You Asked for It! CE


© Can Stock Photo/sCukrov

Special Considerations for Special Conditions: The Community Pharmacist's Guide to Specialty Medications

ABSTRACT: Specialty medications are used to treat complex, chronic, or rare conditions, such as Crohn's disease, cystic fibrosis, growth hormone disorders, hepatitis C, HIV/AIDS, multiple sclerosis, oncology, and rheumatoid arthritis. They often require special storage and administration, increasing the need for support programs and patient education services. Specialty-at-retail programs provide the option for patients to pick up their specialty drugs at a local retail pharmacy. This provides an additional opportunity for pharmacist counseling before the medication reaches the patient. Oncolytics, medications to treat neutropenia, and drugs to treat rheumatologic and dermatologic conditions are among the most common dispensed via specialty-at-retail programs. Pharmacy teams are positioned to recognize patients who would benefit from additional counseling and teaching. Many specialty medications require specific storage and handling, and may have complicated administration techniques. Damaged medication due to improper storage and improper administration can lead to treatment failure. Pharmacists and pharmacy technicians should be able to assist patients with specialty medications and be aware of reputable resources to consult when they are unfamiliar with a specialty medication or condition. With proper education and training, pharmacy teams will be prepared and comfortable with counseling for medications dispensed via specialty-at-retail programs.

FACULTY: Kelsey Giara, Pharm.D. is a community pharmacist and freelance medical writer based in New Hampshire.

FACULTY DISCLOSURE: The author has no actual or potential conflicts of interest associated with this article.

DISCLOSURE OF DISCUSSIONS of OFF-LABEL and INVESTIGATIONAL DRUG USE: This activity may contain discussion of off label/unapproved use of drugs. The content and views presented in this educational program are those of the faculty and do not necessarily represent those of the University of Connecticut School of Pharmacy. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications, and warnings.

INTRODUCTION

Specialty medications—given by injection or orally—are used to treat complex, chronic, or rare conditions. They often require special storage and administration, increasing the need for support programs and patient education services. Specialty drugs are loosely defined by two main factors: cost and complexity. The Centers for Medicare and Medicaid Services (CMS) categorizes a specialty drug as one with a minimum cost of $600 per month under the Part D drug benefit.[1,2] Other organizations may establish higher cost thresholds, often exceeding

UCONN

AN ONGOING CE PROGRAM
of the University of Connecticut
School of Pharmacy

EDUCATIONAL OBJECTIVES

After participating in this activity pharmacists will be able to:

- Discuss the rapid growth of specialty pharmacy and the products most likely to be included in this category and provided by specialty-at-retail
- Identify recent changes in oncology/neutropenia, rheumatologic conditions, and dermatology products provided in specialty-at-retail settings
- Distinguish each FDA-approved product by condition it addresses
- Maximize the community pharmacist's role in specialty-at-retail product provision and counseling patients

After participating in this activity pharmacy technicians will be able to:

- Discuss the basic facts about specialty pharmacy and specialty-at-retail
- Acquire reputable sources of information for patients who engage in specialty-at-retail programs
- Distinguish between specialty products for oncology/neutropenia, rheumatologic conditions, and dermatology
- Infer when to refer patients who use specialty-at-retail programs to the pharmacist for recommendations or referral

The University of Connecticut School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacists and pharmacy technicians are eligible to participate in this application-based activity and will receive up to 0.2 CEU (2 contact hours) for completing the activity, passing the quiz with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission

