goal of treatment is to achieve remission or lower disease activity. Several instruments are available to measure the disease activity in RA. The American Clinical Rheumatology (ACR) criteria is one of the most widely adopted measures for RA outcomes.[10] It encompasses seven core set measures that were deemed sensitive to assess changes in RA disease activity. These measures involve counting the number of joints involved, global assessment of disease by patients and physicians, and a laboratory marker of inflammation. In general, a 20% improvement in the ACR score (ACR20) is considered clinically relevant. The ACR criteria, however, is mostly used in clinical trials with limited applicability in real-life practice settings. Six other instruments have been recommended by the ACR to measure RA disease activity in clinical settings.[11] These tools share similar elements as the ACR criteria of joint count, global assessment of disease, and laboratory markers – but are more concise and thus more convenient to administer in a clinical setting.

Initial treatment for RA includes several conventional disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, leflunomide, hydroxyquinolone, minocycline, and sulfasalazine. It is a heterogeneous class of drugs that modulate the immune system or interfere with various molecular pathways associated with inflammation. As a class, DMARDs have been shown to preserve joint function and integrity by slowing or halting disease progression. DMARDs can be used as a

monotherapy or in combination with other DMARDs or biologics in order to achieve these goals.

In addition to DMARDs, non-steroidal inflammatory drugs (NSAIDs) and corticosteroids are commonly used for symptomatic relief and inflammation control. However, since these drugs do not address the underlying mechanism of the disease, they are used in short courses, on an intermittent basis, with the aim to address acute flare-ups.

For patients with who are not adequately controlled using DMARDs, biologic therapies may be used. Biologics are relatively new treatment options introduced to RA patients over the past decade and have become increasing popular. Currently, several biologic therapies are approved by the Food and Drug Administration (FDA) for the treatment of moderate-to-severe RA. According to the clinical guidelines from the ACR, biologics are recommended in patients with early disease but high disease activity or patients with established RA (disease duration $\geq$ 6 months).[12]

TNF-α blockers, also known as anti-TNFs, are the biologic therapy of choice after failure on DMARDs**.** TNF-α is a pro-inflammatory cytokine that mediates acute-phase reactions that are responsible for the hallmark symptoms of swelling, bone erosion, and thickening of the synovial membrane.[9] Anti-TNFs work at the TNF-α receptor sites, preventing activation of TNF-α, and thus intercepting the immunologic pathway. Currently, there are five anti-TNFs indicated for the treatment of RA – infliximab, etanercept, adalimumab, certolizumab, and golimumab. Among these, etanercept, adalimuman, and infliximab are the most commonly used anti-TNFs. Sometimes, anti-TNFs are used in combination with methotrexate. Concomitant use of methotrexate is

required with infliximab and golimumab. Table 1.1 shows the characteristics of anti-TNFs used in RA.

The ACR guideline also recommends switching to another anti-TNF or a non-anti-TNF biologic if a patient continues to have moderate or high disease activity within three months of treatment.[12] Abatacept, anakinra, tocilizumab, and rituximab are non-anti-TNF biologics that target other cytokines in the inflammatory pathway. Abatacept is a co-stimulation blocker that inhibits the co-stimulation pathway that is necessary to activate inflammation; Anakinra blocks the IL-1 proteins and tocilizumab blocks the IL-6 proteins; Rituximab is a monoclonal antibody that binds to the CD20 antigen on B-cells, which, along with T-cells, are believed to be involved in the autoimmune process in RA. Characteristics of non-anti-TNF biologics are also presented in Table 1.1.

Table 1.1: Biologic therapy used to treat rheumatoid arthritis[13-21]

Generic Name	Brand Name	Approval Year[a]	Drug Class	Route of Administration	Dosing Schedule[b]
Adalimumab	Humira®	2002	Anti-TNF	SQ	40 mg every 2 weeks
Certolizumab	Cimzia®	2009	Anti-TNF	SQ	200 mg every 2 weeks
Etanercept	Enbrel®	1998	Anti-TNF	SQ	50 mg weekly
Golimumab	Simponi®	2009	Anti-TNF	SQ	50 mg monthly in combination with MTX
Infliximab	Remicade®	1999	Anti-TNF	IV	3 mg/kg every 8 weeks in combination with MTX
Abatacept	Orencia®	2005	Co-stimulation Modulator	IV, SQ	IV: 750 mg every 4 weeks SQ: 125 mg weekly
Anakinra	Kineret®	2001	IL-1 Inhibitor	SQ	100 mg daily
Rituximab	Rituxan®	2006	CD20 Inhibitor	IV	Two-1000 mg separated by 2 weeks every 24 weeks in combination with MTX
Tocilizumab	Actemra®	2010	IL-6 Inhibitor	IV, SQ	IV: 4 mg/kg every 4 weeks; increase to 8 mg/kg every 4 weeks based on clinical response SQ: 162 mg weekly

SQ=subcutaneous injection; IV=intravenous infusion; TNF=tumor necrosis factor; IL=interleukin; MTX=methotrexate

[a] Year of FDA approval of indication specific to rheumatoid arthritis

[b] Dosing for adult rheumatoid arthritis patients. Only maintenance dose is listed.

SWITCHING TO A SECOND BIOLOGIC AFTER FAILURE OF AN INITIAL BIOLOGIC

The introduction of biologic treatments in the past decade has shifted the disease management paradigm in RA. Treatment for RA has become increasingly aggressive due to the belief that early and aggressive treatment can provide better clinical and humanistic outcomes and delay or prevent irreversible joint damage.[22,23] Although anti-TNF biologics have been well-established as the first-line biologic treatment, the choice for the second biologic is less clear when a patient fails to respond to the first biologic.

As more biologic treatment options become available, switching from the first biologic to another has become a common practice to address the lack of efficacy and/or the problem of intolerance.[24,25] A review of literature suggests the switch rate ranges from 7% to 15%, with most studies reporting a switch rate of about 12%.[26-31] Bonafede et al. also reported a median time to switch ranging from 107 to 207 days across different anti-TNF agents within the first year of treatment initation.[27] Similarly, Yazici et al. reported a median time to switch ranging from 97 to 154 days across different anti-TNF agents.[29] Switching between biologic DMARDs, especially between anti-TNF drugs, has become an increasing important topic because of the lack of clinical consensus on the appropriate choice due to limited head-to-head comparative evidence, as well as a lack of sufficient information to guide the health care payers when making reimbursement decisions.[32,33]

Treatment inefficacy and intolerance are the main reasons for switching.[25,34-36] Hyrich et al. examined RA patients from a United Kingdom (UK) national register of patients newly started on anti-TNF drugs and found 60% and 35% of the patients

switched to a second agent due to inefficacy and adverse events, respectively.[37] Virkki et al. conducted a similar analysis on a Finnish population and found 51% of the switches were attributable to loss of efficacy and 12% were due to adverse events.[38] A more recent meta-analysis conducted by Remy et al. focusing only on switching from the first anti-TNF to a second anti-TNF revealed that up to 81% of switches were due to lack of efficacy and 35% were due to adverse events.[26] Although the rates of switching due to inefficacy versus adverse events vary widely across study populations and biologics, the rates of switching due to inefficacy appear to have increased over time, perhaps due to the increasing availability of biologic options.

FACTORS ASSOCIATED WITH SWITCHING

Understanding the factors associated with switching is an important topic because it helps clinicians and health care payers identify patients that are likely to experience treatment inefficacy or adverse events. Some previous work has been published that identified predictors for treatment response and remission. Hyrich et al. tested 12 variables related to patient characteristics, treatment, and disease activity and found patients with greater physical impairments, smokers, NSAID use and methotrexate use are significant predictors of better response to anti-TNF biologic.[39] A study by van der Heijde et al. found that male gender, disease activity, number of DMARDs prior biologic initiation, physical disability, disease duration, and concomitant methotrexate use are significant predictors of long-term remission in patients using etanercept.[40] Overall, the

most well documented variable that is significantly associated with remission is concurrent use of methotrexate with a biologic.[39-42]

While these studies provide useful insight into portraying patients who are likely to respond to biologic therapy, many of these variables cannot be captured in administrative claims database. Claims data lack the clinical information required to assess disease activity. As previously mentioned, validated measures used to assess disease activity rely on calculations of joint count, global assessment of disease, and laboratory markers, which are not routinely performed and are not captured in administrative claims. In addition, many predictors of treatment response, such as baseline disease activity and physical impairment, are also absent in claims data. To address such limitations of claims data, Curtis et al. developed a claims-based algorithm to measure the effectiveness of RA medications.[43] Components of the algorithm include dichotomous measures (yes or no) of 1) medication possession ratio (MPR) of less than 80 %, 2) an increase in biologic dose, 3) the addition of a non-biologic DMARD, 4) the initiation of chronic glucocorticoids, 5) an increase in glucocorticoid dose, and 6) the use of more than one intra-articular injection. If the answer to any of these criteria was 'Yes', the treatment was deemed to be ineffective. If the answer to all criteria were 'No', the treatment was deemed to be effective. In the Curtis et al. study, the most common reason for failing the effectiveness criteria was discontinuation or switching to a different biologic.

The switching of biologic agents can be used as a reasonable proxy for treatment inefficacy in retrospective claims analyses.[44] Meissner et al. found that patients who

switched to a different biologic within the first year of biologic initiation were younger (53 years vs. 55 years, $p<.001$), had greater hospitalization rates (9.5% vs. 7.2%, $p=.015$) and higher total monthly health care costs ($1,025 vs. $796, $p<.001$) compared to non-switchers within 6 months prior to the initiation of biologics.[25] The authors also found that the odds of switching were significantly lower in patients started on abatacept compared to other anti-TNFs (OR=0.24; 95% confidence interval [CI]=0.14, 0.44). This study revealed that patterns of health care resource utilization may be useful as signals to predict switching.

OBJECTIVES

The objective of this study was to identify the predictors of switching from the first biologic to a second biologic in rheumatoid arthritis patients newly initiated on biologic treatments. Specific objectives and hypotheses include:

1. To describe the rates of switching within one year of initiating biologic therapy in patients with RA.
2. To describe the time to switch among patients who experienced a switch within one year of biologic initiation.
3. To describe characteristics of RA patients who were newly initiated on biologic therapy with respect to demographics and RA-related health care resource utilization.

4. To examine differences in patient characteristics between patients who experienced a switch and patients who did not experience a switch within one year of biologic initiation.

    $H_0$4.1: There is no statistically significant difference between switchers and non-switchers in the distributions of gender.

    $H_0$4.2: There is no statistically significant difference between switchers and non-switchers in mean age.

    $H_0$4.3: There is no statistically significant difference between switchers and non-switchers in the distributions of geographic region.

    $H_0$4.4: There is no statistically significant difference between switchers and non-switchers in the proportion of patients using biologic monotherapy at treatment initiation.

    $H_0$4.5: There is no statistically significant difference between switchers and non-switchers in the proportion of patients initiated on an anti-TNF as the first biologic therapy.

    $H_0$4.6: There is no statistically significant difference between switchers and non-switchers in the proportion of patients using different biologics

5. To examine differences in RA-related health care resource utilization between patients who experienced a switch and patients who did not experience a switch within one year of biologic initiation.

    $H_0$5.1: There is no statistically significant difference between switchers and non-switchers in the number of 30-day supplies for oral steroids.

$H_0$5.2: There is no statistically significant difference between switchers and non-switchers in the number of 30-day supplies for DMARDs.

$H_0$5.3: There is no statistically significant difference between switchers and non-switchers in the number of RA-related outpatient visits.

$H_0$5.4: There is no statistically significant difference between switchers and non-switchers in the number of RA-related radiographic procedures.

$H_0$5.5: There is no statistically significant difference between switchers and non-switchers in the number of RA-related laboratory procedures.

$H_0$5.6: There is no statistically significant difference between switchers and non-switchers in the number of RA-related intra-articular injections.

$H_0$5.7: There is no statistically significant difference between switchers and non-switchers in the number of RA-related rehabilitation visits.

$H_0$5.8: There is no statistically significant difference between switchers and non-switchers in the number of RA-related surgical procedures.

6. To identify predictors of switching within one year of initiating biologic therapy.

$H_0$6.1: The number of 30-day supplies for oral steroids prior to switch is not a statistically significant predictor of switching.

$H_0$6.2: The number of 30-day supplies for DMARDs prior to switch is not a statistically significant predictor of switching.

H06.3: The number of RA-related outpatient visits prior to switch is not a statistically significant predictor of switching.

$H_0$6.4: The number of RA-related radiographic procedures prior to switch is not a statistically significant predictor of switching.

$H_0$6.5: The number of RA-related laboratory procedures prior to switch is not a statistically significant predictor of switching.

$H_0$6.6: The number of RA-related intra-articular injections prior to switch is not a statistically significant predictor of switching.

$H_0$6.7: The number of RA-related rehabilitation services prior to switch is not a statistically significant predictor of switching.

$H_0$6.8: The number of RA-related surgical procedures prior to switch is not a statistically significant predictor of switching.

