



# SPECIALTY DRUGS IN WORKERS'

# COMPENSATION UPDATE

A POPULATION-BASED ASSESSMENT  
(2020 UPDATE)

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## AUTHORS:

**Michael Nguyen**, PharmD

**Eljana Angjellari**, PharmD

**Phil Walls**, RPh

# EXECUTIVE SUMMARY

Specialty drugs are typically newer, complex, high-value medications that are rapidly becoming standard treatment for many rare and chronic conditions.<sup>1</sup> According to Information Medical Statistics (IMS) Health, United States specialty net spending rose from 24.7% in 2008 to 46.5% in 2017. Specialty medicines are rapidly approaching half of total drug spend. Across all settings, specialty medicines treat relatively few patients and have costs far higher per patient than traditional medicines.<sup>2</sup>

IN THIS WHITE PAPER, MYMATRIXX WILL IDENTIFY AT LEAST SEVEN SIGNIFICANT PATIENT POPULATIONS WHERE SPECIALTY DRUGS ARE THE TREATMENT OF CHOICE:



**Injured workers who have undergone orthopedic surgery**



**Workers who may have been exposed to HIV through needle-stick injury or other means**



**Workers who have been exposed to hepatitis C virus through blood or other infectious bodily fluids**



**Patients who have symptoms of rheumatoid arthritis or ankylosing spondylitis**



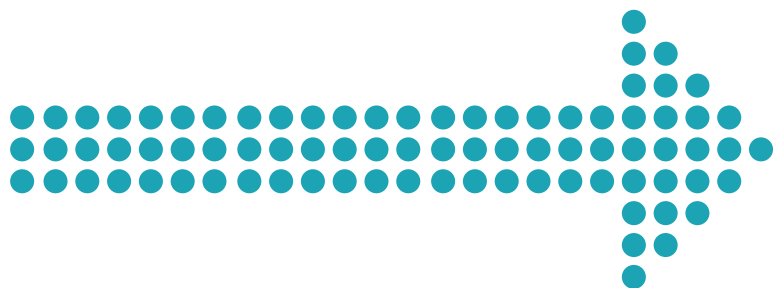
**Workers whose osteoarthritis pain has been exacerbated by their job**



**Injured workers who experience migraine, limb spasticity, cervical dystonia and bladder overactivity due to traumatic brain injury or spinal cord injury**



**Workers who develop cancer from occupational exposure in states with cancer presumption laws**





Along with these medications being so costly, these treatments also require enhanced clinical monitoring and medication management to ensure successful outcomes. The role of the Pharmacy Benefits Manager (PBM), as it pertains to the growing field of specialty medications, is to provide comprehensive utilization and patient management. Additionally, myMatrixx works closely with our network specialty pharmacies to ensure that patients receive the highest level of patient care in order to gain full therapeutic advantage for these complex conditions. Lastly, through myMatrixx's partner specialty pharmacy, Accredo<sup>®</sup>, some conditions qualify for outcome guarantees.



**Specialty medicines are rapidly approaching**

**half of total drug spend.**

# INTRODUCTION

SPECIALTY DRUGS ARE HIGH-COST PRESCRIPTION DRUGS USED TO TREAT COMPLEX, RARE, CHRONIC CONDITIONS, AND MOST SPECIALTY DRUGS REQUIRE PRESCRIBING FROM A SPECIALIZED PHYSICIAN.

THE AMERICAN JOURNAL OF MANAGED CARE (AJMC) DEFINES A SPECIALTY DRUG AS HAVING FIVE KEY COMPONENTS:

- 1 Costs more than \$600 per month
- 2 Treats a rare condition
- 3 Requires special handling
- 4 Uses a limited or restricted distribution network
- 5 Requires enhanced clinical monitoring

The distribution of drug spend has shifted strongly to specialty medicines from traditional therapy. These drugs cost four times as much as other traditional prescription medications for payers. According to the 2018 Drug Trend Report provided by myMatrixx, payers spent an average of \$5,130.57 per injured worker on specialty medications. It also found that spending on specialty medications increased by 18.5% for payers in 2018. In 2017, specialty drugs accounted for 5.8% of total drug spending, which increased to 7.1% in 2018. Although only 1.7% of injured workers use specialty drugs, they contribute to 7.1% of costs spent on all medications prescribed to injured workers.

The financial impact can be significant for payers, making it a critical priority to closely monitor utilization and effectively administer cost containment strategies for specialty medications.

Our partner specialty pharmacy, **Accredo®**, provides individualized care to the needs of patients by connecting them with specialized pharmacists, nurses and other pharmacy experts who have extensive training and experience in specific disease states and specialty medications. Specialists are available for patient counseling at all times. Accredo guarantees the compliance of injured workers infected with Hepatitis C (HCV) by providing full medication cost if the initial trial of antivirals proves to be ineffective after initiation and completion of the first treatment through their specialty pharmacy.

The most common conditions that necessitate specialty drug coverage across workers' compensation patient population include Venous Thromboembolism prophylaxis, HIV, hepatitis C, inflammatory conditions, chronic migraines and cancer. This paper reviews specialty drug trends and provides insights utilizing current treatment guidelines.

# VENOUS THROMBOEMBOLISM

## ANTICOAGULANTS

Lovenox® (enoxaparin), Fragmin® (dalteparin) and Arixtra® (fondaparinux) are specialty injectable anticoagulants used to prevent blood clots. The immobility of an injured worker post orthopedic surgery increases the risk for blood clot formation in the veins known as venous thromboembolism (VTE). Deep vein thrombosis (DVT) occurs when blood clots form in the deep veins, commonly post knee or hip surgery. DVT may break off and travel through the veins and to the lungs, which results in pulmonary embolisms (PE). DVT and PE are forms of VTE.

The incidence of asymptomatic DVT after a major orthopedic surgery ranges from 40% to 60%, whereas the incidence of symptomatic DVT ranges from 0.5% to 4%.<sup>3</sup> Estimates indicate that 40% to 50% of untreated symptomatic DVT patients will develop a PE within 3 months, and 10% of untreated symptomatic PE patients will die within 1 hour of onset.<sup>4</sup> For these reasons, guidelines recommend standard prophylactic anticoagulation therapy post orthopedic surgery.

The specialty injectable anticoagulants and Coumadin® (warfarin) have been the gold standard for VTE prophylaxis and treatment for decades. However, now the American College of Chest Physicians (CHEST) guidelines recommend direct oral anticoagulants (DOACs) such as Eliquis® (apixaban), Pradaxa® (dabigatran) and Xarelto® (rivaroxaban) as first line therapy.<sup>5</sup> The benefit of these novel oral anticoagulants is that they do not require enhanced clinical monitoring. Therefore, they are not considered specialty medications.

Additionally, when comparing DOACs to the specialty injectable anticoagulants, they provide a significant cost savings. Prophylactic anticoagulation therapy may range from 12 to 42 days post surgery, depending on the type of surgery and bleeding risk factors.<sup>6</sup> The following tables provide a cost analysis comparing 30-day regimens. Although generic Lovenox®, enoxaparin, is FDA approved and available on the market, the cost may vary significantly per manufacturer.

The anticoagulation prescribing patterns from myMatrixx prescribers have consistently shifted with the recommended guidelines. In 2018, Eliquis prescriptions accounted for 36% of total anticoagulant transactions, followed by Xarelto (21.8%), Pradaxa (9.73%) and Lovenox (1.98%). Currently the DOACs do not have generics available on the market. However, the patents are set to expire for Pradaxa in 2021, Xarelto in 2024, and Eliquis in 2031.<sup>7,8,9</sup>

Adherence and timely access to anticoagulation therapy significantly reduces the risk of complications from blood clots and therapy cost. According to the CDC, blood clots cost our nation up to \$10 billion each year. Treatment can be as much as \$15,000 to \$20,000 per person and often results in readmission to the hospital.<sup>10</sup> Standard anticoagulation treatment to prevent blood clots post-surgery is strongly recommended per the Chest Guidelines.





### Specialty Injectable Anticoagulants

### Regimen

### Cost of Regimen

Table 1

Lovenox® (enoxaparin)	40 mg once daily	\$285.84 - \$1,070.46
Arixtra® (Fondaparinux)	2.5 mg once daily	\$1,731
Fragmin® (dalteparin)	5,000 units daily	\$1,477.50

### Direct Oral Anticoagulants

### Regimen

### Cost of Regimen

Table 2

Eliquis® (apixaban)	2.5 mg once daily	\$533
Xarelto® (rivaroxaban)	10 mg once daily	\$537.59
Pradaxa® (dabigatran)	220 mg once daily	\$519.14


# HIV

## ANTIRETROVIRALS

Antiretroviral medications used to manage human immunodeficiency virus (HIV) infections are a group of specialty medications used in workers' compensation mainly for post-exposure prophylaxis (PEP). Post-exposure prophylaxis involves taking a short course of antiretroviral medications after a potential occupational exposure to HIV to prevent infection. This approach has been largely accepted as reasonable and necessary. Because of the severe ramifications of an actual infection, PEP is routinely utilized when a work-injury presents the employee with the risk of HIV infection, although data show that the risk of infection is relatively low among healthcare workers. Healthcare workers who have either been exposed to a needle stick involving HIV infected blood at work, have had percutaneous exposure or mucous membrane exposure have a 0.23%, 0.3% and 0.09 % risk infection, respectively.<sup>11,12</sup>

The most current guidelines for treating occupational exposure to HIV are provided by the US Public Health Service (PHS), which was published in 2013. Previous guidance regarding occupational PEP was provided by the Centers for Disease Control and Prevention (CDC) in 2001. The CDC used to recommend PEP therapy based on the severity of exposure (e.g., a two-drug regimen for less severe exposures and three-drug regimens for more severe exposures). The PHS now recommends a regimen of three drugs to be used routinely. The PHS guidelines also specifically recommend Truvada® and Isentress® as the preferred regimen.