ACPE UAN: 0009-0000-19-046-H01-P
0009-0000-19-046-H01-T

Grant funding: Funded by an educational grant from Celgene
Cost: FREE

INITIAL RELEASE DATE: July 15, 2019
EXPIRATION DATE: July 15, 2021

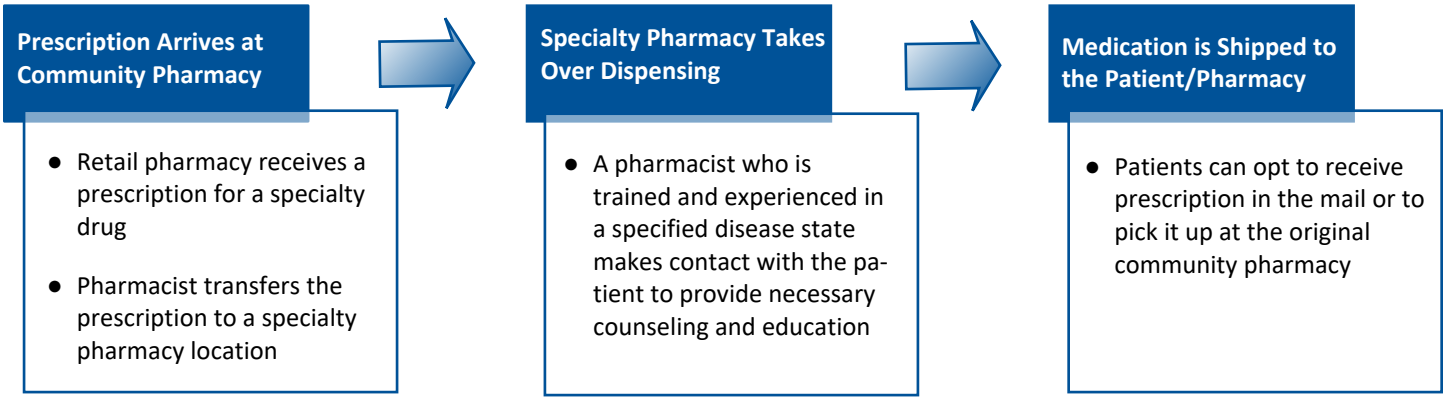
To obtain CPE credit, visit the UConn Online CE Center **https://pharmacyce.uconn.edu/login.php**.

Use your NABP E-profile ID and the **session code 19YC46-FXW93 for pharmacists or 19YC46-TKX48 for pharmacy technicians** to access the online quiz and evaluation. First-time users must pre-register in the Online CE Center. Test results will be displayed immediately and your participation will be recorded with CPE Monitor within 72 hours of completing the requirements.

For questions concerning the online CPE activities, email joanne.nault@uconn.edu.

TO RECEIVE CREDIT FOR THIS CE, go to: https://pharmacyce.uconn.edu/login.php

Figure 1 – Specialty-At-Retail: How Does It Work? [9,10]



$10,000 monthly or $100,000 annually. Specialty drugs encompass many factors, including[2,3]:

- Treatment of complex, chronic, and/or rare conditions
- Availability through restricted or limited distribution
- Special storage, administration, and/or handling requirements
- Risk Evaluation Mitigation Strategy (REMS) program necessity
- Ongoing need for safety and efficacy monitoring

Due to specialty drugs' sensitive nature and price points that are higher than traditional medications', self-identified "specialty pharmacies" are becoming increasingly more common entities. Specialty pharmacies' standard care surpasses the services offered at a typical retail pharmacy. These additional services may include[2]:

- 24-hour access to a pharmacist
- Adherence management
- Dispensing of specialty medications and shipping coordination
- Financial assistance and enrollment in patient assistance programs
- Patient education and adverse effect counseling
- Monitoring for safety and efficacy
- Prior authorization assistance
- Proactive patient outreach for timely refill and renewal

Specialty Pharmacy's Explosive Growth

Specialty pharmacy business is clearly on the rise; retail, mail, specialty, and long-term-care pharmacies dispensed approximately $115 billion in specialty pharmaceuticals in 2016 compared to $98 billion in 2015.[4,5] The number of specialty pharmacies in existence is hard to enumerate given that no universal definition exists and although accreditation is possible, it is not mandatory. A pharmacy can identify as a specialty pharmacy if its business focus is self-administered specialty pharmaceuticals covered under a patient's pharmacy insurance benefit. By one metric, as of April 2017, a market analysis identified more than 2,500 pharmacies in existence with specialty accreditation.[4]

Though the field is difficult to define, pharmacists, regardless of their practice area, should understand specialty pharmacies' role within the industry. Over the past decade, specialty medications have emerged as the fastest growing segment of the pharmaceutical industry and have dominated new drug development. In 2017, of the 46 drugs that the U.S. Food and Drug Administration (FDA) approved, more than 70% were classified as specialty drugs.[6] It is anticipated that by 2020, specialty medications will represent 50% of all U.S. drug spending, while only being used in 4% of the population.[7] Expenditures on specialty drugs are expected to rise to $400 billion in 2020.[8]

Increasing Access and Reducing Waste

A few large entities with central-fill mail pharmacies dominate specialty pharmacy dispensing activities. Many of these entities also offer "specialty-at-retail" programs, outlined in **Figure 1**. Specialty-at-retail programs provide the option for patients to pick up their specialty drug at a local retail pharmacy, reducing the number of specialty medications arriving by mail directly to the patient's residence. This also eliminates the need for patients to remain at home waiting to sign for packages and avoids leaving thousands of dollars of prescription medication sitting on a doorstep unattended.[9,10]

Specialty-at-retail also provides another pharmacy team point of contact before the medication reaches the patient, offering opportunity for counseling and patient follow-up. Pharmacists in the general community setting, however, do not have the same level of training and experience in specialty pharmacy disease states as specialty pharmacists do. Community pharmacists should be prepared to field questions about specialty medications at retail pharmacies as specialty drug utilization increases.[4,11]

PAUSE AND PONDER:

What is your typical process when patients have prescriptions for or pick up specialty drugs at your pharmacy?