Chapter 2: Methodology

STUDY DESIGN AND DATA SOURCE

This was a retrospective analysis using pharmacy and medical claims data from MarketScan Commercial Encounters Database (MCED). The MarketScan Commercial Claims and Encounters Database is a HIPAA-compliant, employer-sponsored health care claims database with broad geographic coverage at the national and state level, with a reported 29.1 million lives. The MCED has fully integrated drug and health care claims records at the patient level with each patient assigned a unique identifier and this patient-level data is derived from multiple sources (employers, health plans, and other carriers), enabling patients to be followed even in some circumstances where they switch health plans. Data from MCED are retrospective in nature and are de-identified. Therefore, the study was determined by the University of Texas at Austin Investigational Review Board (IRB) as a non-human subject research, hence exempting the study from IRB review.

STUDY SAMPLE

Patients with at least one claim for any biologic of interest between January 1st, 2009 to December 31st, 2011 were eligible to be included in the study. Biologics of interest included adalimumab, etanercept, infliximab, certolizumab, golimumab, abatacept, rituximab, tocilizumab, and anakinra. Biologic claims were identified using National Drug Codes (NDC) in pharmacy claims, as well as Healthcare Common Procedure Coding System (HCPCS) codes in medical claims for drugs administered at

the physician's office (Appendix A). The first biologic used during the same period was the index biologic and the date of the first biologic fill was the index date. A rheumatoid arthritis (RA) diagnosis was identified with at least one medical claim for RA (can be either inpatient or outpatient claim with International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] Diagnosis code 714.x) within 365 days prior to index date. Other inclusion criteria were ages between 18 and 64 years old on index date, no biologics of interest within 365 days prior to index, and continuous enrollment in pharmacy and medical benefits 365 days prior to and 365 days post index date. Medicare patients were not included in the study since MCED contains only supplemental Medicare claims, which does not capture the portion of services covered directly under Medicare benefits. In order to increase the likelihood of capturing biologic use related to RA, patients were excluded if they had any confounding diseases that are indications for the biologics of interest. Presence of these disease states were captured using medical claims, which included psoriasis and psoriatic arthritis (ICD-9-CM 696.x), ankylosing spondylitis (ICD-9-CM 720.0), Crohn's disease (ICD-9-CM 555.2), and ulcerative colitis (ICD-9-CM 556.8). Patients using more than one unique biologic drug on index date or with missing information on age or gender were also excluded from analysis.

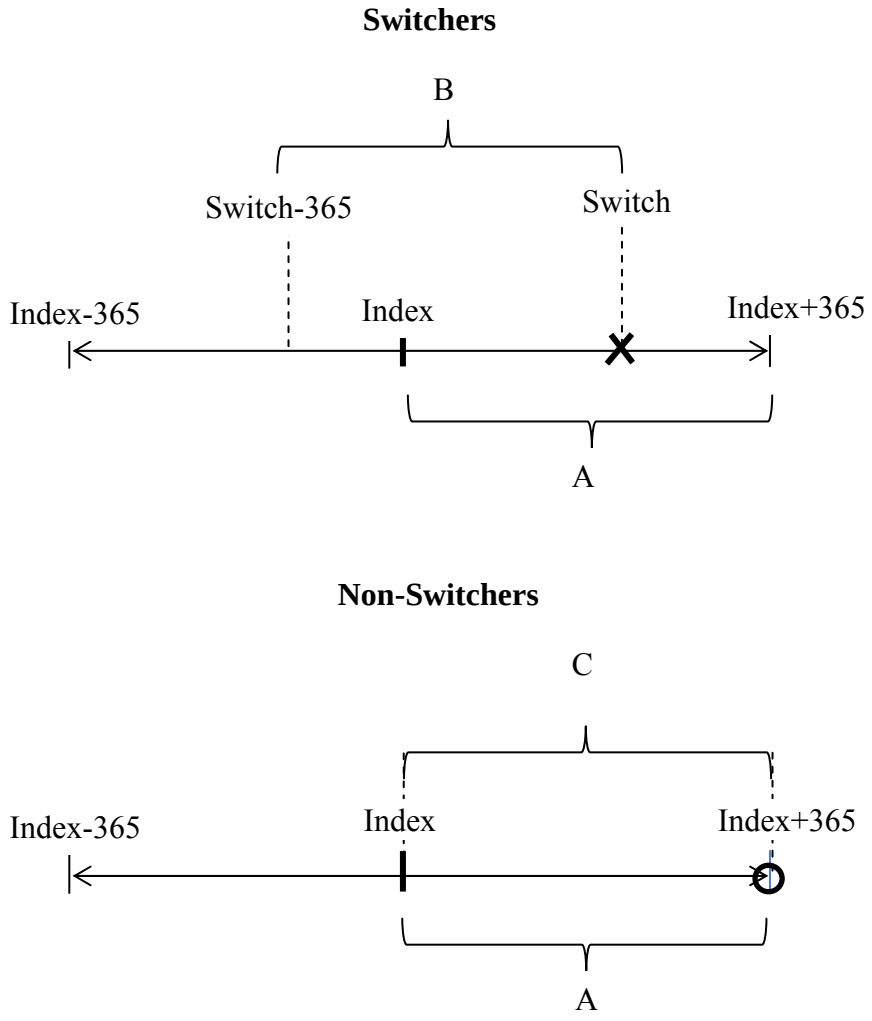
STUDY VARIABLES

The primary dependent (outcome) variable of this study was the event of switching to a second biologic within one year after initiation of biologic treatment. A

switch was defined as the initiation of a biologic that was different from the index biologic, and was captured with at least one pharmacy or medical claim for a non-index biologic within 365 days after the index date. The earliest claim date for the non-index biologic was considered as the switch date. Switching was measured as a dichotomous variable (yes or no). Number of days to switch, number of fills for the index biologic prior to switching, and number of unique biologics filled throughout the follow-up period were also examined.

Independent variables related to health care resource utilization were collected from 365 days prior to switch to the date of switching. For patients who did not experience a switch, variables were collected from 365 days prior to the end of the follow-up period, which was 365 days after index date, resembling the approximate switch date ranges for the group that switched (Figure 1).

Figure 1. Identification Periods for Dependent and Independent Variables



A. The dependent variable (i.e. the event of switching) was identified in Period A (from index to 365 days post index) for all patients.
B. For switchers, the independent variables (i.e. the predictors of switching) were identified in Period B (from 365 days prior to switch to time of switch).
C. For non-switchers, the independent variables were identified in Period C (from 365 days prior to the end of the study period to the end of the study period), which is equivalent to Period A.

Independent variables (predictors) included the number of 30-day supplies for oral steroids and DAMRDs, and the number of medical claims for RA-related outpatient visits, radiographic procedures such as X-rays and magnetic resonate imaging (MRI), laboratory procedures for inflammatory markers (erythrocyte sedimentary rate and C-reactive protein), intra-articular injections, rehabilitation visits, and surgical procedures. These variables were selected based on published algorithms to measure RA severity[45,46] since disease severity has been shown to be associated with the switching of biologics among RA patients.[24] Only variables that could be captured in administrative claims were included in the analysis, most of which reflect health services used for the management of RA. Several surgical options are available to RA patients, which include, but are not limited to, carpal tunnel release, synovectomy, resection of the metatarsal heads, total joint arthroplasty, and joint fusion.[47,48] Acute episodes, or flares, can be managed through intra-articular injections with glucocorticoids, or hyaluronan and its derivative.[49] Rehabilitation therapies such as physical therapy and occupational therapy are also commonly used by RA patients as adjuncts to drug therapies.[48]

Steroid and DMARDs 30-day supply prescription fills were captured using NDC codes in pharmacy claims (Appendix A). All RA-related health care services and procedures were captured from medical claims using Current Procedural Terminology (CPT) codes (Appendix A). In order to ensure the services and procedures received were related to RA, all claims must contain any diagnosis for RA (ICD-9-CM 714.x).

Additional variables examined included demographic and index therapy characteristics such as gender, age at the time of biologic initiation, geographic region

(Northeast, North Central/Midwest, South, and West), index year, index biologic drug, index biologic class (anti-TNF or non-anti-TNF), and index therapy type (whether index biologic was used as a monotherapy or as a combination therapy with DMARDs).

STATISTICAL ANALYSIS

Demographic variables, characteristics of index therapy, independent and dependent variables were summarized using descriptive statistics. Categorical variables including switching, index therapy type, index biologic drug, index biologic class, gender, geographic region, and index year, were summarized using frequencies and proportions. Continuous variables such as age and the number of days to switch among switchers were reported using means and standard deviations. Count variables such as the number of 30-day supplies for steroid and DMARDs, as well as the number of claims for RA-related outpatient visits, radiographic, laboratory, intra-articular injections, rehabilitation, and surgical procedures were summarized using means and standard deviations for normally distributed variables, or medians and ranges for variables with non-normal distributions.

Pairwise comparisons were conducted to test for the differences in demographic and health care resource utilization characteristics between switchers and non-switchers (Objectives 4 and 5). Specifically, independent t-tests were used to examine the differences in means for normally distributed continuous variables and Mann-Whitney U tests were used to examine the difference in medians for count variables with non-normal distributions. Chi-squared tests were used to determine difference in proportions for

categorical variables. Based on preliminary examination of variable distributions, statistical tests used for each variable are listed in Table 2.1.

Table 2.1. Statistical Tests Used for Pair-wise Comparisons between Switchers and Non-Switchers

Variables	Variable Types	Statistical Tests	Objectives
Gender (female, male)	Categorical/ dichotomous	Chi-squared test	$H_0$4.1
Age, in years	Continuous	Independent t-test	$H_0$4.2
Geographic region (Northeast, North Central/Midwest, South, West, or Unknown)	Categorical	Chi-squared test	$H_0$4.3
Index therapy type (monotherapy or combination therapy with DMARDs)	Categorical/ dichotomous	Chi-squared test	$H_0$4.4
Index biologic class (anti-TNF or non-anti-TNF)	Categorical/ dichotomous	Chi-squared test	$H_0$4.5
Index biologic drug (adalimumab, etanercept, infliximab, certolizumab, golimumab, abatacept, rituximab, tocilizumab, or anakinra)	Categorical	Chi-squared test	$H_0$4.6
Number of 30-day supplies for oral steroids	Count	Mann-Whitney U	$H_0$5.1
Number of 30-day supplies for DMARDs	Count	Mann-Whitney U	$H_0$5.2
Number of RA-related outpatient visits	Count	Mann-Whitney U	$H_0$5.3
Number of RA-related radiographic procedures	Count	Mann-Whitney U	$H_0$5.4
Number of RA-related laboratory procedures	Count	Mann-Whitney U	$H_0$5.5
Number of RA-related intra-articular injections	Count	Mann-Whitney U	$H_0$5.6
Number of RA-related rehabilitation visits	Count	Mann-Whitney U	$H_0$5.7
Number of RA-related surgical procedures	Count	Mann-Whitney U	$H_0$5.8

To address Objective 6 ($H_0$6.1–$H_0$6.8), multiple logistic regressions were used to model the odds of switching within 365 days after initiation of biologic therapy. Predictors of the model included the number 30-day supplies for steroids and DMARDs, RA-related outpatient visits, radiographic, laboratory, intra-articular injections, rehabilitation, and surgical procedures, index biologic drug, and index therapy type. Covariates such as patient demographic variables (age, gender, and geographic region) were also included in the models. The logistic regression model can be described with the equations below.

$$Y = \begin{cases} 0, & no\ switch \\ 1, & swtich \end{cases}$$

$$logit\ (P) = \ln\left(\frac{P}{1-P}\right) = \alpha + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 \ldots + \beta_{13} X_{13}$$

P = probability of switching (Y=1)

α = constant

β = regression coefficient of predictors/covariates

X_1 = steroids

X_2 = DMARDs

X_3 = outpatient visits

X_4 = radiographic procedures

X_5 = laboratory procedures

X_6 = intra-articular injections

X_7 = rehabilitation visits

X_8 = surgical procedures

X_9 = index biologic

X_{10} = index therapy type

X_{11} = age

X_{12} = gender

X_{13} = geographic region

A second model with similar variables except the replacement of index biologic (X_9) with index biologic class was also developed to examine whether the class of index biologic would be a stronger predictor for the odds of switching.

All statistical analyses were performed using SAS version 9.3 (Cary, NC). A priori alpha level was set at 0.05 for all analyses.

Chapter 3: Results

SAMPLE SIZE AND CHARACTERISTICS

Overall, a total of 216,387 patients were on at least one biologic of interest during the study period. Among them, 69,942 were adult patients with RA. After all the inclusion and exclusion criteria were applied, the final sample size included 12,370 patients. Table 3.1 reports the sample size for each criterion applied.

Table 3.1. Patient Selection

	Sample size
Inclusion Criteria	
At least one biologic[a] claim from 01/01/2009 to 12/31/2011	216,387
At least one medical claim with diagnoses of Rheumatoid Arthritis (ICD-9-CM 714.x) within 365 days prior to index date	73,243
Between the ages of 18 and 64 at index date	69,942
Continuously enrollment in pharmacy and medical benefit	36,265
Exclusion Criteria	
Any biologic[a] claim from within 365 days prior to index date, excluding index date	14,425
More than one unique biologic at index date	14,424
At least one claim with diagnoses of confounding diseases[b] throughout study period	12,370
Exclude patients with missing gender or age	12,370

[a] Included adalimumab, etanercept, infliximab, certolizumab, golimumab, abatacept, rituximab, tocilizumab, and anakinra

[b] Included psoriasis and psoriatic arthritis (ICD-9-CM 696.x), ankylosing spondylitis (ICD-9-CM 720.0), Crohn's disease (ICD-9-CM 555.2), and ulcerative colitis (ICD-9-CM 556.8)

Of the 12,370 patients included in the study, 18.4% patients (n=2,282) experienced a switch within one year of biologic initiation, while 81.6% did not (n=10,088). Table 3.2 reports the patient characteristics of the final study sample. The average age for all patients was 49.5 years and the majority of the patients were female (78.0%). Patients who had a switch (switchers) were marginally older by less than one year and the percentage of females switching (19.2%) was higher than males (15.9%). Many patients resided in the South Region (43.1%) and the North Central/Midwest Region (25.6%). Similar regional patterns were observed among switchers and the non-switchers (p=.546).