Consistent with these guidelines, myMatrixx providers have been prescribing Truvada® once daily, which is a combination agent containing two drugs (tenofovir 300 mg and emtricitabine 200 mg) and Isentress® (raltegravir 400 mg) twice daily. Some providers, however, are substituting Tivicay® for Isentress®. Tivicay® is in the same drug class as Isentress®, but only needs to be taken once daily. The difference in cost between the two alternative regimens is approximately \$200:

		 Total Cost of PEP course	
<b>Table 3</b>	Most common regimen	Truvada® once daily (\$2,109.48) + Isentress® 400 mg twice daily (\$1,889.28)	\$3,998.76
	Alternative regimen	Truvada® once daily (\$2,109.48) + Tivicay® 50 mg once daily (\$2,088.59)	\$4,198.07

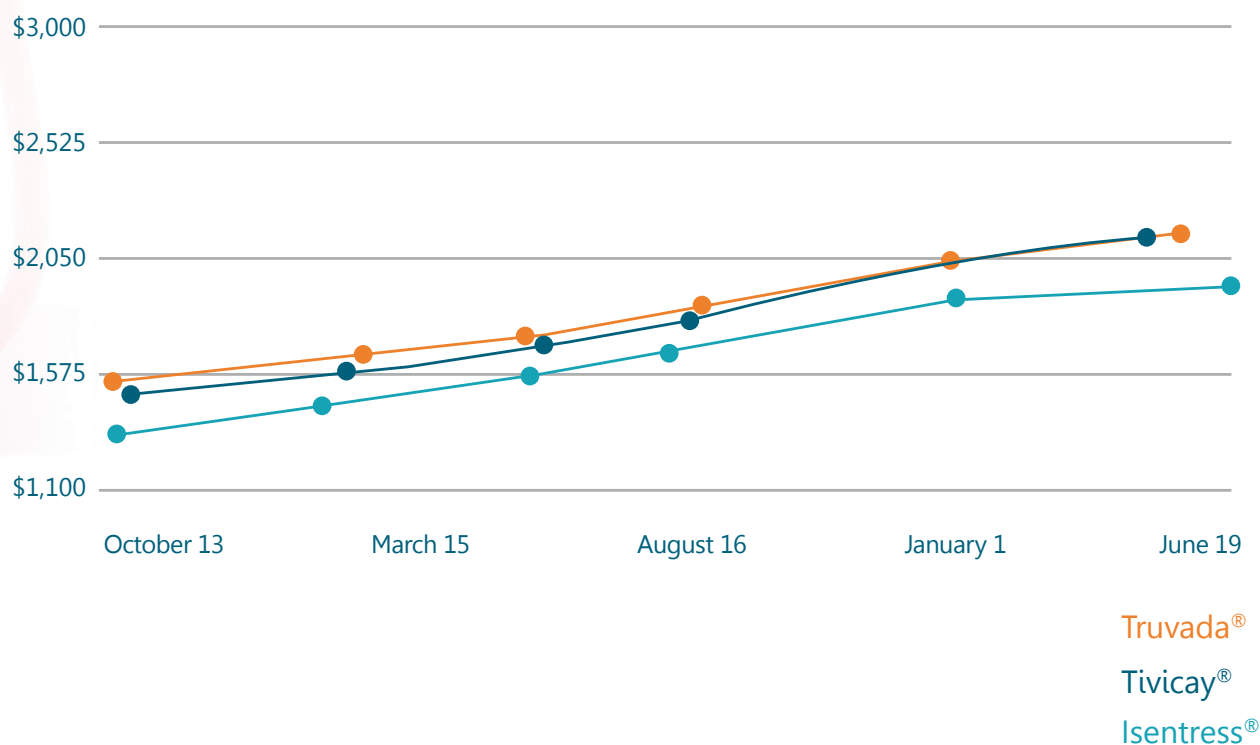


Deviations from the above regimens are rare, but necessary in certain circumstances such as drug interactions (i.e., the exposed patient is taking a medication that interacts with the PEP medications) or other contraindications. Additionally, if the HIV infected person is taking a particular treatment regimen, the exposed person may need to take the same regimen for PEP.

It is plain to see that the decision to use a two-drug or three-drug regimen for PEP presents a significant difference in cost. Although the PHS guidelines will likely drive providers toward using a three-drug regimen routinely, it may still be appropriate to use a two-drug regimen in which Truvada® is the likely drug of choice. According to the PHS, the use of a two-drug regimen for PEP may still be appropriate because, “the optimal number of medications needed for HIV PEP remains unknown”, and “no new definitive data exist to demonstrate increased efficacy of three-drug HIV PEP regimens compared with the previously recommended two-drug HIV PEP regimens for occupational HIV exposures associated with a lower level of transmission risk.”<sup>13</sup> For these reasons, claims handlers may see prescriptions for only Truvada® from time to time for PEP. Common side effects of PEP therapy includes nausea and vomiting, therefore, Zofran® (ondansetron) may be prescribed as supportive care. Although, Zofran® is commonly not recommended due to high cost, for PEP therapy the benefits of treating the nausea and vomiting outweigh the risks of incurring additional cost during the preventative treatment.

When managing pharmacy benefits for HIV PEP, it is necessary to monitor not only utilization, but also cost, particularly of the three most prevalently prescribed drugs: Truvada®, Isentress® and Tivicay®. Our analysis showed that the price of all three drugs increased 37% to 41% over the last five years as a result of consistent annual increases of 6.5% to 7.1%. It is also expected that Truvada® will be the first of these three drugs to go generic and become available on September 30, 2020.<sup>14</sup>

**Figure 1: Five-year Price Increases for Top Three HIV Drugs**



## WHEN MANAGING PATIENT OUTCOMES, THERE ARE SEVERAL IMPORTANT FACTORS THAT SHOULD BE CONSIDERED:



**Occupational exposure to HIV should be prioritized as an urgent medical concern and treated immediately**



**PEP medications should be started as soon as possible, but within 72 hours; If more than 72 hours have passed, PEP therapy should be considered upon expert consultation**



**PEP should be continued for four weeks and only discontinued if the source patient is tested and determined to be HIV negative**



**Because of the potential for intolerable side effects, some patients may have problems completing the four-week course**

Although HIV infection is no longer considered a terminal disease and can be effectively managed with medication therapy, there is no cure. If the injured worker contracts HIV, medications must be continued indefinitely, and therefore, present a substantial lifetime treatment cost. For this reason, PEP can be seen as a highly cost-effective intervention. Current cost of the four-week treatment ranges from \$3,998.76 to \$4,198.07, preventing an estimated lifetime cost of \$379,668 according to the CDC in 2010.<sup>15</sup>



**“...the optimal number of medications needed  
for HIV PEP remains unknown.”**

# HEPATITIS C

## ANTIVIRALS

Hepatitis C virus (HCV) is a blood-borne virus that infects the liver. If left untreated, an acute infection may spontaneously clear or become chronic and progress to eventual liver failure and death. A person may become infected through contact with infected blood. The disease is quite common in the US as there are 2.4 million people estimated to be living with hepatitis C virus infection. The most common risk factor for HCV infection in this population is injection drug use. In the workers' compensation population however, hepatitis C is rare. Guidelines that address occupation exposure to hepatitis focus on needlestick or sharps exposure by health care personnel (HCP) in which recent data estimates the risk of infection to be as low as 0.2% following exposure by percutaneous injuries and 0% for mucocutaneous exposures.<sup>16</sup> However, although the prevalence of hepatitis C is low within workers' compensation, the costs of the specialty medications to treat hepatitis are very high and therefore can have a substantial impact on pharmacy spend.

For guidance on how to manage HCPs infected with HCV, the guidelines by the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA) provide the most up-to-date recommendations. Unlike HIV exposure, in which medications for post-exposure prophylaxis (PEP) are started immediately following a suspected infection, guidelines for HCV do not recommend PEP.<sup>17</sup> It is recommended that regular HCV laboratory monitoring be conducted for a minimum of six months and up to 12 months following exposure to determine spontaneous clearance versus persistence of HCV infection. The six-month period following HCV exposure is referred to as the acute period. It is estimated that the infection has a 20% to 50% chance of spontaneous resolution within

this period. Treatment may proceed if an infection has not spontaneously cleared after six months of laboratory monitoring.

The decision on which medications to use for treatment depends on many factors, but fundamentally the genotype or strain of the virus has to be determined since certain strains do not respond to certain medications. This section focuses on the medications recommended by the AASLD/IDSA guidelines for genotype 1, which is the most common HCV genotype in the US and found in over 70% of all HCV infections. There is also a further classification of genotype 1 into subtype 1a and 1b. Subtype 1b is considered a more severe form. It is also important to determine if the patient has cirrhosis (liver scarring) before therapy is started. The presence of cirrhosis indicates more advanced disease and requires a longer course of therapy, 12 weeks versus eight weeks, but does not call for different medications. Lastly, the choice of medications also depends on whether the patient has been treated previously for hepatitis C, since this may affect which drugs the patient may or may not respond to also.