SPECIALTY CONDITIONS AND TREATMENT

Common disease states managed by specialty pharmacies include Crohn's disease, cystic fibrosis, growth hormone disorders, hepatitis C, HIV/AIDS, multiple sclerosis, oncology, and rheumatoid arthritis.[2] Among the drugs most commonly dispensed via specialty-at-retail programs are oncolytics and medications to treat the resulting neutropenia, and drugs to treat rheumatologic and dermatologic conditions.[9,10]

Oncology and Neutropenia/Anemia

One in every four deaths in the U.S. is caused by cancer, and in 2015, the Centers for Disease Control and Prevention reported more than 1.6 million new cases of cancer.[12] Specialty pharmacy drugs used for cancer treatment are the largest selling class of therapeutic agents within specialty pharmacy.[13] A study found that patients receiving oral oncolytics from a specialty pharmacy are 50% more likely to be adherent than those receiving them through other channels. Pharmacists in this study who were trained to provide disease-specific counseling were shown to lower overall treatment costs by more than $17,000 per patient per year due to increased adherence efforts.[14]

Oncology medications dispensed from specialty pharmacies include injectable drugs, oral formulations, parenteral chemotherapy, and biologic agents. Serious adverse effects—e.g., bone marrow suppression, gastrointestinal (GI) distress—are associated with drugs used to treat cancer, and pharmacists should be prepared to field questions and educate patients. Self-administered therapies increase the importance of counseling patients on how to administer their medication safely and properly in the absence of a healthcare provider.[14] Pharmacists remain the most accessible healthcare provider, and should therefore be familiar with important counseling points.

Oral Chemotherapy

Treatments for non-small cell lung cancer (NSCLC) and blood cancers – leukemia, lymphoma, and myeloma – account for the majority of oral antineoplastic drugs. Lung cancer is the second most common cancer in both men and women. About 13% of all new cancers are lung cancers, and it is the leading cause of cancer death. NSCLC is the most common type of lung cancer, diagnosed in 80% to 85% of all cases. Adenocarcinoma, squamous cell carcinoma, and large cell carcinoma are subtypes of NSCLC.

The most common causes of NSCLC are smoking and environmental toxins (e.g. radon, asbestos).[15] Blood cancers affect blood cell production and function. Most of these cancers originate in the bone marrow where blood is produced; they interrupt blood cell development and cause an uncontrolled growth of abnormal or cancerous cells. The cancerous cells prevent blood from carrying out its normal functions, like clotting or preventing infections. There are three main types of blood cancers[16]:

- **Leukemia:** rapid production of abnormal white blood cells that are unable to fight infection and impair red blood cell and platelet production
- **Lymphoma:** abnormal lymphocytes form into lymphoma cells which multiple and collect in the lymph nodes and other tissues, impairing the immune system
- **Myeloma:** prevents plasma cells from producing antibodies, leaving the immune system weakened and susceptible to infection

The majority of oral drugs to treat NSCLC and blood cancers are tyrosine kinase inhibitors (TKIs), summarized in **Table 1**. Kinases are enzymes that mediate phosphate transfer from adenosine triphosphate (ATP) onto certain amino acid residues to cause cell signal transduction. Kinases are overexpressed in various cancers, especially the receptor tyrosine kinase subtype.[17] For this reason, researchers developed TKIs to inhibit these pathways and stop cell proliferation signaling in cancer. Pharmacists in the community can easily identify TKIs by the "-tinib" suffix of their generic names. TKIs' most common adverse effects are GI distress (nausea, vomiting, diarrhea, constipation), skin rash, and fatigue.[18] Neratinib has a high incidence of diarrhea, and antidiarrheal prophylaxis is recommended upon initiation. Loperamide should be given based on the week of therapy as follows[19]:

- **Weeks 1-2:** 4 mg three times daily
- **Weeks 3-8:** 4 mg twice daily
- **Weeks ≥9:** 4 mg as needed (max of 16 mg daily)