INDEX THERAPY CHARACTERISTICS

Characteristics of index therapy are reported in Table 3.3. About 53% of the patients were started on biologic treatments as combination therapy with DMARDs. The proportions of patients using combination therapy were 51.1% among switchers and 53.3% among non-switchers (p=.061). The majority of the index biologics were anti-TNFs (89.3%). A lower proportion of switchers (6.9%) were initiated on non-anti-TNFs than non-switchers (11.5%), and this difference was statistically significant (p<.001). Etanercept (41.6%) and adalimumab (31.3%) were the most commonly prescribed biologics. The switch rate for each biologic drug ranged from 4.8% for rituximab to 21.0% for golimumab. About one-fifth of the patients taking etanercept (20.2%) and certolizumab (20.0%) switched to another biologic within one year. The overall distribution of patients across different biologic was statistically significantly different between the two groups (p<.001).

Table 3.2. Patient Characteristics

Characteristics	All n=12,370	Switcher n=2,282 [18.4%]	Non-Switcher n=10,088 [81.6%]	*p*-value[a]
Age, mean (SD)	49.5 (10.3)	49.7 (10.2)	48.8 (10.4)	<.001
Gender, n (Column%) [Row%]				<.001
Male	2,725 (22.0%)	434 (19.0%) [15.9%]	2,291 (22.7%) [84.1%]	
Female	9,645 (78.0%)	1,848 (81.0%) [19.2%]	7,797 (77.3%) [80.8%]	
Region, n (Column%) [Row%]				.546
Northeast	1,425 (11.5%)	288 (12.6%) [20.2%]	1,137 (11.3%) [79.8%]	
North Central/ Midwest	3,172 (25.6%)	564 (24.7%) [17.8%]	2,608 (25.9%) [82.2%]	
South	5,336 (43.1%)	957 (41.9%) [17.9%]	4,379 (43.4%) [82.1%]	
West	2,324 (18.8%)	458 (20.1%) [19.7%]	1,866 (18.5%) [80.3%]	
Missing	113 (0.9%)	15 (0.7%) [13.3%]	98 (1.0%) [86.7%]	

[a] The difference in age between switchers and non-switchers was tested using independent t-test and the difference in the distribution of gender and region were tested using Chi-squared test.

Table 3.3. Index Drug Characteristics

Characteristics, n (Column%) [Row%]	All n=12,370		Switcher n=2,282 [18.4%]		Non-Switcher n=10,088 [81.6%]		*p*-value
Index Therapy Type							.061
Monotherapy	5,825	(47.1%)	1,115	(48.9%) [19.1%]	4,710	(46.7%) [80.9%]	
Combination therapy	6,545	(52.9%)	1,167	(51.1%) [17.8%]	5,378	(53.3%) [82.2%]	
Index Biologic Class							<.001
Anti-TNF	11,051	(89.3%)	2,124	(93.1%) [19.2%]	8,927	(88.5%) [80.8%]	
Non-anti-TNF	1,319	(10.7%)	158	(6.9%) [12.0%]	1,161	(11.5%) [88.0%]	
Index Biologic Drug							<.001
Etanercept	5,147	(41.6%)	1,042	(45.7%) [20.2%]	4,105	(40.7%) [79.8%]	
Adalimumab	3,874	(31.3%)	727	(31.9%) [18.8%]	3,147	(31.2%) [81.2%]	
Infliximab	1,274	(10.3%)	199	(8.7%) [15.6%]	1,075	(10.7%) [84.4%]	
Abatacept	643	(5.2%)	112	(4.9%) [17.4%]	531	(5.3%) [82.6%]	
Rituximab	559	(4.5%)	27	(1.2%) [4.8%]	532	(5.3%) [95.2%]	
Golimumab	486	(3.9%)	102	(4.5%) [21.0%]	384	(3.8%) [79.0%]	
Certolizumab	270	(2.2%)	54	(2.4%) [20.0%]	216	(2.1%) [80.0%]	
Tocilizumab	66	(0.5%)	10	(0.4%) [15.2%]	56	(0.6%) [84.8%]	
Anakinra	51	(0.4%)	9	(0.4%) [17.6%]	42	(0.4%) [82.4%]	

SWITCHING PATTERNS

Of those who experienced a switch (n =2,282; 18.4%), the median time to switch was 181 days (range=[1, 365], mean=187.7, SD=91.6). A majority of the switchers were prescribed two unique biologics within one year of biologic initiation (median=2, range=[2, 5], mean=2.2, SD=0.4). The median number of index biologic claim counts prior to switch was four (range=[2, 6]), mean=4.3, SD=2.8).

RA-RELATED HEALTH CARE RESOURCE UTILIZATION

Overall, switchers had more RA-related health care resource utilization than non-switchers. Specifically, switchers filled more steroid and DMARD prescriptions and had more RA-related outpatient visits and laboratory procedures (Table 3.4, all $p<.001$). In addition, a significantly greater proportion of switchers had steroid and DMARD prescription fills and utilized outpatient, radiographic, laboratory, intra-articular injection, and rehabilitation services (Table 3.5, all $p<.001$). Given the small percentage of patients underwent surgery for RA (0.2%), there was no statistically significant difference found in the quantity and frequency of surgical procedure between the two groups (both $p=0.470$).

Table 3.4. Quantity of Use for Rheumatoid Arthritis Related Health Care Resources

Variable	All		Switcher		Non-Switcher		*p*-value
	Median (Range)						
	Mean [SD]						
Steroid - Number of 30-DS	0.4	(0-27)	2	(0-27)	0.2	(0-25)	<.001
	2.6	[3.86]	3.5	[4.03]	2.3	[3.79]	
DMARD - Number of 30-DS	3.8	(0-70)	5	(0-30)	3	(0-70)	<.001
	5.2	[5.33]	5.8	[5.19]	5.0	[5.35]	
Outpatient visit	5	(0-86)	7	(0-54)	5	(0-86)	<.001
	6.7	[5.53]	8.0	[5.01]	6.4	[5.60]	
Radiographic procedure	0	(0-12)	0	(0-6)	0	(0-12)	<.001
	0.2	[0.55]	0.4	[0.67]	0.2	[0.51]	
Laboratory procedure	2	(0-24)	2	(0-24)	1	(0-20)	<.001
	2.1	[2.23]	2.5	[2.32]	2.0	[2.20]	
Intra-articular injection	0	(0-23)	0	(0-23)	0	(0-14)	<.001
	0.5	[1.16]	0.6	[1.29]	0.4	[1.12]	
Rehabilitation visit	0	(0-47)	0	(0-47)	0	(0-45)	<.001
	0.1	[1.50]	0.2	[1.67]	0.1	[1.45]	
Surgical procedure	0	(0-2)	0	(0-2)	0	(0-2)	.470
	0.0	[0.06]	0.0	[0.06]	0.0	[0.06]	

DS=day supply; DMARD=disease modifying anti-rheumatic drug

Table 3.5. Frequency of Patients Using Rheumatoid Arthritis Related Health Care Resources

Variable n (Column%) [Row%]	Frequency[a] (%) All n=12,370	Switcher n=2,282 [18.4%]	Non-Switcher n=10,088 [81.6%]	*p*-value
Steroid - Number of 30-DS	7,232 (58.5%)	1,791 (78.5%) [24.8%]	5,441 (53.9%) [75.2%]	<.001
DMARD - Number of 30-DS	8,142 (65.8%)	1,760 (77.1%) [21.6%]	6,382 (63.3%) [78.4%]	<.001
Outpatient visit	11,882 (96.1%)	2,265 (99.3%) [19.1%]	9,617 (95.3%) [80.9%]	<.001
Radiographic procedure	2,244 (18.1%)	689 (30.2%) [30.7%]	1,555 (15.4%) [69.3%]	<.001
Laboratory procedure	8,303 (67.1%)	1,749 (76.6%) [21.1%]	6,554 (65.0%) [78.9%]	<.001
Intra-articular injection	2,889 (23.4%)	754 (33.0%) [26.1%]	2,135 (21.2%) [73.9%]	<.001
Rehabilitation visit	244 (2.0%)	67 (2.9%) [27.5%]	177 (1.8%) [72.5%]	<.001
Surgical procedure	30 (0.2%)	4 (0.2%) [13.3%]	26 (0.3%) [86.7%]	.470

DS=day supply; DMARD=disease modifying anti-rheumatic drug

[a] The number of patients with at least one medical claim for a rheumatoid arthritis related health care service or procedure.

PREDICTORS OF SWITCHING

Two logistic regression models were performed to predict the odds of switching. They examined the associations between the odds of switching and the use of RA-related health care resources and index therapy characteristics as previously outlined in the Methods Section. Due to the small rates of utilization for surgery (0.2%) and rehabilitation services (2.0%), these two variables were excluded from the logistic regression models.

In Model I (Table 3.6), the number of 30-day supplies for steroids and DMARDs, and the number of outpatient visits, radiographic and laboratory procedures, and intra-articular injections were significant predictors of switching while controlling for age, gender and geographic region. Specifically, with every additional RA-related radiographic procedure performed, the odds of switching increased by a factor of 51% (OR=1.51, 95% CI=[1.40, 1.63]) and with every additional intra-articular injection received, the odds of switching increased by a factor of 17% (OR=1.17, 95% CI=[1.13, 1.22]). The use of certain biologics was associated with lower odds of switching. Compared to the patients who initiated on etanercept, patients who started on infliximab, abatacept, tocilizumab, and rituximab had significantly lower odds of switching. In addition, patients started on combination therapy with a DMARD also had significantly lower odds of switching than those initiated on biologic monotherapy (OR=0.78, 95% CI=[0.69, 0.88]).

Model II (Table 3.7) included similar predictors as Model I, except the index biologic drug variable was replaced with the index biologic class categorization. The purpose of Model II was to examine whether the index biologic class (i.e. whether index biologic drug was an anti-TNF) was associated with the odds of switching. Findings from Model II were similar to Model I. Replacement of the index biologic drug by index

biologic class led to a minor reduction in model predictability as indicated by a decrease of the c-statistic from 0.695 in Model I to 0.684 in Model II. Results from Model II showed that patients who initiated on an anti-TNF biologic had 2.62 times higher odds of switching than those who started on a non-anti-TNF biologic (OR=2.62, 95% CI=[2.17, 3.16]).

Table 3.6. Logistic Regression to Predict the Odds of Switching – Model I[a]

Predictor	Odds Ratio	95% CI	*p*-value
Steroid - Number of 30-DS	1.07	[1.06, 1.08]	<.001
DMARD - Number of 30-DS	1.03	[1.02, 1.05]	<.001
Outpatient visit	1.04	[1.03, 1.05]	<.001
Radiographic procedure	1.51	[1.40, 1.63]	<.001
Laboratory procedure	1.06	[1.03, 1.08]	<.001
Intra-articular injection	1.17	[1.13, 1.22]	<.001
Index Biologic (Ref: Etanercept)			
Golimumab	1.05	[0.83, 1.33]	.690
Certolizumab	0.90	[0.65, 1.24]	.510
Adalimumab	0.90	[0.81, 1.00]	.060
Anakinra	0.63	[0.30, 1.33]	.225
Infliximab	0.51	[0.43, 0.61]	<.001
Abatacept	0.48	[0.38, 0.61]	<.001
Tocilizumab	0.41	[0.20, 0.82]	.012
Rituximab	0.11	[0.07, 0.17]	<.001
Index therapy type (Ref: Monotherapy)			
Combination therapy	0.78	[0.69, 0.88]	<.001
Age	0.99	[0.98, 0.99]	<.001
Gender (Ref: Female)			
Male	0.79	[0.70, 0.89]	<.001
Region (Ref: Northeast)			
North Central/Midwest	0.83	[0.70, 0.98]	.026
South	0.81	[0.69, 0.94]	.007
West	0.95	[0.80, 1.13]	.544
Missing	0.60	[0.34, 1.06]	.076

[a] c-statistic=0.695

Table 3.7. Logistic Regression to Predict the Odds of Switching – Model II[a]

Predictor	Odds Ratio	95% CI	*p*-value
Steroid - Number of 30-DS	1.07	[1.06, 1.08]	<.001
DMARD - Number of 30-DS	1.03	[1.02, 1.04]	<.001
Outpatient visit	1.03	[1.03, 1.04]	<.001
Radiographic procedure	1.53	[1.41, 1.65]	<.001
Laboratory procedure	1.05	[1.03, 1.07]	<.001
Intra-articular injection	1.12	[1.08, 1.16]	<.001
Index Biologic Class[b] (Ref: Non-anti-TNF)			
Anti-TNF	2.62	[2.17, 3.16]	<.001
Index therapy type (Ref: Monotherapy)			
Combination therapy	0.79	[0.70, 0.89]	<.001
Age	0.99	[0.98, 0.99]	<.001
Gender (Ref: Female)			
Male	0.79	[0.70, 0.89]	<.001
Region (Ref: Northeast)			
North Central/Midwest	0.82	[0.70, 0.97]	.020
South	0.82	[0.70, 0.95]	.009
West	0.96	[0.81, 1.14]	.635
Missing	0.60	[0.34, 1.06]	.080

[a] c-statistic=0.684
[b] Replaced index biologic in Model I

RESULT SUMMARY

Results for all the hypotheses tested in this study were summarized in Table 3.8. Statistically significant differences were found between switchers and non-switchers in most patient characteristics (Objective 4) and RA-related health care resource utilization variables (Objective 5). In addition, all the health care resource utilization variables that were included in the final regression models were significant predictors of switching.