For HCPs who have a confirmed HCV infection after six months of laboratory monitoring and have not been previously treated for HCV, the AASLD/IDSA guidelines specifically recommend one of four medications including Zepatier®, Mavyret®, Epclusa® and Harvoni® (see Table 4). According to the AASLD/IDSA guidelines, the four recommended regimens provide comparable efficacy. Two of the four medications are generically available including Epclusa® and Harvoni®. Zepatier® appears to be the most cost-effective regimen at this time, and Harvoni® is the most expensive.



Table 4. AASLD/IDSA Regimen Recommendations for Treatment Naive Patients with Genotype 1a and 1b HCV

Drug	Regimen	Cost of Regimen	Comments
Zepatier® (elbasvir/grazoprevir)	1 tablet once daily for 12 weeks	\$26,208	Same regimen for type 1a or 1b with or without cirrhosis
Mavyret® (glecaprevir/pibrentasvir)	3 tablets once daily for 8 – 12 weeks	\$31,680 – \$46,440	Same regimen for type 1a or 1b; Course duration may be shortened to 8 weeks for patients without cirrhosis
Eplclusa® (sofosbuvir/velpatasvir)	1 tablet once daily for 12 weeks	\$89,712 (\$28,800) generic	Same regimen for type 1a or 1b with or without cirrhosis
Harvoni® (sofosbuvir/ledipasvir)	1 tablet once daily for 8 – 12 weeks	\$75,600 – \$113,400 (\$43,200) generic	Same regimen for type 1a or 1b; Course duration may be shortened to 8 months in patient without cirrhosis, are non-black, HIV uninfected and have virus levels under 6 million IU/ml

Although very costly, these new medications for HCV are highly effective and provide a cure, unlike HIV in which there is no cure. Since non-treatment can lead to dire consequence, which can include the need for a liver transplant, these high-priced medications are considered a cost-effective intervention. Cirrhosis due to hepatitis is the leading indication for liver transplantation in the U.S. and the average cost of a liver transplant is about \$812,500.<sup>18</sup> However, the potential for the virus to spontaneously resolve means that some cases of HCV exposure will not require medication therapy at all.





# INFLAMMATORY CONDITIONS

## DMARDs

Disease modifying anti-rheumatic drugs (DMARDs) work by various mechanisms to slow the disease process and help prevent further joint damage. These medications are approved for the management and treatment of rheumatoid arthritis (RA), but could also be used for psoriasis, ulcerative colitis, Crohn's disease and ankylosing spondylitis (AS). Workers' compensation compensability for DMARDs may be more commonly related to RA and AS.

RA is a chronic, progressive, inflammatory autoimmune disorder that symmetrically affects the joints, typically those in the hand, feet, wrists, elbows, knees and ankles. This causes inflammation that results in swelling and pain around the affected area.<sup>19</sup>

AS is a chronic arthritis that causes inflammation of the joints near the lower spine and pelvis, with inflammation at the insertion sites of tendons or ligaments into the bone. It has a tendency to affect the sacroiliac joints and cause spinal fusion. The result is an inflammation of backbone that may cause abnormal stiffening, immobility of the affected joint and pain in the buttocks, lower back and legs.

An individual's genetic predisposition is generally the cause for development of these conditions, rather than the result of a work-related injury. Experience, however, has dictated that RA and AS claims have been accepted as compensable.



In 2012, the American College of Rheumatology published an update to the 2008 guidelines. To prevent disease progression, the update includes more aggressive recommendations for when to start, resume or switch DMARD therapy.

Non-biologic traditional DMARDs such as methotrexate, leflunomide, hydroxychloroquine, sulfasalazine and minocycline continue to be the first line therapy recommended.<sup>20</sup> These medications are generally oral medications and are more cost effective than the newer biologic DMARDs.

The treatment and goal of therapy is individualized per patient, depending on response to therapy and tolerance of medications. The ideal goal is complete remission of disease or at least slowing the rate of progression. Combination DMARD therapy, including double or triple therapy, may be utilized to achieve treatment goals. Traditional DMARDs may be prescribed together or with a biologic DMARD, however, two biologics should not be prescribed together, because the risks outweigh the benefits.<sup>21</sup>

## continued Inflammatory Conditions DMARDs

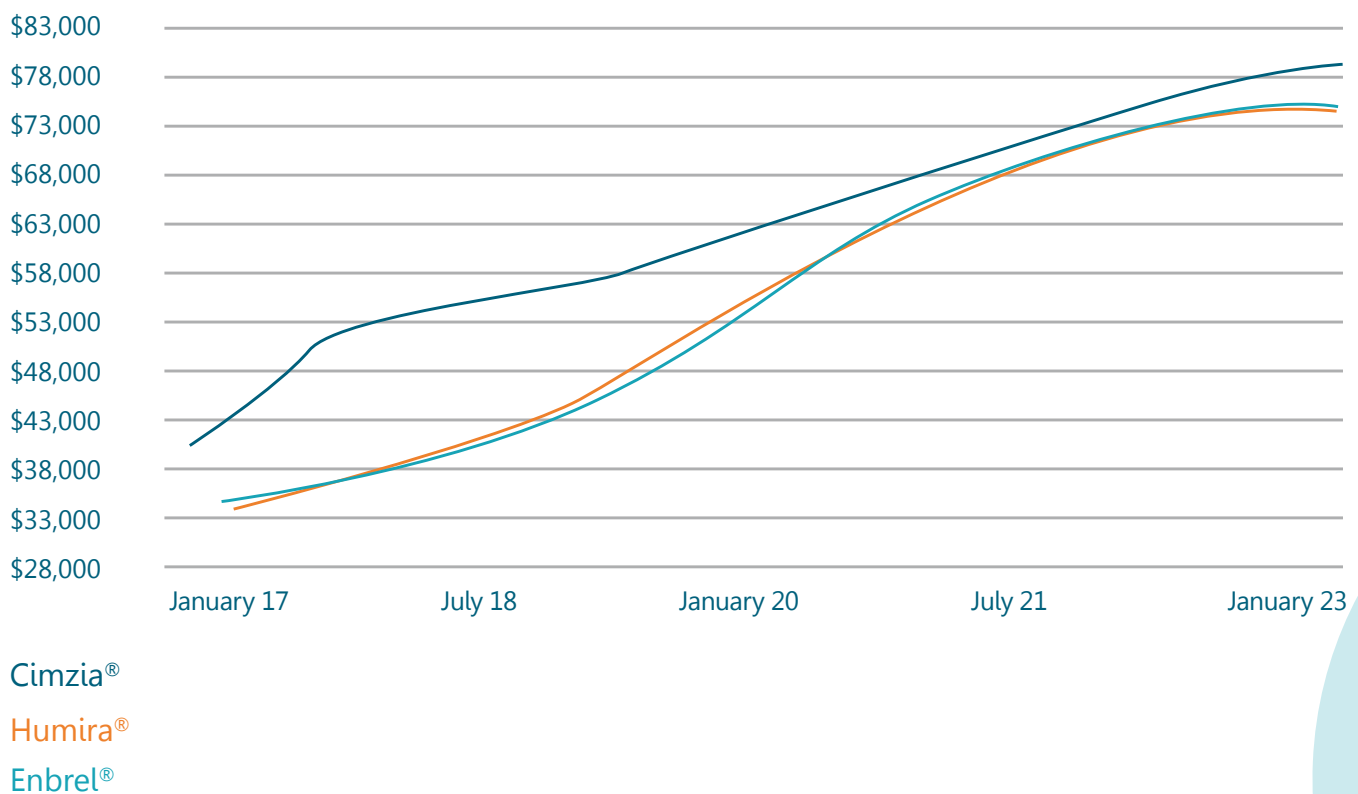
Tumor necrosis factor (TNF) is a pro-inflammatory cytokine that has antitumor and antiviral activities. The toxicity of TNF limits its clinical use for oncological treatment. However, it was discovered that *anti*-TNF biologics are highly effective for autoimmune conditions associated with inflammation and now are extensively utilized.

Tumor necrosis factor alpha-blockers (TNF-alpha) biologics are considered the first-line biological DMARDs and may be used alone or in combination with methotrexate. These include Humira®, Cimzia®, Enbrel®, Simponi® and Remicade®. Remicade® must be prescribed with methotrexate. Other biologic DMARDs, non-TNF agents, include Rituxan®, Orencia®, Actemra® and Kevzara®.