Table 1. Indications and Targets of Oral Tyrosine Kinase Inhibitors[18-38]			
Generic (Brand) names	**Indication**	**Metabolism**	**Initial Dosing and Administration**
Alectinib (Alecensa)	NSCLC	CYP3A4	600 mg BID with food
Axitinib (Inlyta)	Kidney cancer	CYP3A4, 1A2, 2C19 *Inhibitor:* CYP1A2, 2C8	5 mg BID ~12 hours apart with whole glass of water, +/- food
Bosutinib (Bosulif)	Leukemia	CYP3A4	400 mg once daily with food
Brigatinib (Alunbrig)	NSCLC	CYP3A4, 2C8 *Inducer*: CYP3A, CYP2C	90 mg once daily for first 7 days, increase to 180mg if tolerated, +/- food
Cabozantinib (Cabometyx)	Liver, thyroid, renal cell carcinoma	CYP3A4	60 mg once daily on an empty stomach*
Ceritinib (Zykadia)	NSCLC	CYP3A4 *Inhibitor*: CYP3A4, 2C9	450mg once daily with food
Crizotinib (Xalkori)	NSCLC	CYP3A4 *Inhibitor*: CYP3A4	250 mg twice daily, +/- food
Dacomitinib (Vizimpro)	NSCLC	Oxidation & glutathione conjugation; minor CYP2D6, 3A4	45 mg once daily, +/- food
Dasatinib (Sprycel)	Leukemia	CYP3A4 *Inhibitor*: CYP3A4	100 mg once daily, +/- food
Erlotinib (Tarceva)	NSCLC, pancreatic cancer	CYP3A4, 1A2	*NSCLC*: 150 mg *Pancreatic*: 100 mg once daily on an empty stomach*
Gefitinib (Iressa)	NSCLC	CYP3A4, 2C19	250 mg once daily, +/- food
Imatinib (Gleevec)	Leukemia	CYP3A4, 2D6 *Inhibitor*: CYP3A4, 2D6	300-800 mg/day, once or twice daily with a meal and full glass of water
Lapatinib (Tykerb)	Breast cancer	CYP3A4, 2C8 *Inhibitor:* CYP3A4, 2C8	1,250-1,500 mg once daily in combination with capecitabine or letrozole; on an empty stomach*
Lorlatinib (Lorbrena)	NSCLC	CYP3A4 *Inducer*: CYP3A4	100 mg once daily, +/- food
Neratinib (Nerlynx)	Breast cancer	CYP3A4	240 mg once daily with food
Nilotinib (Tasigna)	Leukemia	CYP3A4 *Inhibitor:* CYP3A4, 2C8, 2C9, 2D6 *Inducer*: CYP2B6, 2C8, 2C9	300-400 mg twice daily with water ~12 hours apart on an empty stomach*
Osimertinib (Tagrisso)	NSCLC	CYP3A4	80 mg once daily, +/- food
Ruxolitinib (Jakafi)	Polycythemia Vera, Myelofibrosis	CYP3A4, minor 2C9	5 mg-20 mg twice daily (based on indication & baseline platelet count), +/- food
Sunitinib (Sutent)	GI, neuroendocrine, renal cancer	CYP3A4	50 mg once daily, +/- food
Trametinib (Mekinist)	Thyroid cancer, malignant melanoma, NSCLC	Deacetylation, glucuronidation; no CYP activity	2 mg once daily on an empty stomach*
* Empty stomach is defined as: no food consumed for at least 2 hours before and at least 1 hour after the dose is taken.			

As TKIs are heavily metabolized by the CYP450 enzymes in the liver, drug interactions are common. Almost all TKIs are metabolized by CYP3A4, so pharmacy teams should be familiar with common CYP3A4 inhibitors and inducers[39]:

- **Inhibitors:** amiodarone, protease inhibitors for HIV, macrolide antibiotics, cyclosporine, diltiazem, fluconazole, fluoxetine, fluvoxamine, isoniazid, azole antifungals, miconazole, tamoxifen, verapamil, grapefruit juice
- **Inducers:** carbamazepine, dexamethasone, phenytoin, phenobarbital, oxcarbazepine, modafinil, primidone, rifampin, rifabutin, St. John's wort

Some TKIs – dacomitinib, dasatinib, erlotinib, gefitinib, and neratinib – also interact with drugs that increase gastric pH. Proton pump inhibitors (PPIs), H_2-receptor antagonists (H_2RAs), and antacids reduce the effectiveness of these selected TKIs and should be avoided or limited as follows[19,27-30]:

- **PPIs:** Avoid concomitant use
- **H_2RAs:** Take 10 hours before or six hours after TKI
- **Antacids:** Separate by at least three hours

Thalidomide (Thalomid) and its analogs are also common oral medications used to treat blood cancers. Thalidomide was originally developed as a treatment for respiratory infections and to treat morning sickness in pregnant women in the 1960s. Its manufacturer quickly withdrew thalidomide from the market due to teratogenic effects. Thalidomide binds to a protein called cereblon, which is found in embryonic and adult tissues. Humans need cereblon for normal cell growth and shape development; suppressing it leads to limb malformation. These effects, while detrimental to human development, led to a new therapeutic purpose to thalidomide as treatment for cancer and autoimmune conditions.[40]