Table 3.8. Summary of Hypotheses Tested

Objective		***p*-value**	**Result**
$H_0$4.1	There is no statistically significant difference between switchers and non-switchers in the distributions of gender.	<.001	Rejected
$H_0$4.2	There is no statistically significant difference between switchers and non-switchers in mean age.	<.001	Rejected
$H_0$4.3	There is no statistically significant difference between switchers and non-switchers in the distributions of geographic region.	.546	Failed to reject
$H_0$4.4	There is no statistically significant difference between switchers and non-switchers in the proportion of patients using biologic monotherapy at treatment initiation.	.061	Failed to reject
$H_0$4.5	There is no statistically significant difference between switchers and non-switchers in the proportion of patients initiated on an anti-TNF as the first biologic therapy.	<.001	Rejected
$H_0$4.6	There is no statistically significant difference between switchers and non-switchers in the proportion of patients using different biologics	<.001	Rejected
$H_0$5.1	There is no statistically significant difference between switchers and non-switchers in the number of 30-day supplies for oral steroids.	<.001	Rejected
$H_0$5.2	There is no statistically significant difference between switchers and non-switchers in the number of 30-day supplies for DMARDs.	<.001	Rejected
$H_0$5.3	There is no statistically significant difference between switchers and non-switchers in the number of RA-related outpatient visits.	<.001	Rejected
$H_0$5.4	There is no statistically significant difference between switchers and non-switchers in the number of RA-related radiographic procedures.	<.001	Rejected
$H_0$5.5	There is no statistically significant difference between switchers and non-switchers in the number of RA-related laboratory procedures.	<.001	Rejected
$H_0$5.6	There is no statistically significant difference between switchers and non-switchers in the number of RA-related intra-articular injections.	<.001	Rejected

Table 3.8. (Continued)

Objective		*p*-value	Result
$H_0$5.7	There is no statistically significant difference between switchers and non-switchers in the number of RA-related rehabilitation visits.	<.001	Rejected
$H_0$5.8	There is no statistically significant difference between switchers and non-switchers in the number of RA-related surgical procedures.	.470	Failed to reject
$H_0$6.1	The number of 30-day supplies for oral steroids prior to switch is not a statistically significant predictor of switching.	<.001	Rejected
$H_0$6.2	The number of 30-day supplies for DMARDs prior to switch is not a statistically significant predictor of switching.	<.001	Rejected
$H_0$6.3	The number of RA-related outpatient visits prior to switch is not a statistically significant predictor of switching.	<.001	Rejected
$H_0$6.4	The number of RA-related radiographic procedures prior to switch is not a statistically significant predictor of switching.	<.001	Rejected
$H_0$6.5	The number of RA-related laboratory procedures prior to switch is not a statistically significant predictor of switching.	<.001	Rejected
$H_0$6.6	The number of RA-related intra-articular injections prior to switch is not a statistically significant predictor of switching.	<.001	Rejected
$H_0$6.7[a]	The number of RA-related rehabilitation services prior to switch is not a statistically significant predictor of switching.	N/A	N/A
$H_0$6.8[a]	The number of RA-related surgical procedures prior to switch is not a statistically significant predictor of switching.	N/A	N/A

N/A=not available

[a] The number of RA-related rehabilitation services and surgical procedures were removed from multiple logistic regression analysis due to the small number of patients incurring these services.

Chapter 4: Discussion and Conclusion

DISCUSSION

This study explored the relationship between patterns of health care resource utilization and switching of biologics in RA patients initiated on biologic therapy. The statistically significant differences in the quantity and rate of RA-related health care resource use suggest patients who were inadequately managed by current treatments experienced an increase in intensity and frequency of care prior to switching to another biologic regimen. Findings from this study also support the use of claim-based health care resource variables as a useful tool to predict treatment response to biologics as indicated by a switch in biologic therapy.

Close to one-fifth of the RA patients switched to a different biologic within one year and the majority of the switches occurred within 6 months into biologic treatment initiation. The biologic switch rate observed in this study (i.e., 18.4%) is higher than the switch rates reported in existing literature, which range from 7% to 15%. Meanwhile, the median time to switch is consistent with the findings reported by Bonafede and colleagues.[27] The higher switch rate reported in this study could potentially be related to differences in study populations. While Bonafede et al. utilized the same data source and had similar inclusion criteria as the current study, the study only included patients who initiated on etanercept, adalimumab or infliximab, which are the most commonly prescribed biologic for many auto-immune diseases. Similarly, many other studies examined only patients who either started on one particular biologic, or more specifically, the switch from one particular biologic to another.[26] The expanded inclusion of patients using biologics beyond the most popular anti-TNF agents would likely yield an increase in switch rate as this study found that switch rates were highest in patients started on etanercept, golimumab, and certolizumab. In addition, the definition of a switch also

differs between studies. The definition of switching in Li et al. required a pre-defined discontinuation gap of 90 or 120 days – a period of time where patients are not under any biologic treatment for RA.[28] The absent of such requirement allowed this study to include more patients who experienced a switch. Another possible explanation for the differences in switch rate could be attributable to the accounting of switches regardless of the reasons for switch. Many studies utilized chart review to determine the reason for switch and therefore only accounted for switches due to inefficacy. In this study, it was not feasible to identify the reason for switch since the analyses were performed using administrative claims.

Despite the higher switch rate, similar trends were observed between this study and existing literature.[27, 29] The common age of onset for RA is between 40 to 60 years old.[3] Therefore it is not surprising to find the average age of the study population to be around 50 years old. In this study, patients older than 64 years old were excluded from analysis. Although there was a statistically significant difference in mean age between switchers and non-switchers, the magnitude of the difference was less than one year. More female patients switched within one year than male patients and the logistic regression model confirmed that female patients had higher odds of switching than male patients. This result resonates with the findings from Hyrich et al. and van der Heijde et al. that male gender is positively associated with treatment response.[39, 40] These two studies also echo the finding that concomitant DMARDs use was associated with a lower likelihood of switch. Both authors demonstrated that concomitant methotrexate use is a significant predictor of treatment response.

The logistic regression models reveal that increasing uses of RA-related procedures and services were significantly associated with switching. In particular, patients initiated on anti-TNFs had nearly tripled the odds of switching than those

initiated on non-anti-TNFs. In clinical guidelines and real-world practice, non-TNFs are considered as second- and third-line agents reserved for the use after failure of first-line biologics, either due to inefficacy, intolerance, or the presence of certain comorbidities.[12] Therefore, patients prescribed non-anti-TNFs might already have prior experience with anti-TNFs and were initiated on non-anti-TNFs due to one of the reasons described previously. Although this study employed a 12-month washout period to increase the likelihood of capturing biologic-naïve patients, biologic use longer than 12 months prior to the index date was not examined. Both regression models had a nearly acceptable discrimination of a switcher from a non-switcher (c-statistics close to 0.7), suggesting that claims-based health care resource utilization variables can be potentially useful to predict a patient's likelihood to switch, and therefore allows for the systematic identification of patients who will likely experience sub-optimal treatment early on in therapy initiation.

The use of administrative claims to measure biologic effectiveness in RA is a small area of research but not a novel concept. Curtis et al. developed and validated a claims-based algorithm in 2011.[43] One of the major challenges with Curtis' algorithm is that it requires patients to be highly adherent to the treatment drug as defined by a medication possession ratio (MPR) of 80%. A recent systematic review by Blum et al. found that only 51% of RA patients naïve to biologic were adherent (MPR≥80%) and this percentage dropped to 42% in patients experienced with biologic treatments.[50] The mean MPR reported in the same review was 52%. Based on the low rates of adherence among RA patients, most patients would automatically be considered as having ineffective biologic treatment based on Curtis' algorithm, simply due to their non-adherence to biologics. The variables in the current study's predictive models are similar to those in Curtis' algorithm. Instead of capturing independent variables as dichotomous measures

like in Curtis et al., this study retained the variables in continuous format and therefore could provide richer information on how the quantity of health care resource utilization reflects treatment effectiveness.

LIMITATIONS

This study has several limitations. The reasons for switching could not be identified in this study given the nature of administrative claims. Although literature has shown up to 80% of switches are due to treatment inefficacy[26], patients could also switch to another biologic due to adverse events, newly developed contraindications, and formulary preferences set by insurance companies. As previously mentioned, this study only required patients to have an absence of biologic treatment within 12 months prior to index date and therefore could not completely exclude patients who were experienced with biologic treatments for RA. In addition, the use of DMARDs and oral steroids was determined using prescription fills. The presence of a prescription fill does not necessary confirm that patients are actually taking the medications. Furthermore, both DMARDs and steroids can be used for a whole host of other disease states and thus the true indication for DMARD and/or steroid prescriptions could not be determined using pharmacy claims. The severity of RA also could not be determined due to the lack of clinical information. Therefore, it is uncertain whether there is a difference in severity between switchers and non-switchers. Lastly, patients in the MCED database include employees of large employers, as well as their spouses and dependents, who are covered under private health insurance offered by the employers. Patients enrolled in Medicare or Medicaid were not included in this analysis. Therefore, the findings may not be generalizable to the entire US population.

CONCLUSION

Determining the clinical effectiveness of treatments for RA is difficult in the absence of clinical data and practitioner assessments. With the increasing availability and popularity of costly biologic agents indicated for RA, the ability to identify patients who are likely to experience treatment ineffectiveness on a population level is crucial for the clinical community and managed care organizations to prevent waste and sub-optimal management of RA. Switching of biologic is largely due to treatment ineffectiveness and switching behavior can be conveniently identified in administrative claims. This study demonstrates that patterns of RA-related health care resource utilization can be used to predict switching and thus can potentially serve as useful measures of treatment ineffectiveness.

Appendix

Appendix A: Claim Codes Used to Identify Pharmaceutical and Medical Resource Utilization