Reassessment of disease progression is completed every three months for traditional and anti-TNF DMARDs, and every six months for non-TNF biologics. If disease has not slowed progression, another agent is added or therapy is switched. After two trials of anti-TNF biologic, a non-TNF agent is recommended.<sup>22</sup>

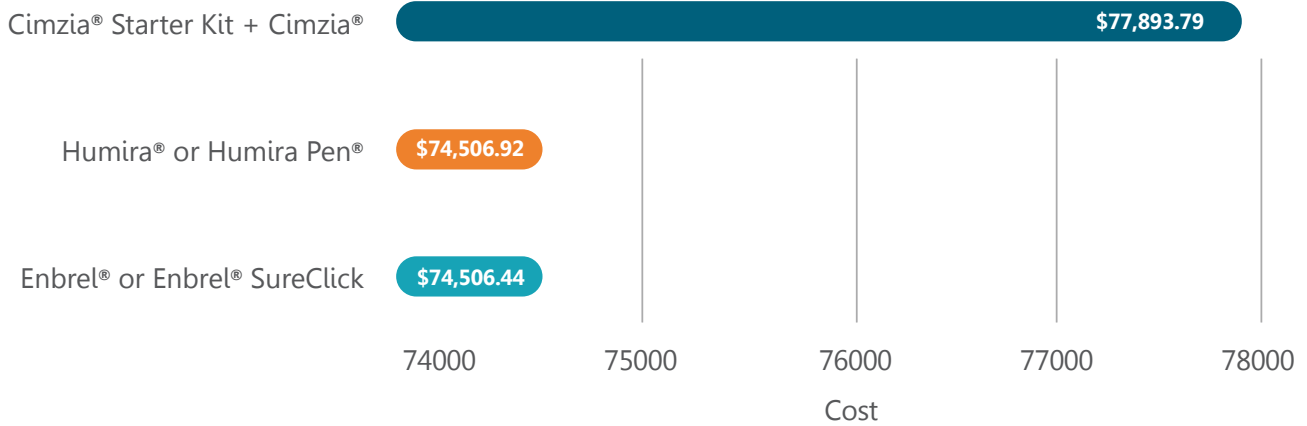
The utilization patterns of myMatrixx prescribers are consistent with the guidelines. Enbrel®, Humira® and Cimzia® are the top biologic DMARDs utilized. Humira® and Enbrel® are in the top three in the top 20 drugs by 2018 U.S. sales according to IQVIA's latest report; Humira® came in first grossing \$13.68 billion. Our cost analysis showed that the price of all three drugs increased 56% to 78% over the last five years.

**Figure 2: Initial TNF-alpha Inhibitors Annual Cost since 2013**





## TNF - Alpha Inhibitors



Cimzia® appears to be most expensive for initiation of treatment, given that the initial annual cost is composed of the Cimzia® Starter Kit and maintenance annual cost. However, following the initial year, Cimzia® is the most cost effective with an annual maintenance cost of \$62,315. Switching between biologic therapies is only recommended by guidelines if the medication is ineffective or intolerable.

Evidence from U.S. National Survey Data estimated the national indirect costs of RA-related absenteeism were \$252 million annually. Individuals with RA have higher probabilities of missing work and missing workdays than those without RA.<sup>23</sup> This indicates the need for early interventions to slow down or stop the progression of the disease and keep people with RA in the work force.



# OSTEOARTHRITIS

## VISCOSUPPLEMENTATION

Osteoarthritis (OA) is a common degenerative joint disease characterized by the breakdown in cartilage of an affected joint that results in pain, inflammation and stiffness. Any joint may be susceptible, but degradation presents more frequently in hands, lumbar and cervical spine, and weight-bearing joints of the knees, hips and feet. OA may be caused when the cartilage between joints wears out due to an injury or repetitive stress. However, some workers might be predisposed genetically, and work could potentially exacerbate the presentation of osteoarthritis.

Such occupational fields that may be at an increased risk for development of OA due to higher physical labor demand include construction, firefighting, fisheries, forestry, mining, agriculture and healthcare.<sup>24</sup> OA does not have a cure, but there are ways to ease pain and maintain mobility of the joints.

## Hyaluronic Acid Derivatives

Table 5

Drug	Recommended Dose	Number of Injections per Course	Cost of Course
Synvisc-One®	Inject 48 mg once	1	\$1,559.34
Hyalgan®	Inject 20 mg once weekly	5	\$1,140
OrthoVisc®	Inject 30 mg once weekly	4	\$2,294.40
Synvisc®	Inject 16 mg once weekly	3	\$1,559.34
Supartz®	Inject 25 mg once weekly	5	\$1,381.80
Monovisc®	Inject 88 mg once	1	\$1,710.73

First-line pharmacologic therapy recommendations include acetaminophen (Tylenol®), oral NSAIDs and local analgesics.<sup>25,26</sup> Local analgesics recommended are capsaicin, methyl salicylate creams and topical NSAIDs (e.g. Voltaren® gel) and oral NSAIDs recommended include OTC formulations such as Motrin® and Aleve®. Non-pharmacologic therapy recommended as initial treatment options have included physical and occupational therapy, therapeutic lifestyle changes, exercise, tai chi and use of assistive devices, such as braces and canes. If a patient fails OTC therapy and therapeutic lifestyle changes, prescription therapy may be considered. Stronger NSAIDs and Cymbalta® (duloxetine) are available by prescription that could be used to treat chronic pain.<sup>27</sup>

Remaining pharmacologic options include opioid analgesic therapy and intra-articular injections, such as corticosteroid injections and viscosupplementation. However, since OA of the knee is the only approved indication for viscosupplementation, it is important to note that the remainder of this discussion pertains only to this condition.

If conservative treatments are not effective, then intra-articular injections, such as corticosteroid injections and viscosupplementation, may be used. Cortisone injections may relieve pain in the joint; however, a limitation of three or four injections per year is set due to the high potential for worsening joint damage over time.<sup>28</sup> Viscosupplementation consists of injections of hyaluronic acid, a component normally found in the joint fluid. This treatment option may offer pain relief by providing some cushioning in the knee.

The 2013 American Academy of Orthopedic Surgeons (AAOS) guidelines strongly recommended against the use of hyaluronic acid injections (viscosupplementation) for patients with knee arthritis, given the lack of benefit shown in randomized trials.<sup>29</sup> Even though guidelines recommend against the use of these medications, the hyaluronic acid derivatives in table 5 continue to be utilized by myMatrixx prescribers in a constant utilization rate since 2013.

# BOTOX®

Botox® is indicated for a variety of conditions — axillary hyperhidrosis, chronic migraine, bladder dysfunction, certain eye disorders (e.g. strabismus, blepharospasm), cervical dystonia, spasticity and cosmetic purposes (e.g. wrinkle reduction).<sup>30</sup>

Although there are the many approved indications, only a few can be potentially related to workers’ compensation injuries. These include chronic migraine headaches, limb spasticity associated with traumatic brain injury (TBI) or spinal cord injury (SCI), cervical dystonia associated with trauma and neurogenic (overactive) bladder associated with SCI.

**Table 6: Use and Cost of Botox® Therapy per Indication**

Condition Treated	Recommended as First-Line Agent	Dosing & Frequency	Cost Per Injection	First-Line Pharmacologic Options for Condition
Chronic Migraine	Yes	Max 155 units every 12 weeks	\$1,442.40	Prophylaxis: BoNT-A, topiramate, amitriptyline, beta-blockers  Acute Treatment: • Mild to moderate: NSAIDs, combination product (acetaminophen, aspirin, caffeine) • Moderate to severe: triptans
Upper Limb Spasticity	Yes	Max 200 units every 12 weeks	\$1,442.40	Focal: BoNT-A, BoNT-B
Lower Limb Spasticity	Yes	Max 75 units every 12 weeks	\$721.20	Generalized: baclofen, tizanidine
Cervical Dystonia	Yes	198 – 300 units every 8 weeks	\$1,442.40 – \$2,163.60	BoNT-A
Neurogenic Bladder	No	Max 200 units every 12 weeks	\$1,442.40	Oral anticholinergic agents (i.e. oxybutynin, tolterodine, solifenacin)

**Migraines:** Approved by the FDA as treatment for chronic migraines, Botox® injections are an effective treatment option in treating migraines and tension type headaches. Chronic migraines are “attacks occurring 15 days or more monthly for at least 3 months, with attacks lasting 4 hours or more.”



# ALTERNATIVE MIGRAINE TREATMENTS

Calcitonin gene-related peptide (CGRP) inhibitors, the most recent novel migraine treatment to enter the market in 2018 for the treatment of episodic and chronic migraines. Although CGRP inhibitors are not recognized as specialty medications, their high cost compared to existing therapeutic alternatives demands an assessment.

The American Headache Society (AHS) released a consensus statement in December 2018 regarding the use of CGRP inhibitors in treatment therapy, there is insufficient evidence at this time to provide an anti-CGRP treatment guideline for migraine therapy. ,

**Monthly Cost of Anti-CGRP Migraine Prophylaxis Treatment**

Medication	Dosage	Monthly Cost
Aimovig® (erenumab)	70 – 140 mg once monthly	\$345.00 – \$690.00
Ajovy® (fremanezumab)	225 mg once monthly	\$690.00
Emgality® (galcanezumab)	120 mg once monthly	\$690.00

Due to the high monthly cost and insufficient evidence available regarding the use of anti-CGRP treatment in migraine therapy, the potential benefits of therapy do not outweigh the therapy cost. Therefore, use of first-line oral treatment options are recommended over anti-CGRP therapy.



**Although CGRP inhibitors are not recognized as specialty medications, their high cost compared to existing therapeutic alternatives demands an assessment.**

**Limb Spasticity:** Initially indicated for upper limb (elbow, wrist, fingers) spasticity or stiffness, the FDA expanded the indications of Botox® to include treatment of lower limb (ankle and toe flexors) spasticity in 2016. Limb spasticity is a condition that causes stiffness and flexing of muscles, twitching of limbs or loss of limb movement control. Spasticity can be the result of damage to the nervous system due to a TBI or SCI.