Thalidomide analogues – lenalidomide (Revlimid) and pomalidomide (Pomalyst)– (hereafter referred to as "thalidomides") have been synthesized to further combat toxicity and to improve efficacy. Thalidomides have immunomodulatory, anti-inflammatory, anti-angiogenesis, and cell proliferation inhibitory properties. They are also immune system modulators, and they effectively suppress tumor development and prevent secondary spread. [40]

Thalidomides' most common adverse effects include[41-43]:

- Fever
- Fatigue/muscle weakness
- GI distress (nausea, diarrhea, constipation)
- Rash/desquamation

Additionally, thalidomide itself can cause[41]:

- Weight changes
- Mood changes (confusion, anxiety, agitation)
- Thrombosis/embolism
- Tremor/neuropathy
- Hypocalcemia

Of the three thalidomides, lenalidomide is the best tolerated; it does not cause the change in blood cell counts

© Can Stock Photo / AndreyPopov

(neutropenia/anemia) that thalidomide and pomalidomide do. Lenalidomide does, however, carry the risk of cough, whereas the other thalidomides do not.[41-43]

All three thalidomides also come with Boxed Warnings for embryo-fetal toxicity and for venous and arterial thromboembolism. Boxed Warnings are part of FDA labeling and can be found in the package insert.[41-43] Due to the serious teratogenic risk, patients are required to participate in a Risk Evaluation and Mitigation Strategies (REMS) program to ensure the patient or patient's sexual partner is not and does not become pregnant. Participation in this program requires females of reproductive potential to use two forms of contraception or continuously abstain from heterosexual sex during and for four weeks after stopping treatment with thalidomide or its analogues. Even a single dose taken by a pregnant woman can cause severe birth defects or embryo-fetal death.[41-43] Pharmacy teams should be conscious of birth control adherence in females taking thalidomides and follow up with these patients regarding available refills. Pharmacists should also counsel patients on thromboembolism's signs and symptoms, and urge them to seek medical care immediately if they develop shortness of breath, chest pain, or arm/leg swelling. Pharmacists should also encourage prescribers to consider thromboprophylaxis in patients with underlying risk factors.

Not all oral chemotherapy falls into these two classes, so recognizing where to find more information is important for pharmacy teams. Package inserts are the most reliable source for storage, administration, and dosing recommendations. Generally, oral chemotherapy should be stored in its original container whenever possible, away from light, heat, and moisture. Additionally, the patient should be the only one exposed to the drug, so caregivers should be cautious when handling or administering. Counsel caregivers to avoid handling with bare hands, empty pills into the cap lid or a small cup for dispensing, or wear gloves if contact is unavoidable.[44]

Sidebar: Recognizing Neutropenia[61]

Neutropenia itself may not cause any symptoms, but patients should always take signs of infection seriously. Pharmacy teams should instruct cancer patients with any of the following to contact their oncology team:

- Fever (≥100.5°F [38°C])
- Chills or sweating
- Sore throat, mouth sores, or toothache
- Abdominal pain
- Pain around or near the anus
- Diarrhea
- Frequent or painful urination
- Bloody or cloudy urine
- Cough or shortness of breath
- Unusual vaginal discharge or itching
- Any redness, swelling, or pain (especially near a wound)

Pharmacists should also make patients and caregivers aware that chemotherapy stays in the body for hours or even days, and it is excreted into vomit, urine, stool, and sweat. Caregivers should take extra care in cleaning surfaces or clothes that have been soiled, and wear gloves when doing so. Importantly, pregnant caregivers should never handle the patient's body waste. Last, unused oral chemotherapy should never be flushed down the toilet or thrown in the trash. Counsel patients to return unused antineoplastics to the pharmacy or discuss a safe disposal plan with their oncologist.[45]

Injectable Chemotherapy

Most injectable chemotherapy dispensed via specialty-at-retail is not self-administered. These medications should only be handled and administered by a trained professional with proper protective equipment. Most are intravenous (IV) formulations, while some are given subcutaneously or intramuscularly. Therefore, storage requirements are the most important counseling points for pharmacists. Patients should store injectable chemotherapy in the original container, protect from light, and refrain from shaking. Most should also be stored in the refrigerator (36°F-46°F or 2°C-8°C), but caution patients not to freeze the medication. [46-59]

There are exceptions to refrigeration requirements. Injectable chemotherapy that should be kept at controlled room temperature (59°F-86°F or 15°C-30°C) includes[46-59]:

- Belinostat
- Decitabine
- Melphalan
- Levoleucovorin
- Eribulin mesylate
- Romidepsin
- Cabazitaxel
- Leuprolide
- Peginterferon alfa-2b
- Bendamustine
- Triptorelin
- Bortezomib
- Azacitidine
- Goserelin

Improperly stored medication can lead to treatment failure or delays in treatment while waiting for a replacement. When in doubt, consult the drug packaging or package insert to determine proper storage requirements and always communicate this information to the patient.