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone)	NDC 00006-0219-68, 00009-0015-01, 00009-0023-01, 00009-0034-01, 00143-1202-01, 00182-1648-01, 00536-3530-01, 00536-3530-05, 00603-3062-21, 00615-0502-53, 00615-0502-63, 00615-0502-65, 00677-0046-01, 00839-5084-06, 00904-2043-60, 51432-0114-03, 52544-0798-01, 60429-0015-01, 00006-0020-68, 00006-0041-68, 00006-0063-12, 00006-0063-68, 00006-0095-50, 00006-0097-28, 00006-0097-50, 00006-0147-50, 00006-7622-55, 00006-7622-66, 00032-3205-01, 00032-3210-01, 00032-3215-01, 00032-3220-01, 00052-0790-91, 00052-0793-04, 00052-0795-14, 00052-0798-90, 00052-0798-91, 00054-3177-57, 00054-3177-63, 00054-4179-25, 00054-4179-31, 00054-4180-25, 00054-4181-25, 00054-4182-25, 00054-4183-25, 00054-4184-25, 00054-4186-25, 00054-8168-16, 00054-8174-25, 00054-8175-25, 00054-8176-25, 00054-8177-16, 00054-8179-25, 00054-8180-25, 00054-8181-25, 00054-8183-25, 00095-0086-35, 00095-0086-51, 00095-0087-35, 00095-0088-51, 00095-0089-21, 00182-0488-01, 00182-1013-44, 00182-1612-01, 00182-1613-19, 00182-1614-01, 00182-1614-19, 00223-0790-01, 00223-0791-01, 00223-0791-02, 00223-0792-01, 00223-6496-01, 00223-6496-02, 00247-0624-07, 00247-0624-12, 00247-0624-20, 00247-0624-21, 00247-1010-04, 00247-1010-12, 00254-2667-06, 00364-0098-01, 00364-0098-02, 00364-0397-01, 00364-0397-02, 00364-0398-01, 00364-0399-01, 00364-7182-61, 00364-7182-76, 00403-0738-91, 00403-0755-18, 00403-0756-18, 00405-2625-77, 00405-4313-01, 00405-4314-01, 00405-4315-01, 00405-4316-01, 00405-4317-01, 00405-4318-01, 00426-8466-00, 00426-8466-08, 00472-0972-08, 00472-0972-28, 00472-0972-33, 00536-0452-59, 00536-3580-06, 00536-3581-01, 00536-3582-01, 00536-3583-01, 00536-3583-10, 00536-3584-01, 00603-1145-56, 00603-1147-56, 00603-3190-21, 00603-3191-11, 00603-3191-21, 00603-3192-21, 00603-3194-21, 00615-0506-52, 00659-2501-05, 00677-0340-01, 00677-0601-42, 00677-0849-01, 00686-0506-21, 00686-0972-33, 00781-6400-08, 00814-2358-14, 00814-2360-14, 00814-2362-14, 00814-2364-14, 00814-2365-14, 00839-1228-03, 00839-1228-06, 00839-6019-06, 00839-6020-06, 00839-6044-66, 00839-6734-06, 00839-7997-66, 00904-0243-60, 00904-0244-12, 00904-0244-60, 00904-0245-60, 00904-0246-60, 00904-0972-04, 00904-0972-09, 00998-0615-05, 16590-0269-10, 21695-0290-30, 21695-0382-04, 21695-0382-06, 21695-0382-08, 21695-0382-20, 21695-0382-60, 21695-0728-12, 21695-0745-10, 21695-0745-12, 23490-5404-01, 23490-5407-01, 23490-5407-02, 35356-0359-30, 43063-0266-07, 44183-0507-35, 44183-0508-51, 44183-0509-21, 49727-0105-02, 49884-0083-01, 49884-0083-10, 49884-0084-01, 49884-0084-10, 49884-0085-01, 49884-0085-05, 49884-0085-10, 49884-0086-01, 49884-0086-03, 49884-0086-05, 49884-0086-10, 49884-0087-01, 49884-0087-03, 49884-0087-05, 49884-0087-10, 49884-0129-01, 49884-0129-03, 49999-0059-06, 49999-0059-30, 51432-0126-03, 51432-0128-03, 51432-0130-03, 51432-0132-03, 51432-0560-19, 51432-0925-03, 52555-0064-01, 52555-0066-01, 52959-0392-12, 52959-0392-21, 52959-0392-28, 52959-0392-30, 52959-0547-10, 52959-0547-11, 52959-0547-12, 52959-0547-16, 52959-0547-20, 52959-0547-30, 52959-0547-50, 52959-1504-00, 52959-1504-21, 53002-0412-05, 53002-0412-12, 53002-0412-30, 53002-0471-30, 53002-0508-15, 53002-0614-91, 53002-0614-92, 53002-0614-97, 54124-0488-30, 54569-0320-00, 54569-0321-00, 54569-0322-00, 54569-0322-01, 54569-0322-03, 54569-0322-04, 54569-0322-05, 54569-0324-02, 54569-0324-04, 54569-0324-05, 54569-0324-06, 54569-0324-07, 54569-0324-08, 54569-0324-09, 54569-0336-01, 54569-0336-02, 54569-0336-03, 54569-1034-00, 54569-1035-00, 54569-1302-00, 54569-3110-00, 54569-5729-00, 54868-0218-00, 54868-0218-01, 54868-0218-02, 54868-0218-03, 54868-0218-04, 54868-0218-05, 54868-0218-06, 54868-0218-07, 54868-0218-08, 54868-0218-09, 54868-0911-01, 54868-0916-00, 54868-0927-00, 54868-1744-00, 54868-3157-01, 54868-5334-00, 54868-5903-00, 54879-0003-08, 55045-1308-04, 55045-1308-05, 55045-1428-01, 55045-1970-02, 55045-1970-05, 55045-1970-08, 55045-2665-02, 55175-1104-01, 55175-1341-01, 55175-1341-02, 55175-1341-03, 55175-1341-06, 55175-1342-04, 55175-1342-07, 55175-1855-00, 55175-1855-02, 55175-1855-03, 55289-0410-04, 55289-0582-04, 55289-0582-06, 55289-0582-10, 55289-0582-28, 55289-0903-10, 55289-0903-12, 55289-0903-20, 57866-3581-01, 58016-0290-00, 58016-0290-02, 58016-0290-03, 58016-0290-12, 58016-0290-15, 58016-0290-20, 58016-0290-30, 58016-0290-73, 58016-0290-89, 58016-0293-00, 58016-0293-12, 58016-0293-15, 58016-0293-20, 58016-0293-30, 58016-0349-12, 58016-0781-00, 58016-0781-10, 58016-0781-12, 58016-0781-14, 58016-0781-15, 58016-0781-20, 58016-0781-21, 58016-0781-24, 58016-0781-28, 58016-0781-30, 58016-0781-40, 58016-0781-50

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone) (Continued)	58016-2931-00, 58016-2931-12, 58016-2931-15, 58016-2931-20, 58016-2931-30, 58729-0085-27, 60346-0173-12, 60346-0286-34, 60346-0356-12, 60346-0479-06, 60346-0479-08, 60346-0479-15, 60346-0479-19, 60346-0479-50, 60346-0550-12, 60346-0550-15, 60346-0550-30, 60346-0977-31, 60432-0466-00, 60432-0466-08, 60904-0085-27, 62584-0357-01, 63629-3742-01, 63629-3742-02, 63629-3742-03, 63629-4127-01, 63629-4129-01, 63874-0444-01, 63874-0444-12, 63874-0444-15, 63874-0444-20, 63874-0444-21, 63874-0444-30, 64679-0810-08, 64980-0509-24, 66267-0066-12, 66267-0066-30, 66267-0067-04, 66267-0067-08, 66267-0067-10, 66267-0067-12, 66267-0067-20, 66267-0067-21, 66336-0479-06, 66336-0479-15, 66336-0479-44, 66336-0550-12, 66336-0550-21, 68115-0096-12, 68115-0096-14, 68115-0097-20, 68115-0435-10, 68387-0172-21, 68850-0001-08, 00006-0619-68, 00006-0625-68, 00009-0012-01, 00009-0031-01, 00009-0044-01, 00115-3685-01, 00143-1254-01, 00143-1254-25, 00223-1063-01, 00223-1063-02, 00536-3913-01, 00603-3899-19, 00603-3900-21, 00603-3901-21, 00677-0076-01, 00686-1254-25, 00722-5220-01, 00814-3735-14, 00839-1365-06, 00904-2674-60, 43063-0208-01, 43063-0208-30, 43063-0208-60, 43063-0386-30, 51432-0214-03, 54505-0331-05, 54505-0332-10, 54505-0333-10, 54569-0328-00, 54569-0329-00, 54569-1982-00, 54868-1743-00, 54868-1743-01, 54868-1743-02, 54868-1743-03, 54868-1743-04, 54868-3924-00, 55045-3458-00, 59366-2807-02, 59366-2817-03, 59366-2827-03, 59762-0073-01, 59762-0074-01, 59762-0075-01, 60429-0262-01, 64720-0331-05, 64720-0332-10, 64720-0333-10, 67263-0282-01, 67263-0381-50, 68084-0224-11, 68084-0224-21, 68084-0469-01, 68084-0469-11, 68258-9074-01, 68258-9075-01, 00009-0142-01, 00009-0020-01, 00009-0022-01, 00009-0049-02, 00009-0056-01, 00009-0056-02, 00009-0056-03, 00009-0056-04, 00009-0056-05, 00009-0073-01, 00009-0073-02, 00009-0155-01, 00009-0176-01, 00182-1050-01, 00182-1050-03, 00247-0012-21, 00247-1365-01, 00247-1365-20, 00247-1365-21, 00247-1365-30, 00254-4216-13, 00254-4216-28, 00349-8279-01, 00349-8279-21, 00364-0467-01, 00364-0467-21, 00403-1304-18, 00405-4666-01, 00405-4666-21, 00440-7760-21, 00527-1296-07, 00536-4036-01, 00536-4036-44, 00555-0301-02, 00555-0301-38, 00591-0790-01, 00591-0790-21, 00603-4593-15, 00603-4593-21, 00677-0565-01, 00677-0565-13, 00677-1831-01, 00677-1831-13, 00781-1402-01, 00781-1402-07, 00781-5022-01, 00781-5022-07, 00814-4781-14, 00814-4781-21, 00839-6224-06, 00839-6224-58, 00904-2175-19, 00904-2175-60, 10544-0322-21, 11845-0120-19, 16590-0149-21, 18837-0086-21, 21695-0080-21, 23490-5902-01, 23629-0047-01, 23629-0047-10, 33358-0241-21, 35356-0194-21, 35356-0763-21, 42549-0522-21, 49884-0158-03, 49884-0490-01, 49884-0490-59, 49999-0153-21, 49999-0153-30, 50436-4037-01, 51285-0301-02, 51285-0301-21, 51432-0282-03, 51432-0282-21, 51432-0830-01, 51991-0188-01, 51991-0188-21, 51991-0188-31, 52544-0790-01, 52544-0790-21, 52959-0100-00, 52959-1083-00, 53002-0312-21, 53002-0312-30, 53261-0278-21, 54569-0327-00, 54569-0370-00, 54569-0370-01, 54569-1036-00, 54569-2014-00, 54569-4516-00, 54569-4580-00, 54569-7084-00, 54868-0776-01, 54868-2913-00, 54868-2913-01, 54868-2913-02, 54868-2913-03, 54868-4952-00, 54868-4952-01, 54868-6624-01, 55034-0123-21, 55045-1259-09, 55045-1811-08, 55045-3513-01, 55175-1103-01, 55289-0649-30, 55289-0649-98, 55887-0544-25, 55887-0554-50, 55887-0953-21, 56126-0326-11, 57866-4037-01, 57866-7100-01, 58016-2001-01, 58016-2004-01, 58016-4719-01, 59723-0035-01, 59746-0001-03, 59746-0001-06, 59746-0001-09, 59746-0002-04, 59746-0002-06, 59746-0003-14, 59746-0015-04, 59762-0049-01, 59762-0050-01, 59762-0051-01, 59762-3327-01, 59762-3327-02, 59762-4440-02, 59762-4440-03, 60346-0360-21, 60346-0608-10, 60346-0608-20, 60346-0608-44, 60346-0764-14, 61392-0136-30, 61392-0136-31, 61392-0136-32, 61392-0136-39, 61392-0136-45, 61392-0136-51, 61392-0136-54, 61392-0136-60, 61392-0136-90, 61392-0136-91, 62269-0351-21, 62269-0351-24, 63304-0591-22, 63629-3910-01, 63739-0161-10, 63739-0161-15, 63874-0413-21, 66116-0662-21, 66267-0961-21, 66993-0840-02, 66993-0840-21, 66993-0842-25, 67253-0360-10, 67253-0360-21, 67263-0400-86, 68001-0005-01, 68030-4037-01, 68084-0149-01, 68084-0149-11, 68115-0960-21, 68387-0170-01, 00093-6118-16, 00093-6118-87, 00115-4280-01, 00115-4280-03, 00121-0687-05, 00121-0687-08, 00121-0687-16, 00223-1512-01, 00223-1512-02, 00364-0217-01, 00364-0217-02, 00378-3425-24, 00378-3425-48, 00405-4823-01, 00405-4823-03, 00451-1500-08, 00451-1500-16, 00451-2201-04, 00472-0212-08, 00472-0212-16, 00472-0250-08, 00472-0250-16, 00527-1201-01, 00527-1201-05, 00527-1201-10, 00536-4346-10, 00536-4346-50, 00591-0520-38, 00591-5059-01, 00591-5059-10, 00603-1567-56, 00603-1567-58, 00603-1570-56, 00603-1570-58, 00677-0116-01,