According to the Official Disability Guidelines (ODG), “multiple clinical trials suggest that botulinum toxin A may be useful in the management of spasticity following a traumatic brain injury,” and is therefore recommended as a first-line treatment option. Botox® has not yet proven an increase in functional ability and is not intended to replace existing physical therapy.

**Cervical dystonia:** Characterized by involuntary neck contractions, cervical dystonia results in abnormal movements and awkward posture of the head and neck. Initially mild, symptoms may start as an invisible tremor of the head, followed by involuntary head pulling, turning or jerking that may increase in frequency and strength over time.

Though it is not generally related to a workers’ compensation injury by ODG standards, BoNT-A treatment is a recommended first-line therapy for cervical dystonia. This treatment has shown to improve posture, pain and disability. BoNT-B is also effective in treating cervical dystonia, but is reserved as an alternative for patients who fail to get clinical benefit after using BoNT-A due to its high antigenicity effects.

**Neurogenic Bladder:** Overactive bladder (OAB) is a syndrome of bladder dysfunction symptoms (e.g. urinary urgency with or without incontinence, urinary frequency, nocturia, urinary incontinence) which may all lead to a reduction in quality of life. The cause of this overactivity may be due to neurogenic detrusor overactivity stemming from an SCI or multiple sclerosis.

First-line pharmacologic therapies for detrusor hyperreflexia are oral anticholinergic agents and BoNT. For patients whose symptoms are refractory to first-line oral therapy, the use of BoNT provides an effective alternative to more invasive and aggressive treatments (e.g. sacral nerve stimulation, bladder augmentation cystoplasty).

Patients cannot receive treatment with Botox® if they have an infection at the target injection site, a urinary tract infection or urinary retention. Prophylactic antibiotic therapy should be administered 1 to 3 days prior to treatment, on the day of treatment and one to three days following treatment with Botox®.

**Though it is not generally related to a workers’  
compensation injury by ODG standards, BoNT-A treatment  
is a recommended first-line therapy for cervical dystonia.**

# CHEMOTHERAPEUTIC AGENTS

As cancer treatment medications meet all criteria for specialty classification as defined by the American Journal of Managed Care, it is important to discuss its impact in patient care.

The National Institute for Occupational Safety and Health (NIOSH) estimates between 45,872 to 91,725 of new cancer cases reported in the U.S. in 2012 were associated with past occupational exposure. This estimated range is an underestimate and may change over time as further information regarding agents in the workplace and number of cancers in the U.S. is determined.<sup>40</sup>

Employees exposed to radiation and toxic substances during employment may be eligible for compensation and medical benefits through the Energy Employees Occupational Illness Compensation Program Act of 2000 (the Act/EEOICPA). This act outlines compensation for employees (or survivors if the worker is deceased) who are employed through the Department of Energy (DOE), its contractors or members at subcontracted facilities and had developed certain diseases as a result of occupational exposure to certain materials or radiation.<sup>41</sup>

The Special Exposure Cohort (SEC) was established as a result of the Act/EEOICPA, and specifies qualifications that an employee must meet in order to be deemed compensable as well as established classes of employees and work sites. In order to qualify for compensation through the act, the employee must have at least one of the following cancer types, in addition to having worked at an associated SEC site.<sup>42, 43</sup>

## The Special Exposure Cohort Compensability Qualifications

### Cancer Type

### Comment

Bone, renal	
Leukemia (other than chronic)	Disease onset was at least two years after initial exposure
Lung	Other than in-situ discovered during or after post-mortem exam
Multiple myeloma, lymphomas (other than Hodgkin's)	

### Primary Cancer of the:

• Bile ducts	• Gall bladder	• Pharynx
• Brain	• Liver (except cirrhosis or hepatitis B)	• Salivary gland
• Breast (male and female)	• Ovary	• Small intestine
• Colon	• Pancreas	• Stomach
• Esophagus		• Thyroid
		• Urinary bladder

**Disease onset was at least five years after initial exposure**

Table 8

Cancer presumption laws affecting firefighters and emergency medical service (EMS) workers have remained a controversial topic due to the removal of traditional burden of proof that an injury, illness or disease is the result of an occupational injury. Prior studies, including a multi-year study conducted by NIOSH and the U.S. Fire Administration, concluded that firefighters were among an occupational field with an increased risk of cancer.<sup>44</sup>

Federal regulations, such as the Firefighter Cancer Registry Act (enacted July 2018) require the CDC and NIOSH to establish a registry of firefighters in order to determine correlation between occupational exposure and cancer development. Additionally, the James Zadroga 9/11 Health and Compensation Reauthorization Act of 2015 provides funding for first responders and survivors with health complications resulting from terrorist attacks.<sup>45</sup>

Cancer presumption laws enacted by 33 states have extended workers' compensation coverage to include firefighters who have developed one or more cancer types due to occupational exposure. The language and specifications, however, vary from state to state, regarding compensability of certain cancer types and compensation qualifications, as there is no current federal legislation available for guidance.<sup>46</sup> There are 10 additional states that have written legislation stating workers' compensation benefits are managed by the local jurisdiction or the respective Fire Commission, though in some states this does not guarantee state approval.<sup>47</sup>










**Cancer presumption laws enacted by 33 states have extended workers' compensation coverage to include firefighters who have developed one or more cancer types due to occupational exposure.**

- Alabama
- Alaska
- Arizona
- Arkansas
- California
- Colorado
- Connecticut
- District of Columbia
- Florida
- Georgia
- Idaho
- Illinois
- Indiana
- Iowa
- Kansas
- Kentucky
- Louisiana
- Maine
- Maryland
- Massachusetts
- Michigan
- Minnesota
- Missouri
- Montana
- New Mexico
- Nebraska
- Nevada
- New Hampshire
- New York
- North Dakota
- Ohio
- Oklahoma
- Oregon
- Pennsylvania
- Rhode Island
- South Dakota
- Tennessee
- Texas
- Utah
- Vermont
- Virginia
- Washington
- Wisconsin
- Wyoming

The statute language and specificity regarding presumption varied. For example, language written in some states' statutes are not specific in terms of cancer types that are covered, whereas other state statutes specify certain cancers such as leukemia, brain, bladder, non-Hodgkin lymphoma and gastrointestinal. Though legislation may vary, the coverage criteria for presumption generally consider the following:

## THOUGH LEGISLATION MAY VARY, THE COVERAGE CRITERIA FOR PRESUMPTION GENERALLY CONSIDER THE FOLLOWING:

-  **Type of cancer**
-  **Type of occupation**
-  **Pre-claim or pre-employment physical exam**
-  **Employee's current work status**
-  **Time frame of employment or onset of disease**
-  **Retroactivity**
-  **Disability**

As the amount of spending for specialty medications and treatment costs continue to climb, it is important to determine whether the state legislations describe specific conditions for workers' compensation coverage for cancer presumption. It may be anticipated that as further research relating occupational exposure and cancer development emerge through laws such as the Firefighter Cancer Registry Act, cancer presumption legislation may further develop and outline how affected workers may be compensated for their condition.



# RISK OF NONCOMPLIANCE

SEVERAL COMPLICATIONS CAN ARISE DUE TO INSUFFICIENT TREATMENT AND/OR NONCOMPLIANCE. THESE COMPLICATIONS COULD LEAD TO EXTRANEIOUS COSTS THAT INSURERS MUST PAY, WHICH COULD POTENTIALLY BE MUCH MORE THAN STANDARD TREATMENT THERAPY.

## ANTICOAGULANTS

The use of DOACs are known to reduce the risk of CV events such as PEs, VTEs and stroke. Therefore, it is important to ensure that these patients are being treated effectively to prevent such events from occurring. Non-adherence to these medications leads to poor outcomes and increase cost in healthcare expenditure. Although, there are many unwanted side effects of taking DOACs, with clinical monitoring and supervision, the likelihood of these adverse events are less likely.

## HIV ANTIRETROVIRAL

Lack of adherence to HIV treatment regimen could be fatal. More than 1.1 million people in the U.S. are living with HIV, and about one out of seven are unaware that they are infected.<sup>48,49</sup> This makes it crucial to ensure that if an injured worker comes into contact with potential blood borne pathogens that he or she seeks medical attention right away. By ensuring medication adherence, the risk of HIV becoming treatment resistant is reduced. Without proper drug therapy, HIV can progress to AIDS, and these patients can develop multiple infections from opportunistic microbes such as cytomegalovirus, Kaposi's sarcoma, jiroveci pneumonia, etc.<sup>50</sup> According to the CDC, the lifetime cost of HIV treatment is \$379,668.<sup>51</sup> There are multiple resources for injured workers to learn more about HIV such as the CDC and AIDSinfo.