Neutropenia & Neutropenic Fever

Each year in the U.S., approximately 60,000 cancer patients are hospitalized with neutropenia – a decrease in white blood cells – and infections linked to neutropenia, which are some of chemotherapy's most serious side effects. In 2012 alone, the total cost of treating cancer patients with neutropenia was more than $2 billion for adults and nearly $440 million for children.[60] Neutropenia is especially common in patients with leukemia and other blood cancers. It leaves patients without enough neutrophils to kill infectious organisms and therefore susceptible to serious infections. Additionally, patients aged 70 years or older and immunocompromised patients (e.g. HIV, organ transplant) are more likely to develop neutropenia.[61] Pharmacists can increase patients' knowledge of neutropenic fever and counsel on early detection to prevent subsequent infection. Pharmacy teams should also reinforce that while over-the counter (OTC) remedies – aspirin, acetaminophen, etc. – are effective at lowering fever, they can also mask or hide signs of a more serious problem.

© Can Stock Photo / urfingus

PAUSE AND PONDER: What questions can you ask to ensure that patients who pick up specialty medications don't need more help?

Medications available via specialty-at-retail for neutropenia include filgrastim, pegfilgrastim, and sargramostim, and their biosimilars. These medications are colony stimulating factors (CSFs), which bind to receptors on hematopoietic cells to stimulate proliferation, differentiation, and activation of neutrophils.[62-64] All CSFs should be stored in the refrigerator in the original carton to protect them from light. Patients should not leave them in direct sunlight, so pharmacy teams should recommend delivery to the pharmacy, rather than the patient's home so the delivery company doesn't leave them in a sunny location. Additionally, freezing CSFs should be avoided; if frozen, patients should thaw filgrastim or pegfilgrastim in the refrigerator before administration and discard the product if frozen more than once or left at room temperature for more than 48 hours. If sargramostim is frozen, it should be discarded. Also, counsel patients to avoid shaking CSFs.[62-64] Adherence to CSFs is especially important to avoid neutropenic fever, so pharmacists should be prepared to counsel on the drugs' storage and handling so improper handling doesn't disrupt therapy.

Rheumatologic Conditions

Rheumatoid arthritis (RA), a chronic, inflammatory, autoimmune disease, affects approximately 1% of the world population. Census data from 2005 showed 1.3 million adults in the U.S. suffered from this affliction.[65,66] While inflammation is normally a controlled and regulated process, this process breaks down in RA, causing the joints – mainly in hands, wrists, and knees – to become inflamed. This leads to eventual cartilage and bone destruction. Patients suffer from chronic pain, fatigue, unsteadiness, and loss of bodily function.[66,67] Patients with RA experience many physical and social consequences leading to lowered quality of life. They are more likely to develop premature heart disease and less likely to be able to hold a job.[67]

Pharmacy teams should be familiar with specialty-at-retail drugs for RA summarized in **Table 2.** The most common mechanism of action for RA treatment is tumor necrosis factor alpha (TNF-a) inhibition. TNF-a is a cytokine released in the body during inflammation, and therefore over-produced in RA patients whose inflammatory process is poorly regulated. TNF-a causes the release of other cytokines in the body as well, cascading the inflammatory effects. Blocking TNF-a can reduce inflammation and therefore joint damage.[68] TNF-a inhibitors' most common adverse effects are injection site reactions, rash, upper respiratory infection, sinusitis, and urinary tract infection. Pharmacists should refer patients on TNF-a inhibitors to their rheumatologist when they present with any signs of infection – fever, cough, flu-like symptoms, or open cuts/sores – as these drugs can make infections worse.[69-72] Infliximab also carries the risk of infusion reactions – fever, chills, hypertension, dyspnea, etc. – and should only be administered intravenously by a trained healthcare provider.[73]

Pharmacists should be prepared to counsel patients on proper storage and handling and adequate injection technique and adherence. Patients must store all TNF-a inhibitors in their original cartons in the refrigerator at 36°F to 46°F (2°C to 8°C) and never freeze them or expose them to extreme heat. Adalimumab and etanercept can be stored at room temperature for up to 14 days but should not be returned to the refrigerator once brought to room temperature.[69-87] As infection is especially risky in RA patients on TNF-a inhibitors, always counsel patients to wash their hands with soap and water and to clean the injection site with an alcohol swab prior to administration. Each TNF-a injector requires a different injection technique, so pharmacists should review the specifics with patients whenever possible, especially when a change in therapy occurs.