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone) (Continued)	00677-0116-10, 00781-1540-01, 00814-6250-14, 00814-6250-30, 00814-6250-32, 00839-5076-06, 00839-5076-16, 00879-0128-01, 00879-0128-10, 00879-0801-08, 00879-0801-16, 00904-2155-60, 16477-0505-01, 16477-0505-21, 16477-0505-48, 16477-0507-48, 21695-0365-08, 21695-0365-16, 23490-6144-01, 23490-6144-02, 23490-6144-03, 23490-6145-01, 23490-6145-02, 23490-6145-03, 33358-0291-08, 38739-0150-08, 49999-0335-08, 49999-0335-24, 49999-0929-01, 50383-0042-24, 50383-0042-48, 51432-0354-06, 52544-0520-16, 52544-0520-38, 52959-0622-60, 54569-4012-00, 54569-4012-01, 54569-4012-02, 54569-4012-03, 54569-4012-04, 54569-4807-00, 54569-4827-00, 54569-4827-01, 54868-3220-00, 54868-4748-00, 54868-4749-00, 54868-4749-01, 55045-1825-02, 55175-1842-03, 55175-1842-06, 55175-1844-06, 55289-0952-02, 55289-0952-04, 57866-4327-01, 57866-4327-02, 58016-0673-12, 58016-0673-24, 58016-0673-48, 58016-4843-01, 58177-0910-05, 58177-0910-07, 58177-0912-03, 59196-0010-24, 59196-0010-48, 60432-0137-08, 60432-0137-16, 63629-1862-01, 66116-0174-82, 66440-0150-08, 66440-0150-16, 67870-0103-08, 67870-0103-16, 68071-1532-08, 68094-0524-58, 68115-0898-08, 68258-8987-02, 00065-0638-25, 00065-0638-27, 00247-0470-10, 00403-1731-18, 00998-0635-05, 00998-0635-10, 00998-0637-05, 00998-0637-10, 11980-0108-05, 11980-0174-05, 11980-0174-10, 11980-0180-01, 11980-0180-05, 11980-0180-10, 11980-0180-15, 16590-0189-05, 21695-0409-05, 51672-1338-03, 52959-0265-05, 52959-0265-10, 52959-0265-15, 52959-1501-05, 53002-0848-71, 53002-0848-72, 54569-0871-00, 54569-1203-00, 54569-1214-00, 54569-1858-00, 54569-2868-00, 54569-4293-00, 54569-4293-01, 54569-4309-00, 54569-4309-01, 54569-4401-00, 54868-0636-00, 54868-0636-01, 54868-1152-00, 54868-1152-01, 54868-4293-00, 54868-4293-01, 54868-4293-02, 55045-2176-02, 55175-4420-01, 55175-4420-05, 55175-5010-05, 58016-6057-01, 58016-6557-01, 60346-0188-77, 60346-0367-51, 60346-0934-77, 60758-0119-05, 60758-0119-10, 60758-0119-15, 61314-0637-05, 61314-0637-10, 61314-0637-15, 68115-0814-05, 68115-0814-10, 68115-0814-15, 68258-8997-01, 68387-0642-01, 00121-0711-04, 00121-0711-05, 00121-0711-10, 00121-0711-20, 00121-0759-08, 00178-0582-08, 00403-1611-18, 00574-0148-04, 00585-2250-01, 00603-9388-56, 13925-0501-04, 16477-0510-08, 17856-0759-05, 21695-0405-08, 35356-0488-04, 42254-0102-08, 50383-0040-04, 50383-0177-08, 53002-0624-92, 53014-0250-01, 54569-1335-00, 54569-5204-00, 54569-5204-01, 54569-5749-00, 54569-5749-01, 54569-6478-00, 54868-0821-00, 54868-0954-00, 54868-1720-00, 54868-5242-00, 55045-2885-00, 55045-2885-08, 55175-4004-01, 55289-0511-02, 58016-4144-01, 58177-0932-05, 59196-0011-04, 59196-0012-24, 59212-0700-48, 59439-0455-02, 59630-0700-14, 59630-0700-48, 59630-0701-14, 59630-0701-48, 59630-0702-14, 59630-0702-48, 59630-0710-08, 59630-0710-10, 60346-0451-04, 60432-0089-04, 60432-0212-08, 63717-0915-08, 65162-0667-88, 65162-0667-90, 65580-0251-01, 68135-0455-02, 68135-0455-03, 68188-0480-02, 68188-0482-02, 68188-0484-02, 68791-0100-04, 23589-0067-93, 23589-0070-93, 00009-0032-01, 00009-0045-01, 00009-0045-02, 00009-0045-04, 00009-0045-05, 00009-0045-16, 00009-0165-01, 00009-0165-02, 00009-0165-03, 00009-0193-01, 00009-0193-02, 00009-0193-03, 00009-0388-01, 00032-2808-01, 00032-2808-10, 00032-2810-01, 00032-2810-10, 00032-2812-01, 00032-2812-10, 00032-2814-01, 00032-2814-10, 00032-2816-01, 00054-0017-20, 00054-0017-25, 00054-0017-29, 00054-0018-20, 00054-0018-25, 00054-0018-29, 00054-0019-20, 00054-0019-25, 00054-3721-44, 00054-3722-50, 00054-3722-63, 00054-4728-25, 00054-4728-31, 00054-4729-25, 00054-4729-29, 00054-4730-25, 00054-4730-29, 00054-4733-25, 00054-4741-25, 00054-4741-31, 00054-4742-25, 00054-4747-25, 00054-8722-16, 00054-8724-25, 00054-8725-25, 00054-8726-25, 00054-8729-25, 00054-8730-04, 00054-8730-16, 00054-8736-16, 00054-8739-25, 00054-8740-25, 00054-8747-25, 00085-0843-03, 00131-2228-81, 00143-1425-01, 00143-1473-01, 00143-1473-10, 00143-1473-25, 00143-1475-01, 00143-1475-10, 00143-1477-01, 00143-1477-05, 00143-1477-10, 00143-1477-25, 00143-9738-01, 00143-9738-05, 00143-9738-10, 00143-9739-01, 00143-9739-10, 00143-9740-01, 00143-9740-10, 00182-0201-00, 00182-0201-10, 00182-0201-89, 00182-1086-00, 00182-1086-01, 00182-1086-10, 00182-1086-89, 00182-1334-00, 00182-1334-01, 00182-1334-10, 00182-1334-89, 00223-1515-01, 00223-1515-02, 00223-1516-01, 00228-2336-96, 00228-2337-10, 00228-2337-50, 00228-2338-10, 00228-2338-50, 00247-0071-35, 00247-0071-40, 00247-0071-42, 00247-0071-43, 00247-0071-50, 00247-0072-00, 00247-0072-03, 00247-0072-04, 00247-0072-10, 00247-0072-15, 00247-0072-20, 00247-0072-21, 00247-0072-22, 00247-0072-24, 00247-0072-27, 00247-0072-30, 00247-0072-36, 00247-0072-40, 00247-0072-42, 00247-0072-44, 00247-0072-45

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone) (Continued)	00247-0072-48, 00247-0072-50, 00247-0072-52, 00247-0072-54, 00247-0072-60, 00247-0072-61, 00247-0072-80, 00247-0072-99, 00247-0100-00, 00247-0100-03, 00247-0100-04, 00247-0100-07, 00247-0100-08, 00247-0100-09, 00247-0100-10, 00247-0100-12, 00247-0100-13, 00247-0100-14, 00247-0100-15, 00247-0100-18, 00247-0100-20, 00247-0100-21, 00247-0100-27, 00247-0100-30, 00247-0100-42, 00247-0973-40, 00247-1176-21, 00247-1323-21, 00247-1323-60, 00247-1417-30, 00254-5093-13, 00254-5093-23, 00254-5094-13, 00254-5094-23, 00259-0284-01, 00259-0364-21, 00259-0364-48, 00259-0389-48, 00259-0390-21, 00259-0391-48, 00259-0400-49, 00304-0229-00, 00339-5293-12, 00339-5295-12, 00339-5296-12, 00339-5775-12, 00339-5777-12, 00349-8933-10, 00349-8934-01, 00349-8934-05, 00349-8935-01, 00364-0218-01, 00364-0218-02, 00364-0218-90, 00364-0442-01, 00364-0442-02, 00364-0442-05, 00364-0442-90, 00364-0461-01, 00364-0461-02, 00364-0461-05, 00364-0461-90, 00403-0770-01, 00403-0770-21, 00403-0770-30, 00403-0770-40, 00403-0770-42, 00403-0770-50, 00403-0772-14, 00403-0772-20, 00403-0772-30, 00403-0774-01, 00403-0774-15, 00403-0774-21, 00403-0774-36, 00403-0774-50, 00403-0774-71, 00403-1965-18, 00403-1967-18, 00405-4828-01, 00405-4828-03, 00405-4829-01, 00405-4829-02, 00405-4829-03, 00405-4830-01, 00405-4830-02, 00440-2165-12, 00440-2167-15, 00440-2167-20, 00440-8164-30, 00440-8165-06, 00440-8165-10, 00440-8165-12, 00440-8165-20, 00440-8165-21, 00440-8165-30, 00440-8165-60, 00440-8165-90, 00440-8166-04, 00440-8166-10, 00440-8166-12, 00440-8166-20, 00440-8166-30, 00440-8167-03, 00440-8167-04, 00440-8167-06, 00440-8167-10, 00440-8167-15, 00440-8167-18, 00440-8167-20, 00440-8167-21, 00440-8167-30, 00440-8167-60, 00440-8168-03, 00440-8168-05, 00440-8168-10, 00451-1201-04, 00451-1201-08, 00536-4324-10, 00536-4324-50, 00536-4325-01, 00536-4325-10, 00536-4326-01, 00536-4326-05, 00536-4326-10, 00536-4328-01, 00591-5052-01, 00591-5052-10, 00591-5442-01, 00591-5442-05, 00591-5442-10, 00591-5443-01, 00591-5443-05, 00591-5443-10, 00603-5332-15, 00603-5332-21, 00603-5332-31, 00603-5332-32, 00603-5333-15, 00603-5333-21, 00603-5333-31, 00603-5333-32, 00603-5334-21, 00603-5334-32, 00603-5335-21, 00603-5335-32, 00603-5336-21, 00603-5337-15, 00603-5337-21, 00603-5337-31, 00603-5337-32, 00603-5338-15, 00603-5338-21, 00603-5338-28, 00603-5338-31, 00603-5338-32, 00603-5339-21, 00603-5339-28, 00603-5339-32, 00615-0536-13, 00615-0536-21, 00615-0536-29, 00615-0536-43, 00615-0536-53, 00615-0536-63, 00615-0536-65, 00615-1542-29, 00615-1542-43, 00615-1542-53, 00615-1542-63, 00615-1542-65, 00615-3593-29, 00615-3593-43, 00615-3593-53, 00615-3593-63, 00615-3593-65, 00659-2502-21, 00659-2503-21, 00659-2504-21, 00677-0117-01, 00677-0117-10, 00677-0427-01, 00677-0427-05, 00677-0427-10, 00677-0698-01, 00677-0698-05, 00677-0698-10, 00686-0536-13, 00686-1542-13, 00781-1450-01, 00781-1450-13, 00781-1485-01, 00781-1485-13, 00781-1495-01, 00781-1495-10, 00781-1495-13, 00781-1500-01, 00781-1500-10, 00814-6285-14, 00814-6285-30, 00814-6288-14, 00814-6288-28, 00814-6290-14, 00814-6290-28, 00839-1517-06, 00839-1517-12, 00839-1520-06, 00839-1520-12, 00839-1520-16, 00839-5143-06, 00839-5143-16, 00839-5143-58, 00879-0129-01, 00879-0129-10, 00879-0438-01, 00879-0438-05, 00879-0438-10, 00904-0527-60, 00904-2140-60, 00904-2140-80, 00904-2141-60, 00904-2141-80, 00904-2157-19, 00904-2157-46, 00904-2157-52, 00904-2157-60, 00904-2157-80, 10768-7085-01, 10768-7283-01, 10768-7283-02, 10768-7283-03, 10768-7283-04, 10768-7733-01, 10768-7733-02, 10768-7733-03, 10768-7733-04, 11845-0178-04, 11845-0179-04, 11845-0180-01, 11845-0180-04, 16590-0326-10, 16590-0326-15, 16590-0326-20, 16590-0326-21, 16590-0326-30, 16590-0326-45, 16590-0326-60, 16590-0365-21, 16590-0365-48, 16590-0373-21, 16590-0373-28, 16590-0373-30, 16590-0404-20, 16590-0404-21, 16590-0404-30, 16590-0404-40, 16590-0404-45, 16590-0404-48, 16590-0624-21, 16590-0624-48, 18837-0267-21, 18837-0267-30, 18837-0267-48, 18837-0353-10, 18837-0353-30, 21695-0305-21, 21695-0305-30, 21695-0305-90, 21695-0306-20, 21695-0306-21, 21695-0306-28, 21695-0306-30, 21695-0306-36, 21695-0306-39, 21695-0306-40, 21695-0306-42, 21695-0306-45, 21695-0306-48, 21695-0306-50, 21695-0306-90, 21695-0307-05, 21695-0307-06, 21695-0307-07, 21695-0307-09, 21695-0307-10, 21695-0307-12, 21695-0307-13, 21695-0307-14, 21695-0307-15, 21695-0307-18, 21695-0307-20, 21695-0307-21, 21695-0307-30, 21695-0307-90, 21695-0580-05, 21695-0580-07, 21695-0580-14, 21695-0764-21, 21695-0765-21, 21695-0765-48, 23490-6157-01, 23490-6157-02, 23490-6157-03, 23490-6157-04, 23490-6157-05, 23490-6157-06, 23490-6157-07, 23490-6157-08, 23490-6158-00, 23490-6158-01, 23490-6158-02, 23490-6158-03, 23490-6158-04, 23490-6158-05