## HEPATITIS C ANTIVIRALS

HCV infection is one of the most common chronic infections, affecting an estimated 170 million people worldwide, and is the leading cause of chronic liver disease. For HCV, treatment care should include medical education, laboratory testing, imaging, diet management and an individualized treatment regimen.<sup>52</sup> Adherence is critical in avoiding further liver damage with leads to cirrhosis and possible liver cancer. Cirrhosis due to hepatitis is the leading indication for liver transplantation in the U.S. and the average cost of a liver transplant is about \$812,500.<sup>53</sup>

## BIOLOGIC DMARDS

There are many factors that lead to medication non-compliance with biological DMARDs. These include therapy-related factors such as tolerability, administration and convenience, as well as patient related factors such as age, health literacy, social support and patient beliefs. Unfortunately, with medication non-adherence, many complications can arise, such as further joint damage, osteoporosis, carpal tunnel syndrome and even heart and lung problems. This can result in cardiovascular events, such as a stroke or heart attack. The current average cost of treatment after a severe heart attack, including direct and indirect costs, is about \$1 million dollars, according to an article from the National Business Group on Health.<sup>54</sup>

# CONCLUSION

Specialty drugs are the fastest growing medications in the pharmaceutical market and have a massive impact on healthcare spending and professional involvement. These medications require in-depth patient counseling, clinical monitoring, medication management and financial strategies in order to increase cost-effectiveness while ensuring full patient compliance. Communication and collaboration between all stakeholders involved in the patients' care may ultimately lead to improved health outcomes while maintaining cost of therapy.

This paper discussed the highest utilized specialty drugs and conditions represented in the 2018 myMatrixx Drug Trend Report. However, claims handlers may also encounter anomalies for rare disorders, such as hereditary angioedema, that can present a significant cost impact.

Undoubtedly, our data shows that when specialty drugs are added to the injured worker's regimen, the total cost of treating that patient rises exponentially. We stratified our claimants in three spending categories, what was found is that in the group of patients that utilized less than \$50K per year total in drug spend attributed to specialty only accounted for 5.6% of drug spend and 1.8% of total patients. In the second group, total annual drug spend exceeded \$50K but was less than \$1M, we saw the percentage of specialty drug use approached almost 40%. Those who used over \$1M of medications annually were found to be using specialty drugs almost exclusively.

**Table 9**

myMatrixx Total Drug Cost 2019	% of Total Spend	% of Total Patients	% of Spend that is Specialty Drugs	% of Patients on Specialty Drugs
< \$50K	91.4%	99.9%	5.6%	1.8%
\$50K to \$1M	8.2%	0.1%	37.7%	29.8%
> \$1M	0.4%	< 0.1%	100.0%	100.0%

As managed care pharmacist we recognize the strategy that these pharmaceutical companies are using to market these drugs and gain profit share, is similar to what the industry has done for traditional drugs in that innovators can almost guarantee immediate competition. These competing companies often use the progenitor drug to formulate their own replicator of the drug. Most of the money is spent copying other drugs in order to compete and market "copy-cat" drugs, which presents us with the challenge of distinguishing between specialty medications in the same therapeutic class. There is a bigger challenge with presenting a therapeutic alternative for specialty medications to physicians, due to the manufacturers marketing specialty medications as exclusively effective for a specific patient population. Although this culture and adversities exist and acceptance rate is lower than traditional medications, when clinical interventions lead to a change in therapy for specialty medications, the impact is substantial. Our goal as the PBM is to provide solutions that improve the injured worker's health while promoting financial accountability for the prescribing of specialty medications.



# ABOUT MYMATRIX

myMatrixx is a full-service pharmacy benefit management company focused on the workers' compensation market. By combining advanced technology, clinical expertise and comprehensive reporting, myMatrixx simplifies the management of claims. Our results-driven solutions deliver reduced costs for our clients and improve outcomes for their injured workers. For more information, visit [www.mymatrixx.com](http://www.mymatrixx.com). For drug inquiries or clinical services, email [clinical@mymatrixx.com](mailto:clinical@mymatrixx.com) or contact your Clinical Account Executive.

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# APPENDICES A – SPECIALTY MEDICATIONS

Samsca®  
Sandostatin® (octreotide acetate)  
Sandostatin LAR Depot®  
Signifor® LAR  
Signifor®  
Somatuline Depot®  
Somavert®  
Supprelin LA®  
Testopel®  
Triptodur™  
Xermelo™

## ENZYME DEFICIENCIES

Adagen®  
Aldurazyme®  
Brineura™  
Carbaglu®  
Cerdelga™  
Cerezyme®  
Cystadane®  
Elaprase®  
Elelyso™  
Fabrazyme®  
Galafold™  
Kanuma™  
Kuvan®  
Lumizyme™  
Mepsevii™  
Naglazyme®  
Nityr™  
Orfadin® (nitisinone)  
Palynziq™  
Ravicti™  
Revcovi™  
Strensiq™  
Sucraid®  
Vimizim™  
VPRIV™  
Zavesca® (miglustat)

## GROWTH DEFICIENCY

Genotropin®  
Humatrope®  
Increlex®  
Macrlen®  
Norditropin®  
Nutropin AQ®  
Omnitrope®  
Saizen®  
Serostim®  
Zomacton®  
Zorbtive®

## HEMOPHILIA

Advate®  
Adynovate™  
Afstyla®  
Alphanate®  
Alphanine SD®  
Alprolix™  
Bebulin®  
Benefix®  
Coagadex®  
Corifact®  
DDAVP® (desmopressin acetate) (oral/nasal forms are not specialty)  
Eloctate™  
Feiba®  
Fibryga®  
Hemlibra®  
Hemofil M®

Humate-P®  
Idelvion®  
Ixinity®  
Jivi®  
Koate®  
Kogenate FS®  
Kovaltry®  
Mononine®  
Novoeight®  
Novoseven RT®  
Nuwiq®  
Obizur™  
Profilnine SD®  
Rebinyn®  
Recombinate™  
RiaSTAP®  
Rixubis™  
Stimate®  
Tretten®  
Vonvendi™  
Wilate®  
Xyntha®

## HEPATITIS C

Epclusa® (sofosbuvir/velpatasvir)  
Harvoni® (ledipasvir/sofosbuvir)  
Mavyret™  
Ribavirin (Rebetol®, Ribasphere®, Ribapak®, Moderiba™)  
Sovaldi®  
Viekira Pak®  
Vosevi®  
Zepatier®

## HEREDITARY ANGIOEDEMA

Berinert®  
Cinryze®  
Firazyr® (icatibant)  
Haegarda®  
Kalbitor®  
Ruconest®  
Takhzyro™

## HIGH BLOOD CHOLESTEROL

Juxtapid®

## HIV

Aptivus®\*  
Atripla®\*  
Biktarvy®  
Cimduo™  
Combivir®\* (lamivudine/zidovudine)  
Complera®\*  
Crixivan®\*  
Delstrigo™\*  
Descovy®\*  
Dovato®  
Edurant®\*  
Emtriva®\*  
Epivir®\* (lamivudine)  
Epzicom®\* (abacavir/lamivudine)  
Evotaz™ \*  
Fuzeon®\*  
Genvoya®\*  
Intelligence®\*  
Invirase®\*  
Isentress®\*  
Juluca®  
Kaletra®\* (lopinavir/ritonavir)  
Lexiva®\* (fosamprenavir)  
Norvir®\* (ritonavir)

Odefsey®\*  
Pifeltro™\*  
Prezcobix™\*  
Prezista®\*  
Rescriptor®\*  
Retrovir®\* (zidovudine)  
Reyataz®\* (atazanavir)  
Sustiva®\* (efavirenz)  
Selzentry®\*  
Stribild®\*  
SymFi™  
SymFi Lo™  
Symtuza™  
Tivicay®\*  
Triumeq®\*  
Trizivir®\* (abacavir/lamivudine/zidovudine)  
Trogarzo™  
Truvada®\*  
Tybost®\*  
Videx®\* (didanosine)  
Videx EC®\* (didanosine DR)  
Yiracept®\*  
Viramune®\* (nevirapine)  
Viramune XR®\* (nevirapine ER)  
Viread®\* (tenofovir disoproxil fumarate)  
Vitekta®\*  
Zerit®\* (stavudine)  
Ziagen®\* (abacavir)

## IDIOPATHIC PULMONARY FIBROSIS

Esbriet™  
OFEV®

## IMMUNE DEFICIENCY

Bivigam™  
Cutaquig®  
Cuvitru™  
Cytogam®  
Flebogamma®  
Gamastan S-D®  
Gammagard Liquid®  
Gammagard S-D®  
Gammaked™  
Gammplex®  
Gamunex-C®  
Hizentra™  
HyQvia™  
Octagam®  
Panzyga®  
Privigen®

## INFERTILITY

(oral forms are not specialty)  
Bravelle®  
Cetrotide®  
Chorionic Gonadotropin (brands include Novarel®, Pregnyl®)  
Crinone®  
Endometrin®  
Follistim AQ®  
Ganirelix (ganirelix acetate)  
Gonal-F®  
leuprolide  
Menopur®  
Ovidrel®  
progesterone injection

**INFLAMMATORY CONDITIONS**

Actemra®  
 Arcalyst®  
 Benlysta®  
 Cimzia®  
 Cosentyx™  
 Enbrel®  
 Entyvio™  
 Humira®  
 Humira® (Pediatric)  
 Ilaris®  
 Ilumya™  
 Inflectra™  
 Kevzara®  
 Kineret®  
 Olumiant®  
 Orencia®  
 Otezla®  
 Remicade®  
 Renflexis™  
 Rinvoq™  
 Siliq™  
 Simponi™  
 Simponi Aria®  
 Skyrizi™  
 Stelara™  
 Taltz®  
 Tremfya™  
 Xeljanz®  
 Xeljanz XR®