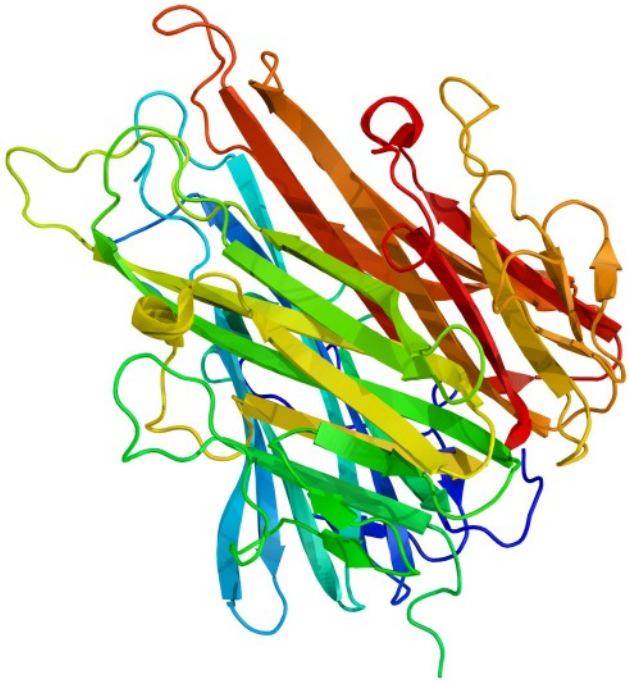
Use of the adalimumab auto-injector pen can be explained to patients by the "four P's" [88]:

- **PICK** *an injection site on your thigh or stomach that is free of bruising, soreness, scarring, or other abnormalities.* This spot should be at least one inch from your most recent injection site, and stomach sites should be at least two inches from the belly button.
- **PULL** *the caps off of the auto-injector.* Holding the middle of the pen with one hand with the gray cap facing up, use your other hand to pull the gray cap straight off the top and the plum-colored cap straight off the bottom, revealing a plum button. Flip the pen so the plum button is facing up.
- **PLACE** *the white end of the pen on the selected injection site.* With your free hand, gently pinch the area of skin you've cleaned and place the white needle sleeve of the pen straight at a 90° angle and flat against your skin.
- **PRESS** *the plum-colored button.* Hold this button down until ~10-15 seconds after the yellow indicator has stopped moving, indicating the dose has been completely delivered. Dispose of the pen in a Sharps container.

Certolizumab pegol's injection technique is similar to adalimumab, with a few key differences. Certolizumab pegol is supplied in a prefilled syringe, rather than a pen injector. Patients should remove the needle cap by gripping the plastic ring and pulling it straight off. Counsel patients that air bubbles in the syringe are normal and safe and not to attempt to expel them. Also, the needle should be inserted and removed at a 45° angle to the injection site, rather than 90°.[89]

A newer AutoTouch injector has been developed for etanercept administration. The device is reusable for up to two years or

© Can Stock Photo / ibreakstock



Tumor necrosis factor (TNF, cachexin, cachectin) protein, a cytokine that plays an important role in inflammation and immunity

130 injections, whichever comes first. Patients load a single dose prefilled cartridge into the device after bringing it to room temperature for about 30 minutes. The AutoTouch injector allows patients the ability to choose an injection speed, and the injector uses blinking lights and sounds to aid in administration technique.[90] Pharmacists who are unsure how to use a device should always consult the package insert or the manufacturer's web site for accurate and concise instructions.

Counsel patients injecting TNF-a inhibitors **not** to do any of the following[88,89]:

- Rub the injection site
- Try to recap needles
- Reuse any injection supplies
- Dispose of loose syringes and needles in household trash

Pharmacy teams should know where patients can access safe needle disposal. Most pharmaceutical manufacturers will aid their patients in accessing a sharps container, so instruct patients to call the customer service number on their medication packaging. (This is also a great project for technicians; assembling a list of disposal sites and keeping it up-to-date is helpful to all customers.) In the meantime, patients can use household containers, like an empty laundry detergent bottle, for safe needle disposal. Direct patients who need more information to www.fda.gov/safesharpsdisposal.