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone) (Continued)	23490-6158-07, 23490-6158-08, 23490-6158-09, 23490-6159-01, 23490-6159-02, 23490-6159-03, 23490-6159-04, 23490-6159-05, 23490-6159-06, 23490-7854-00, 23629-0167-10, 33358-0292-12, 33358-0292-15, 33358-0292-21, 33358-0292-30, 33358-0292-78, 33358-0293-20, 33358-0293-30, 33358-0293-40, 33358-0294-15, 33358-0294-20, 33358-0294-30, 33358-0294-40, 33358-0294-60, 35356-0581-30, 35356-0673-20, 35356-0673-21, 35356-0673-30, 35356-0674-15, 35356-0674-18, 35356-0674-20, 35356-0674-30, 35356-0675-60, 35356-0676-48, 35356-0677-15, 35356-0677-20, 35356-0677-21, 35356-0677-30, 35356-0677-40, 35356-0818-10, 35356-0818-14, 35356-0818-15, 35356-0818-18, 35356-0818-20, 35356-0818-21, 35356-0818-30, 35356-0819-15, 35356-0819-20, 35356-0819-21, 35356-0819-30, 35356-0819-40, 35356-0819-42, 42254-0240-21, 42254-0276-21, 42254-0361-08, 42254-0361-14, 42254-0361-15, 42254-0361-20, 42254-0361-21, 42254-0361-28, 42254-0361-30, 42254-0361-36, 42254-0361-40, 42254-0361-42, 42254-0361-45, 42254-0361-48, 42549-0647-14, 43063-0097-03, 43063-0097-06, 43063-0109-10, 43063-0415-01, 43063-0415-30, 43063-0426-10, 43063-0426-20, 43063-0426-21, 43063-0426-30, 43063-0426-40, 43063-0426-42, 43063-0426-50, 43063-0426-60, 43063-0432-10, 43063-0432-12, 43063-0432-15, 43063-0432-20, 43063-0432-21, 43063-0432-30, 43353-0080-60, 43353-0657-60, 43353-0819-60, 45802-0303-21, 45802-0303-67, 45802-0733-21, 45802-0733-67, 46703-0007-10, 49999-0008-00, 49999-0008-05, 49999-0008-20, 49999-0008-21, 49999-0008-30, 49999-0008-40, 49999-0008-42, 49999-0008-55, 49999-0028-05, 49999-0028-12, 49999-0028-14, 49999-0028-15, 49999-0028-20, 49999-0028-21, 49999-0028-28, 49999-0028-30, 49999-0028-40, 49999-0028-48, 49999-0028-50, 49999-0028-60, 49999-0028-90, 49999-0110-00, 49999-0110-06, 49999-0110-07, 49999-0110-10, 49999-0110-12, 49999-0110-14, 49999-0110-15, 49999-0110-18, 49999-0110-20, 49999-0110-21, 49999-0110-30, 49999-0390-21, 49999-0437-03, 50319-0505-01, 51079-0022-01, 51079-0022-17, 51079-0022-19, 51079-0022-20, 51079-0032-01, 51079-0032-17, 51079-0032-19, 51079-0032-20, 51079-0033-01, 51079-0033-17, 51079-0033-19, 51079-0033-20, 51138-0144-30, 51138-0145-15, 51138-0145-20, 51138-0145-30, 51138-0146-15, 51138-0146-20, 51138-0146-21, 51138-0146-28, 51138-0146-36, 51138-0146-39, 51138-0146-42, 51138-0146-50, 51138-0147-10, 51138-0147-12, 51138-0147-14, 51138-0147-15, 51138-0147-20, 51138-0147-21, 51138-0147-30, 51138-0154-15, 51138-0154-20, 51138-0154-30, 51138-0155-15, 51138-0155-20, 51138-0155-21, 51138-0155-28, 51138-0155-36, 51138-0155-39, 51138-0155-42, 51138-0155-50, 51138-0156-10, 51138-0156-12, 51138-0156-14, 51138-0156-15, 51138-0156-20, 51138-0156-21, 51138-0156-30, 51285-0311-02, 51285-0311-05, 51285-0312-02, 51285-0312-05, 51285-0313-02, 51285-0313-05, 51432-0356-03, 51432-0356-06, 51432-0358-03, 51432-0358-06, 51432-0359-03, 51432-0360-06, 51655-0020-24, 51655-0020-25, 51655-0020-28, 51655-0020-52, 51655-0020-53, 51655-0020-77, 51655-0023-24, 51655-0023-25, 51655-0086-24, 51655-0086-25, 51655-0086-27, 51655-0086-28, 51655-0086-30, 51655-0086-51, 51655-0086-72, 51655-0087-24, 51655-0087-28, 51655-0087-77, 51991-0458-01, 51991-0458-10, 51991-0462-01, 51991-0462-05, 52544-0797-01, 52544-0830-01, 52544-0830-10, 52544-0830-51, 52544-0831-01, 52544-0831-10, 52544-0832-01, 52544-0832-05, 52765-1252-00, 52959-0126-00, 52959-0126-05, 52959-0126-07, 52959-0126-10, 52959-0126-12, 52959-0126-15, 52959-0126-18, 52959-0126-20, 52959-0126-21, 52959-0126-25, 52959-0126-30, 52959-0126-40, 52959-0126-42, 52959-0126-44, 52959-0126-50, 52959-0126-60, 52959-0126-70, 52959-0127-00, 52959-0127-07, 52959-0127-10, 52959-0127-12, 52959-0127-15, 52959-0127-18, 52959-0127-20, 52959-0127-21, 52959-0127-25, 52959-0127-30, 52959-0127-37, 52959-0127-42, 52959-0220-00, 52959-0220-10, 52959-0220-20, 52959-0220-21, 52959-0220-30, 52959-0220-36, 52959-0220-40, 52959-0220-60, 52959-0220-75, 52959-0650-01, 52959-0954-05, 53002-0309-10, 53002-0309-20, 53002-0309-25, 53002-0309-27, 53002-0309-30, 53002-0309-35, 53002-0309-40, 53002-0309-42, 53002-0309-45, 53002-0309-50, 53002-0309-60, 53002-0325-08, 53002-0325-12, 53002-0325-15, 53002-0325-20, 53002-0325-21, 53002-0325-23, 53002-0325-24, 53002-0325-30, 53002-0325-40, 53002-0325-42, 53002-0352-00, 53002-0352-14, 53002-0352-20, 53002-0352-21, 53002-0352-24, 53002-0352-30, 53002-0352-36, 53002-0352-40, 53002-0352-50, 53002-0352-55, 53002-0352-60, 53002-0483-00, 53002-0638-20, 53489-0138-01, 53489-0138-10, 53489-0139-01, 53489-0139-05, 53489-0139-10, 53489-0140-01, 53489-0140-05, 53489-0140-10, 54124-0026-02, 54124-0026-30, 54124-0026-60, 54124-0157-02, 54124-0157-15, 54124-0157-20, 54124-0157-30, 54124-0165-15, 54124-0233-02, 54124-0233-20, 54124-0233-30

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone) (Continued)	54124-0694-20, 54569-0330-00, 54569-0330-01, 54569-0330-02, 54569-0330-03, 54569-0330-04, 54569-0330-05, 54569-0330-06, 54569-0330-07, 54569-0330-08, 54569-0330-09, 54569-0331-00, 54569-0331-01, 54569-0331-02, 54569-0331-03, 54569-0331-04, 54569-0331-05, 54569-0331-06, 54569-0331-07, 54569-0331-08, 54569-0331-09, 54569-0332-00, 54569-0332-01, 54569-0332-02, 54569-0332-03, 54569-0332-04, 54569-0332-05, 54569-0332-08, 54569-0332-09, 54569-0333-00, 54569-0333-04, 54569-1469-00, 54569-2785-00, 54569-2828-00, 54569-3043-00, 54569-3043-01, 54569-3043-02, 54569-3043-03, 54569-3043-04, 54569-3043-05, 54569-3043-06, 54569-3241-00, 54569-3241-01, 54569-3302-00, 54569-3302-01, 54569-3302-02, 54569-3302-03, 54569-3302-04, 54569-3302-05, 54569-3302-06, 54569-3302-07, 54569-3302-08, 54569-3302-09, 54569-3413-00, 54569-3798-00, 54569-3847-00, 54569-4017-00, 54569-4017-01, 54569-4026-00, 54569-4026-01, 54569-4026-03, 54569-4026-04, 54569-4026-05, 54569-4226-00, 54569-4227-00, 54569-7104-00, 54569-7139-00, 54868-0258-00, 54868-0258-01, 54868-0258-02, 54868-0258-03, 54868-0258-04, 54868-0258-05, 54868-0258-06, 54868-0258-07, 54868-0258-08, 54868-0258-09, 54868-0836-00, 54868-0836-01, 54868-0836-02, 54868-0836-03, 54868-0836-04, 54868-0836-05, 54868-0836-07, 54868-0836-08, 54868-0836-09, 54868-0908-00, 54868-0908-01, 54868-0908-02, 54868-0908-03, 54868-0908-04, 54868-0908-05, 54868-0923-01, 54868-1119-01, 54868-1119-02, 54868-1119-03, 54868-1119-04, 54868-1119-05, 54868-1183-00, 54868-1183-01, 54868-1183-02, 54868-1183-03, 54868-1183-04, 54868-1183-06, 54868-1183-07, 54868-1183-08, 54868-1183-09, 54868-3234-00, 54868-4095-00, 54868-4096-00, 54868-5213-00, 54868-5230-00, 55045-1260-09, 55045-1444-01, 55045-1444-02, 55045-1444-03, 55045-1444-04, 55045-1444-07, 55045-1444-08, 55045-1480-00, 55045-1480-01, 55045-1480-02, 55045-1480-05, 55045-1480-06, 55045-1480-07, 55045-1480-08, 55045-1480-09, 55045-1533-03, 55045-1533-06, 55045-1533-07, 55045-1533-08, 55045-1533-09, 55045-1809-02, 55045-2963-01, 55175-1843-01, 55175-2765-01, 55175-2766-01, 55175-2766-08, 55175-3918-00, 55175-3918-01, 55175-3918-02, 55175-3918-03, 55175-3918-04, 55175-3918-05, 55175-3918-06, 55175-3918-07, 55175-3918-08, 55175-3918-09, 55175-3919-01, 55175-3920-01, 55175-3921-08, 55175-3992-00, 55175-3992-01, 55175-3992-02, 55175-3992-03, 55175-3992-04, 55175-3992-05, 55175-3992-06, 55175-3992-07, 55175-3992-09, 55175-4158-00, 55175-4158-01, 55175-4158-02, 55175-4158-03, 55175-4158-04, 55175-4158-05, 55175-4158-06, 55175-4158-07, 55175-4158-08, 55175-4158-09, 55289-0330-05, 55289-0330-07, 55289-0330-10, 55289-0352-05, 55289-0352-07, 55289-0352-09, 55289-0352-10, 55289-0352-12, 55289-0352-14, 55289-0352-15, 55289-0352-20, 55289-0352-21, 55289-0352-30, 55289-0373-01, 55289-0373-12, 55289-0373-21, 55289-0373-30, 55289-0373-36, 55289-0373-42, 55289-0373-46, 55289-0373-55, 55289-0373-60, 55289-0373-72, 55289-0438-01, 55289-0438-15, 55289-0438-20, 55289-0438-21, 55289-0438-30, 55289-0438-36, 55289-0438-38, 55289-0438-40, 55289-0438-42, 55289-0438-50, 55289-0438-60, 55289-0859-02, 55289-0948-01, 55829-0422-10, 55829-0423-10, 55829-0424-10, 55887-0643-21, 55887-0643-30, 55887-0643-40, 55887-0643-42, 55887-0643-90, 55887-0696-21, 55887-0696-48, 55887-0770-21, 55887-0770-48, 55887-0796-20, 55887-0796-30, 57480-0351-01, 57480-0351-06, 57480-0352-01, 57480-0352-06, 57480-0472-01, 57480-0472-06, 57866-4324-01, 57866-4324-04, 57866-4324-05, 57866-4324-06, 57866-4325-01, 57866-4325-02, 57866-4325-03, 57866-4325-07, 57866-4325-08, 57866-4326-01, 57866-4326-02, 57866-4326-04, 57866-4326-05, 57866-4326-06, 57866-4326-07, 57866-4326-08, 57866-4328-01, 57866-4328-02, 57866-4328-03, 58016-0216-00, 58016-0216-12, 58016-0216-14, 58016-0216-15, 58016-0216-20, 58016-0216-21, 58016-0216-24, 58016-0216-28, 58016-0216-30, 58016-0216-32, 58016-0216-40, 58016-0216-50, 58016-0216-60, 58016-0216-90, 58016-0217-00, 58016-0217-10, 58016-0217-15, 58016-0217-16, 58016-0217-18, 58016-0217-20, 58016-0217-21, 58016-0217-22, 58016-0217-24, 58016-0217-28, 58016-0217-30, 58016-0217-40, 58016-0217-60, 58016-0218-00, 58016-0218-20, 58016-0218-21, 58016-0218-24, 58016-0218-30, 58016-0218-33, 58016-0218-36, 58016-0218-40, 58016-0218-50, 58016-0218-55, 58016-0218-60, 58016-0218-90, 58016-0672-20, 58016-2222-01, 58016-4832-01, 58729-0286-20, 58864-0362-20, 58864-0362-56, 58864-0423-15, 58864-0423-20, 58864-0423-30, 58864-0423-40, 58864-0424-09, 58864-0424-14, 58864-0424-20, 58864-0424-30, 59746-0171-06, 59746-0171-10, 59746-0172-06, 59746-0172-10, 59746-0173-06, 59746-0173-09, 59746-0173-10, 59746-0175-06, 59746-0175-09, 59746-0175-10, 60346-0058-12, 60346-0058-15, 60346-0058-18, 60346-0058-20, 60346-0058-21, 60346-0058-27