**IRON TOXICITY**

Exjade® (deferasirox)  
 Ferriprox®  
 Jadenu™

**MISCELLANEOUS DISEASES**

Acthar H.P. Gel®  
 Actimmune®  
 Apokyn®  
 Arestin®  
 Arikayce®  
 Austedo®  
 Botox®  
 Botox Cosmetic®  
 Ceprotin™  
 Chenodal®  
 Cholbam®  
 Cystagon®  
 Daraprim®  
 Diacomit®  
 Duopa™  
 Dysport®  
 Endari™  
 Epidiolex®  
 Gamifant®  
 Gattex®  
 Gocovri™  
 Hemangeol™  
 Hetlioz™  
 Inbrija™  
 Ingrezza™  
 Jynarque™  
 Keveyis®  
 Krystexxa®  
 Makena™ (hydroxyprogesterone caproate)  
 Myobloc®  
 Northra™

Nourianz™  
 Nuplazid™  
 Ocaliva™  
 Onpattro™  
 Prialt®  
 Procybsi™  
 Probuphine®  
 Prothelia™  
 Qutenza®  
 Sabril® (vigabatrin)  
 Sinuva™  
 Solesta®  
 Soliris®  
 Sprix®  
 Spravato™  
 Sublocade™  
 Tegsedi™  
 Thiola®  
 Thyrogen®  
 Ultomiris™  
 Varithena®  
 Vigadrone™  
 Vivitrol®  
 Vyleesi™  
 Vyndamax™  
 Vyndaqel®  
 Wakix®  
 Xenazine® (tetrabenazine)  
 Xeomin®  
 Xiaflex™  
 Xuriden™  
 Xyrem®2  
 Zecuity®  
 Zulresso™

**MULTIPLE SCLEROSIS**

Ampyra® (dalfampridine)  
 Aubagio®  
 Avonex®  
 Betaseron®  
 Copaxone® (glatiramer, Glatopa®)  
 Extavia®  
 Gilenya®  
 Lemtrada®  
 Mavenclad®  
 Mayzent®  
 mitoxantrone®  
 Ocrevus®  
 Plegridy®  
 Rebif®  
 Tecfidera®  
 Tysabri®

**MUSCULAR DYSTROPHIES**

Emflaza™  
 Exondys 51™  
 Firdapse®  
 Radicava™  
 Ruzurgi®  
 Spinraza™  
 Zolgensma®

**OPHTHALMIC CONDITIONS**

Cystaran™  
 Eylea®  
 Iluvien™  
 Jetrea®  
 Lucentis®

Luxturna™  
 Macugen®  
 Oxervate™  
 Ozurdex™  
 Retisert®  
 Visudyne®  
 Yutiq™

**OSTEOARTHRITIS**

Durolane®  
 Euflexxa®  
 Gel-One®  
 Gelsyn-3™  
 Genvisc 850®  
 Hyalgan®  
 Hymovis®  
 Monovisc®  
 Orthovisc®  
 Sodium hyaluronate  
 Supartz FX®  
 Synvisc®  
 Synvisc-One®  
 Visco-3™  
 Zilretta™

**OSTEOPOROSIS**

Boniva® (ibandronate) (oral forms are not specialty)  
 Eventy™  
 Forteo®  
 Prolia™  
 Reclast® (zoledronic acid)  
 Tymlos™

**PULMONARY HYPERTENSION**

Adcirca® (tadalafil)  
 Adempas®  
 Flolan® (epoprostenol)  
 Flolan Diluent® (epoprostenol diluent)  
 Letairis® (ambrisentan)  
 Opsumit®  
 Orenitram™  
 Remodulin® (treprostinil)  
 Remodulin Diluent®  
 Revatio® (sildenafil citrate)  
 Tracleer® (bosentan)  
 Tyvaso®  
 Uptravi®  
 Veletri®  
 Ventavis®

**RESPIRATORY SYNCYTIAL VIRUS**

Synagis®

**TRANSPLANT**

azathioprine (AZASAN, IMURAN)  
 Astagraf XL™\*  
 Cellcept®\* (mycophenolate mofetil)  
 Neoral®, Sandimmune®\* (cyclosporine, Gengraf®)  
 Envarsus® XR\*  
 Myfortic®\* (mycophenolic acid)  
 Nulojix®\*  
 Prograf®\* (tacrolimus)  
 Rapamune®\* (sirolimus)  
 Simulect®\*  
 Thymoglobulin®\*  
 Zortress®\*



# APPENDICES B – PIPELINE

## Specialty Medications

abicipar pegol	inebilizumab	ripretinib
abrocitinib	lisocabtagene maraleucel	risdiplam
beta beglogene darolentivec	obeticholic acid	satralizumab
entinostat	ozanimod	selumetinib
fenfluramine	pemigatinib	valoctocogene
filgotinib	ponesimod	roxaparvovec
idecabtagene vicleucel	quizartinib	viltolarsen

## Biosimilar

Biosimilar	Manufacturer(s)	Reference Biologic	Possible FDA Approval Date	Potential Launch Date
1. bevacizumab biosimilar	Samsung Bioepis	Avastin (bevacizumab)	9.19.2020	TBD
2. filgrastim biosimilar	Adello Biologic	Neupogen (filgrastim)	2020	TBD (FDA Approval)
3. pegfilgrastim biosimilar (Lapelga)	Apotex/Intas	Neulasta (pegfilgrastim)	2020	TBD (FDA Approval)
4. filgrastim biosimilar (Grastofil)	Apotex/Intas	Neupogen filgrasyim)	2020	TBD (FDA Approval)
5. filgrastim biosimilar	Tanvex BioPharma	Neupogen filgrasyim)	2020	TBD (2020)

## FDA – Approved Biosimilars Pending Launch

Biosimilar	Manufacturer(s)	Reference Biologic	Approval Date	Potential Launch Date
1. etanercept-szszs (Erelzi)	Sandoz	Enbrel (etanercept)	8.30.2016	TBD (2028/2029)
2. adalimumab-atto (Amjevita)	Amgen	Humira (adalimumab)	9.23.2016	Settlement: 3.31.2023
3. adalimumab-adbm (Cyltezo)	Boehringer Ingelheim	Humira (adalimumab)	8.25.2017	Settlement: 7.1.2023
4. infliximab-qbtx (Ixifi)	Pfizer	Remicade (infliximab)	12.13.2017	No US Launch Plans
5. adalimumab-adaz (Hyrimoz)	Sandoz	Humira (adalimumab)	10.31.2018	Settlement: 9.30.2023
6. trastuzumab-pkrb (Herzuma)	Celltrion/Teva	Herceptin (trastuzumab)	12.17.2018	Feb. – Apr. 2020
7. trastuzumab-dttb (Ontruzant)	Merck/Samsung Bioepis	Herceptin (trastuzumab)	1.18.2019	Feb. – Apr. 2020
8. trastuzumab-gyyp (Trazimera)	Pfizer	Herceptin (trastuzumab)	3.11.2019	Feb. 15th, 2020
9. etanercept-ykro (Eticovo)	Merck/Samsung Bioepis	Enbrel (etanercept)	4.25.2019	TBD (2028/2029)
10. adalimumab-bwwd (Hadilma)	Biogen/Samsung Bioepis	Humira (adalimumab)	7.23.2019	Settlement: 6.30.2023
11. adalimumab-afzb (Abrilada)	Pfizer	Humira (adalimumab)	11.15.2019	Settlement: 11.20.2023
12. infliximab-axxq (Avsola)	Amgen	Remicade (infliximab)	12.6.2019	TBD (2020)

# REFERENCES

- <sup>1</sup> Patel BN, Audet PR. A review of approaches for the management of specialty pharmaceuticals in the United States. *Pharmacoeconomics*. 2014;32(11):1105–1114.
- <sup>2</sup> [https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us-a-review-of-2017-and-outlook-to-2022.pdf?&\\_=1563751862716](https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/medicine-use-and-spending-in-the-us-a-review-of-2017-and-outlook-to-2022.pdf?&_=1563751862716)
- <sup>3</sup> Flevas DA, Megaloikononimos PD, Dimopoulos L, et al. (2018). Thromboembolism prophylaxis in orthopedics: An update. *General Orthopedics*, 3, 136-148.
- <sup>4</sup> Lee SY, Ro D, Chung CY, et al. Incidence of deep vein thrombosis after major limb orthopedic surgery: analysis of a nationwide claim registry. *Yonsei Medical Journal*. 2014;56(1):139-145.
- <sup>5</sup> Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e278S-e325S.
- <sup>6</sup> Flevas, Dimitrios A, et al. "Thromboembolism prophylaxis in orthopedics: an update." *EFORT open reviews*. 2018;3(4):136-148.
- <sup>7</sup> Palmer E. BMS and Pfizer file 16 Eliquis patent lawsuits to waylay generic makers. April 12, 2017. <https://www.fiercepharma.com/legal/bms-and-pfizer-file-16-eliquis-patent-lawsuits-to-waylay-generic-makers>. (Accessed April 22, 2019).
- <sup>8</sup> Kass D. Mylan Pradaxa generic delayed in Boehringer patent deal. January 26, 2018. <https://www.law360.com/articles/1006299/mylan-pradaxa-generic-delayed-in-boehringer-patent-deal>. (Accessed April 2, 2019).
- <sup>9</sup> Food and Drug Administration. Tentative approval. Aurobindo generic Xarelto. June 22, 2018. [https://www.accessdata.fda.gov/drugsatfda\\_docs/applletter/2018/208544Orig1s000TAltr.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/applletter/2018/208544Orig1s000TAltr.pdf). (Accessed May 8, 2019).
- <sup>10</sup> Learn About Healthcare-Associated Venous Thromboembolism | CDC. (n.d.). Retrieved July 24, 2019, from <https://www.cdc.gov/ncbddd/dvt/ha-vte.html>
- <sup>11</sup> Kuhar DT, et al. (2013, September 25). Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis. Retrieved from <https://stacks.cdc.gov/view/cdc/20711>
- <sup>12</sup> Occupational HIV Transmission and Prevention among Health Care Workers. (2016, November 7). Retrieved December 13, 2018, from <https://www.cdc.gov/hiv/workplace/healthcareworkers.html>
- <sup>13</sup> Kuhar DT, et al. (2013, September 25). Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis. Retrieved from <https://stacks.cdc.gov/view/cdc/20711>
- <sup>14</sup> United States Securities and Exchange Commission. Retrieved July 21, 2019, from <http://investors.gilead.com/static-files/0ff8d741-b9eb-4162-bcb4-f16094d37254>
- <sup>15</sup> Center for Disease Control and Prevention. (n.d.). HIV cost-effectiveness. Retrieved from <http://www.cdc.gov/hivprevention/ongoing/costeffectiveness/>
- <sup>16</sup> Hepatitis C Questions and Answers 16 for Health Professionals | CDC. (n.d.). Retrieved from <https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#section1>
- <sup>17</sup> Management of Acute HCV Infection: HCV Guidance. (n.d.). Retrieved from <https://www.hcvguidelines.org/unique-populations/acute-infection>
- <sup>18</sup> 2017 US Organ and tissue transplant cost estimates and discussion. Milliman Research Report. <http://www.milliman.com/uploadedFiles/insight/2017/2017-Transplant-Report.pdf>.
- <sup>19</sup> What is Rheumatoid Arthritis? (n.d.). Retrieved July 8, 2019, from <https://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/what-is-rheumatoid-arthritis.php>
- <sup>20</sup> American College of Rheumatology. Rheumatoid arthritis. August 2012. [http://www.rheumatology.org/practice/clinical/patients/diseases\\_and\\_conditions/ra.pdf#toolbar=1](http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.pdf#toolbar=1). (Accessed July 17, 2019).
- <sup>21</sup> American College of Rheumatology. Rheumatoid arthritis. August 2012. [http://www.rheumatology.org/practice/clinical/patients/diseases\\_and\\_conditions/ra.pdf#toolbar=1](http://www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/ra.pdf#toolbar=1). (Accessed July 17, 2019).
- <sup>22</sup> Singh JA, Furst DE, Bharat A et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res (Hoboken)* 2012;64:625-39.
- <sup>23</sup> Gunnarsson C, Chen J, Rizzo JA, Ladapo JA, Naim A, Lofland JH. The Employee Absenteeism Costs of Rheumatoid Arthritis: Evidence From US National Survey Data. *J Occup Environ Med*. 2015;57(6):635-42.
- <sup>24</sup> Yucesoy, Berran et al. "Occupational and genetic risk factors for osteoarthritis: a review." *Work (Reading, Mass.)* 2015;50(2):261-273. doi:10.3233/WOR-131739
- <sup>25</sup> Hochberg MC, Altman R, April KT, et al. American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care & Research*. 2012;64(4):465-474.
- <sup>26</sup> A. (2015, December 4). Surgical Management of Osteoarthritis of the Knee: Evidence-Based Clinical Practice Guidelines. Retrieved from <http://content.guidelinecentral.com/guideline/get/pdf/2437>.

- <sup>27</sup> A. (2015, December 4). Surgical Management of Osteoarthritis of the Knee: Evidence-Based Clinical Practice Guidelines. Retrieved from <http://content-guide-linecentral.com/guideline/get/pdf/2437>.
- <sup>28</sup> Hochberg MC, Altman R, April KT, et al. (2012, April). American College of Rheumatology 2012 Recommendations for the Use of Nonpharmacologic and Pharmacologic Therapies in Osteoarthritis of the Hand, Hip, and Knee. *Arthritis Care & Research*. 2012;64(4):465-474.
- <sup>29</sup> American Association of Orthopaedic Surgeons. Treatment of Osteoarthritis of the Knee: Evidence-Based Guideline, 2nd Edition, 2013.
- <sup>30</sup> Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2016;86(19):1818-1826.
- <sup>31</sup> Simpson DM, Hallett M, Ashman EJ, et al. Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache: Report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. 2016;86(19):1818-1826.
- <sup>32</sup> Rosenberg, J. (2019, January 14). American Headache Society Includes CGRP Inhibitors in Updated Consensus Statement. Retrieved July 16, 2019, from <https://www.ajmc.com/newsroom/american-headache-society-includes-cgrp-inhibitors-in-updated-consensus-statement>.
- <sup>33</sup> DiGrande, S. (2019, March 14). Insufficient Evidence for Anti-CGRP Treatment Guideline for Migraine. Retrieved July 16, 2019, from <https://www.ajmc.com/newsroom/insufficient-evidence-for-anticgrp-treatmentguideline-for-migraine>.
- <sup>34</sup> Anderson, P. (2016, January 26). FDA Approves Botox for Lower Limb Spasticity. Retrieved July 16, 2019, from <https://www.medscape.com/viewarticle/857757>.
- <sup>35</sup> Official Disability Guidelines. Integrated Treatment/Disability Duration Guidelines: Head. Updated 6/21/2019.
- <sup>36</sup> Official Disability Guidelines. Integrated Treatment/Disability Duration Guidelines: Head. Updated 6/21/2019.
- <sup>37</sup> Jinnah, HA. Diagnosis & Treatment of Dystonia. *Neurol Clin*. 2015 Feb; 33(1): 77-100
- <sup>38</sup> Official Disability Guidelines. Integrated Treatment/Disability Duration Guidelines: Neck. Updated 6/21/2019.
- <sup>39</sup> Middleton J, Ramakrishnan K, Cameron I. Management of the Neurogenic Bladder for Adults with Spinal Cord Injuries. Agency for Clinical Innovation. (2014).
- <sup>40</sup> CDC - Cancer Policy - NIOSH Workplace Safety and Health Topic. (n.d.). Retrieved July 23, 2019, from <https://www.cdc.gov/niosh/topics/cancer/default.html>
- <sup>41</sup> CDC - NIOSH - Radiation Dose Reconstruction - The Act/EEOICPA. (n.d.). Retrieved from <https://www.cdc.gov/niosh/ocas/ocaseeoi.html>
- <sup>42</sup> CDC - NIOSH - Radiation Dose Reconstruction - Special Exposure Cohort (SEC). (n.d.). Retrieved from <https://www.cdc.gov/niosh/ocas/ocassec.html>
- <sup>43</sup> CDC - NIOSH - Radiation Dose Reconstruction - Work Site Information. (n.d.). Retrieved from <https://www.cdc.gov/niosh/ocas/worksite.html>
- <sup>44</sup> Fire Fighter Resources, Cancer and Other Illnesses | NIOSH | CDC. (n.d.). Retrieved July 23, 2019, from <https://www.cdc.gov/niosh/firefighters/health.html>
- <sup>45</sup> Presumptive Legislation for Firefighter Cancer by State. (n.d.). Retrieved from <https://www.firstrespondercenter.org/cancer/toolsresources/presumptive-legislation-firefighter-cancer-state/>
- <sup>46</sup> Presumptive Legislation for Firefighter Cancer by State. (n.d.). Retrieved from <https://www.firstrespondercenter.org/cancer/toolsresources/presumptive-legislation-firefighter-cancer-state/>
- <sup>47</sup> Presumptive Legislation for Firefighter Cancer by State. (n.d.). Retrieved from <https://www.firstrespondercenter.org/cancer/toolsresources/presumptive-legislation-firefighter-cancer-state/>
- <sup>48</sup> CDC - Monitoring selected national HIV prevention and care objectives by using HIV surveillance data — United States and 6 dependent areas, 2016. *HIV Surveillance Supplemental Report 2018*; 23(4).
- <sup>49</sup> CDC - Estimated HIV incidence and prevalence in the United States, 2010–2016. *HIV Surveillance Supplemental Report 2019*;24 (No. 1)
- <sup>50</sup> Aids.gov. (n.d.). Opportunistic infections. Retrieved from <http://aids.gov/hiv-aids-basics/50-staying-healthywith-hiv-aids/potential-related-health-problems/opportunistic-infections/>.
- <sup>51</sup> Center for Disease Control and Prevention. (n.d.). HIV cost-effectiveness. Retrieved from <http://www.cdc.gov/hivprevention/ongoing/costeffectiveness/>
- <sup>52</sup> Larrey D, Ripault MP, Pageaux GP. Patient adherence issues in the treatment of hepatitis C. *Patient Prefer Adherence*. 2014;8:763-773.
- <sup>53</sup> 2017 US Organ and tissue transplant cost estimates and discussion. Milliman Research Report. <http://www.milliman.com/uploadedFiles/insight/2017/2017-Transplant-Report.pdf>.
- <sup>54</sup> CDC - Health and Safety Practices Survey of Healthcare Workers - NIOSH Workplace Safety and Health Topic. Centers for Disease Control and Prevention. <https://www.cdc.gov/niosh/topics/healthcarehsp/antioadmin.html>. Accessed June 17, 2019.