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
Steroids (Cortisone, dexamethasone, hydrocortisone, methylprednisolone, prednisolone, prednisone) (Continued)	60346-0058-30, 60346-0058-40, 60346-0058-50, 60346-0058-54, 60346-0058-60, 60346-0058-90, 60346-0094-09, 60346-0094-10, 60346-0094-12, 60346-0094-15, 60346-0094-18, 60346-0094-20, 60346-0094-24, 60346-0094-30, 60346-0094-40, 60346-0094-90, 60346-0249-04, 60346-0515-12, 60346-0515-20, 60346-0515-30, 60346-0515-36, 60346-0515-40, 60346-0515-50, 60346-0515-60, 60346-0515-75, 60346-0515-90, 60346-0721-40, 60429-0130-01, 60429-0130-10, 60429-0131-01, 60429-0131-10, 60429-0132-01, 60429-0132-10, 60760-0002-21, 60760-0138-30, 60760-0629-21, 60760-0630-28, 60904-0286-20, 61392-0408-15, 61392-0408-30, 61392-0408-31, 61392-0408-32, 61392-0408-39, 61392-0408-45, 61392-0408-51, 61392-0408-54, 61392-0408-56, 61392-0408-60, 61392-0408-90, 61392-0408-91, 61392-0417-15, 61392-0417-30, 61392-0417-31, 61392-0417-32, 61392-0417-39, 61392-0417-45, 61392-0417-51, 61392-0417-54, 61392-0417-56, 61392-0417-60, 61392-0417-90, 61392-0417-91, 61392-0761-30, 61392-0761-31, 61392-0761-32, 61392-0761-39, 61392-0761-45, 61392-0761-51, 61392-0761-54, 61392-0761-60, 61392-0761-90, 61392-0761-91, 62584-0832-01, 62584-0832-33, 62584-0833-01, 62584-0833-33, 62584-0834-01, 63629-1579-00, 63629-1579-01, 63629-1579-02, 63629-1579-03, 63629-1579-04, 63629-1579-05, 63629-1579-06, 63629-1579-07, 63629-1579-08, 63629-1579-09, 63629-1587-01, 63629-1587-02, 63629-1587-03, 63629-1587-04, 63629-1587-05, 63629-1587-06, 63629-1587-07, 63629-1587-08, 63629-1605-01, 63629-1605-02, 63629-1605-03, 63629-1605-04, 63629-1605-05, 63629-1605-06, 63629-1605-07, 63629-1605-08, 63629-4624-01, 63739-0207-01, 63739-0207-02, 63739-0207-03, 63739-0207-10, 63739-0207-15, 63739-0208-01, 63739-0208-02, 63739-0208-03, 63739-0208-10, 63739-0208-15, 63739-0209-10, 63739-0209-15, 63739-0518-10, 63739-0519-10, 63739-0520-10, 63874-0327-01, 63874-0327-02, 63874-0327-10, 63874-0327-12, 63874-0327-14, 63874-0327-15, 63874-0327-18, 63874-0327-19, 63874-0327-20, 63874-0327-21, 63874-0327-24, 63874-0327-25, 63874-0327-28, 63874-0327-30, 63874-0327-32, 63874-0327-40, 63874-0327-42, 63874-0327-50, 63874-0327-60, 63874-0327-90, 63874-0373-01, 63874-0373-02, 63874-0373-10, 63874-0373-15, 63874-0373-20, 63874-0373-21, 63874-0373-30, 63874-0373-33, 63874-0373-36, 63874-0373-40, 63874-0373-50, 63874-0373-60, 63874-0392-01, 63874-0392-02, 63874-0392-06, 63874-0392-10, 63874-0392-14, 63874-0392-15, 63874-0392-20, 63874-0392-21, 63874-0392-24, 63874-0392-28, 63874-0392-30, 63874-0392-40, 63874-0772-01, 63874-0772-30, 66116-0410-05, 66116-0410-30, 66116-0420-05, 66116-0420-15, 66116-0465-30, 66116-0465-50, 66116-0625-30, 66267-0171-15, 66267-0171-20, 66267-0171-21, 66267-0171-30, 66267-0171-40, 66267-0171-42, 66267-0172-10, 66267-0172-12, 66267-0172-15, 66267-0172-20, 66267-0172-30, 66267-0172-42, 66267-0173-20, 66267-0173-30, 66267-0173-40, 66267-0173-42, 66267-0173-60, 66267-0860-04, 66267-0948-21, 66336-0058-10, 66336-0058-12, 66336-0058-20, 66336-0058-21, 66336-0058-30, 66336-0058-40, 66336-0058-60, 66336-0094-10, 66336-0094-12, 66336-0094-18, 66336-0094-20, 66336-0094-21, 66336-0094-30, 66336-0219-30, 66336-0515-10, 66336-0515-21, 66336-0515-30, 66336-0515-40, 67544-0399-60, 68030-4325-01, 68030-4326-02, 68030-4326-08, 68030-9786-01, 68084-0035-80, 68084-0035-85, 68115-0289-10, 68115-0289-21, 68115-0289-30, 68115-0289-42, 68115-0290-20, 68115-0290-30, 68115-0291-21, 68115-0291-30, 68115-0947-21, 68258-3013-01, 68387-0240-10, 68387-0240-25, 68387-0241-15, 75987-0020-01, 75987-0021-01, 75987-0022-01

Appendix A. (Continued)

Drugs/Procedures	Claim Codes
DMARDs (Sulfasalazine, methotrexate, minocycline, hydroxychloroquine, leflunomide)	NDC 00005-3960-31, 00005-4507-04, 00005-4507-05, 00005-4507-07, 00005-4507-09, 00005-4507-23, 00005-4507-91, 00005-5313-56, 00005-5343-23, 00005-5343-27, 00005-5344-18, 00005-5344-27, 00005-9375-23, 00005-9376-18, 00013-0101-01, 00013-0101-05, 00013-0101-11, 00013-0101-20, 00013-0102-01, 00013-0102-05, 00013-0102-20, 00016-0101-01, 00016-0101-05, 00016-0101-11, 00016-0102-01, 00016-0102-05, 00024-1562-10, 00047-0615-24, 00047-0615-32, 00047-0616-19, 00047-0616-32, 00047-0687-24, 00047-0688-19, 00054-4550-15, 00054-4550-25, 00054-8550-03, 00054-8550-05, 00054-8550-06, 00054-8550-07, 00054-8550-10, 00054-8550-25, 00088-2160-30, 00088-2161-30, 00088-2162-03, 00093-0173-56, 00093-0174-56, 00093-3165-01, 00093-3167-53, 00093-7300-01, 00093-9774-01, 00093-9774-05, 00115-1245-01, 00115-1245-08, 00115-1246-01, 00115-1246-08, 00115-1247-01, 00115-1247-08, 00115-7017-01, 00115-7018-06, 00115-7018-13, 00115-7054-01, 00143-2128-01, 00182-1016-01, 00182-1016-05, 00182-1102-01, 00182-1103-19, 00182-1430-01, 00182-1431-19, 00182-1539-01, 00182-1539-95, 00182-2609-01, 00223-1727-01, 00223-1727-02, 00223-1727-05, 00254-5905-28, 00332-3165-09, 00332-3167-07, 00364-2497-01, 00364-2498-50, 00364-2499-01, 00364-2499-36, 00364-2627-01, 00378-0014-01, 00378-0014-50, 00378-0373-01, 00378-4296-01, 00378-4296-93, 00378-4297-01, 00378-4297-93, 00378-4298-01, 00378-4298-93, 00405-4643-01, 00405-4643-36, 00405-4680-01, 00405-4681-50, 00405-4956-01, 00405-4956-02, 00406-2096-01, 00406-2096-05, 00440-7615-30, 00440-7805-60, 00440-7820-60, 00440-7821-60, 00440-8420-91, 00536-1382-01, 00536-1392-06, 00536-1482-01, 00536-1492-06, 00536-3998-01, 00536-3998-36, 00536-4617-01, 00536-4617-05, 00536-4617-10, 00536-5710-01, 00555-0351-01, 00555-0352-01, 00555-0572-02, 00555-0572-35, 00591-0698-01, 00591-0698-05, 00591-0796-01, 00591-0796-05, 00591-0796-10, 00603-3944-21, 00603-5801-04, 00603-5801-21, 00603-5801-28, 00603-5801-32, 00603-5802-21, 00603-5802-28, 00603-5803-21, 00603-5803-25, 00615-1522-53, 00615-1522-63, 00615-1522-65, 00659-0106-05, 00677-0483-01, 00677-0483-05, 00677-1590-01, 00781-1407-01, 00781-1407-05, 00781-5056-31, 00781-5057-31, 00814-7230-14, 00814-7230-28, 00839-6098-06, 00839-6098-12, 00839-7963-06, 00904-1152-40, 00904-1152-60, 00904-5107-60, 00955-0790-01, 00955-0790-05, 11845-0121-01, 11845-0121-03, 16714-0321-01, 16714-0331-01, 17236-0610-01, 17236-0610-05, 21695-0486-30, 23155-0043-03, 23155-0044-03, 23490-5724-03, 23490-5724-06, 23490-5724-09, 23629-0026-01, 23629-0026-10, 24987-0562-10, 29936-0377-01, 38245-0774-10, 38245-0774-50, 42291-0320-01, 42291-0320-18, 43353-0761-53, 43353-0761-80, 43353-0794-53, 43353-0794-80, 47463-3017-30, 49884-0888-05, 49884-0888-11, 49884-0889-05, 49884-0889-11, 49999-0372-60, 51875-0377-01, 51875-0377-02, 52544-0698-01, 52544-0698-05, 52555-0642-01, 52761-0377-01, 54868-2319-00, 54868-4385-00, 54868-4902-00, 54868-6170-00, 60429-0319-30, 60429-0320-30, 60505-2502-01, 60505-2502-03, 60505-2503-01, 60505-2503-03, 63629-1263-01, 66993-0160-30, 66993-0161-30, 68115-0817-30
Anti-TNFs (Adalimumab, etancercept, certolizumab, glolimumab, infliximab)	NDC 00074-3799-02, 00074-4339-02, 00074-4339-06, 00074-4339-07, 00074-9374-02, 50474-0700-62, 50474-0710-79, 50474-0710-81, 54569-5524-00, 54868-4782-00, 54868-4822-00, 54868-5444-00, 57894-0030-01, 57894-0070-01, 57894-0070-02, 57894-0071-01, 57894-0071-02, 57894-0350-01, 58406-0425-34, 58406-0425-41, 58406-0435-01, 58406-0435-04, 58406-0445-01, 58406-0445-04, 58406-0455-01, 58406-0455-04 HCPCS J0135, C9249, J0718, J1438, J1745, J1602

Appendix A. (Continued)

Drugs/Procedures	**Claim Codes**
Non-anti-TNFs (Abatacept, anakinra, rituximab, tocilizumab)	NDC 00003-2187-10, 00003-2188-11, 00003-2188-31, 50242-0051-21, 50242-0053-06, 50242-0135-01, 50242-0136-01, 50242-0137-01, 50242-0138-01, 55513-0177-01, 55513-0177-07, 55513-0177-28, 66658-0234-01, 66658-0234-07, 66658-0234-28 HCPCS J0129, C9230, J9310, J3262, C9264
RA-related Radiographic Procedures	CPT X-rays : 72010, 72040, 72069, 72070, 72080, 72100, 72240, 72255, 72265, 72270, 72200, 72202, 73010, 73020, 73030, 73040, 73050, 73070, 73080, 73085, 73100, 73110, 73115, 73120, 73130, 73140, 73500, 73510, 73520, 73525, 73530, 73540, 73542, 73560, 73562, 73564, 73565, 73580, 73600, 73610, 73615, 73620, 73630, 73660 MRIs : 73218, 73219, 73220, 73221, 73222, 73223, 73721, 73722, 73723, 73221, 73222, 73223, 73721, 73722, 73723, 72146, 72147, 72157, 73718, 73719, 73720, 72148, 72158, 72149, 72141, 72142, 72156
RA-related Laboratory Procedures	CPT 85651, 85652, 86140, 86141
RA-related Intra-articular Injections	CPT 20256, 20550, 20551, 20552, 20553, 20600, 20605, 20610 HCPCS J0702, J0704, J1020, J1030, J1040, J1700, J1710, J1720, J2920, J2930, J3303, J7319, Q4083, Q4084, Q4085, Q4086
RA-related Rehabilitation Services	CPT 97010, 97012, 97014, 97018, 97022, 97024, 97032, 97035, 97110, 97112, 97113, 97114, 97116, 97118, 97124, 97128, 97139, 97154, 97250, 97260, 97265, 97500, 97501, 97504, 97530, 97540, 97703, 97750, 97799
RA-related Surgical Procedures	CPT 22532, 22533, 22534, 22548, 22554, 22556, 22558, 22585, 22590, 22595, 22600, 22610, 22612, 22614, 22630, 22632, 22800, 22802, 22804, 22808, 22810, 22812, 23800, 23802, 24800, 24802, 25800, 25805, 25810, 25820, 25825, 25830, 26841, 26842, 26843, 26844, 26850, 26852, 26860, 26861, 26862, 26863, 27280, 27282, 27284, 27286, 27580, 27870, 27871, 28705, 28715, 28725, 28730, 28735, 28737, 28740, 28750, 28755, 28760, 29899

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15. Product Information: HUMIRA(R) subcutaneous injection, adalimumab subcutaneous injection. 2012. North Chicago, IL, Abbott Laboratories.

16. Product Information: KINERET(R) subcutaneous injection, anakinra subcutaneous injection. 2012. Boyds, MD, Swedish Orphan Biovitrum AB .

17. Product Information: ENBREL(R) subcutaneous injection solution, etanercept subcutaneous injection solution. 2013. Thousand Oaks, CA, Amgen Inc. and Pfizer Inc.

18. Product Information: SIMPONI(R) subcutaneous injection, golimumab subcutaneous injection. 2013. Horsham, PA, Janssen Biotech, Inc.

19. Product Information: CIMZIA(R) subcutaneous injection lyophilized powder for solution, subcutaneous injection solution, certolizumab pegol subcutaneous injection lyophilized powder for solution, subcutaneous injection solution. 2013. Smyrna, GA, UCB, Inc.

20. Product Information: ACTEMRA(R) intravenous infusion, tocilizumab intravenous infustion. 2013. South San Francisco, CA, Genentech, Inc.

21. Product Information: ORENCIA(R) intravenous, subcutaneous injection, abatacept intravenous, subcutaneous injection. 2013. Princeton, NJ, Bristol-Myers Squibb .

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