Two oral medications for RA are also available through specialty-at-retail pharmacy programs. Baricitinib and tofacitinib are

PAUSE AND PONDER: Look at the tables of drugs and biologics and take a few minutes to look up the brand names associated with each. How often do you see these medications?

both Janus kinase (JAK) inhibitors – also known as "jakinibs" –indicated for RA treatment. JAK is a tyrosine kinase that activates cytokine receptors involved in inflammation. JAK inhibitors, therefore, halt the inflammatory process's cascade. Tofacitinib is the first jakinib developed to treat autoimmune diseases like RA.[91] It can be administered without regard to food and dosed twice daily with the original formulation or once daily with the extended-release formulation. Tofacitinib's most common adverse reactions are headache, diarrhea, upper respiratory infection, and nasopharyngitis.[86]

Baricitinib is dosed once daily without regards to food. Its most common adverse reactions are nausea, upper respiratory tract infection, and infections with herpes simplex and zoster viruses.[76] Tofacitinib is metabolized primarily by CYP3A4 with minor contribution from CYP2C19, so pharmacists should be vigilant in monitoring for drug interactions. Baricitinib, however, is metabolized mainly by the kidneys with very little contribution from CYP3A4; it is unaffected by inducers or inhibitors of the CYP enzymes.[76,86,91] Pharmacists should counsel patients to store oral JAK inhibitors at controlled room temperature in the original container only. Patients should also alert their rheumatologist if they have any signs of infection, discussed above, as JAK inhibitors can weaken the immune system's ability to fight infection.[76,86]

Dermatologic Conditions

Psoriasis, the most common autoimmune disease in the U.S., affects as many as 7.5 million Americans, approximately 2.2% of the U.S. population.[92] Like rheumatoid arthritis, psoriasis is an overactivation of the inflammatory system. In psoriasis patients, T-cells are activated by surface cell proteins, migrate from lymph nodes and the blood stream into the skin, and secrete various cytokines. These cytokines cause skin cells to over-proliferate and rapidly replicate, leading to red, scaly, raised patches on the skin. These patches can occur anywhere, but most commonly affect the outside of the elbows, knees, or scalp. These is a significant genetic link to psoriasis, but symptoms can be aggravated by stress, alcohol, smoking, infection, and trauma. Climate is important too; warm seasons and sunlight can improve symptoms in 80% of patients, while cold weather can worsen them in 90% of patients. Lithium carbonate, beta blockers, some antimalarials, nonsteroidal anti-inflammatory drugs (NSAIDs), and tetracyclines have been reported to exacerbate psoriasis.[93]

Between 10% and 30% of people with psoriasis also develop psoriatic arthritis, chronic inflammation in the joints and the places where tendons and ligaments connect to bone. This leads to

Table 2. Drugs and Biologics Dispensed via Specialty-At-Retail for Psoriasis, Psoriatic Arthritis, and Rheumatoid Arthritis[9,10,69-87]

Drug	Description
Abatacept (Orencia)	Subcutaneous selective costimulation modulator injected once a week for the treatment of moderate to severe rheumatoid arthritis
Adalimumab (Humira)	Subcutaneous TNF-a inhibitor injected every 2 weeks for the treatment of moderate to severe rheumatoid arthritis, psoriasis, or psoriatic arthritis
Apremilast (Otezla)	Twice-daily oral PDE-4 inhibitor for the treatment of moderate to severe plaque psoriasis or psoriatic arthritis
Baricitinib (Olumiant)	Once-daily oral JAK inhibitor for the treatment of moderate to severe rheumatoid arthritis
Brodalumab (Siliq)	Subcutaneous IL-17RA antagonist injected every 2 weeks for the treatment of moderate to severe plaque psoriasis
certolizumab pegol (Cimzia)	Subcutaneous TNF-a inhibitor injected every 2-4 weeks for the treatment of moderate to severe rheumatoid arthritis, psoriasis, or psoriatic arthritis
Etanercept (Enbrel)	Subcutaneous TNF-a inhibitor injected once or twice weekly for the treatment of moderate to severe rheumatoid arthritis, psoriasis, or psoriatic arthritis
Golimumab (Simponi)	Subcutaneous TNF-a inhibitor injected once monthly for the treatment of moderate to severe rheumatoid arthritis or psoriatic arthritis
Guselkumab (Tremfya)	Subcutaneous IL-23 blocker injected every 8 weeks for the treatment of moderate to severe plaque psoriasis
Infliximab (Remicade)	Intravenous infusion of TNF-a inhibitor injected every 8 weeks for the treatment of moderate to severe rheumatoid arthritis, psoriasis, or psoriatic arthritis
Ixekizumab (Taltz)	Subcutaneous IL-17RA antagonist injected every 4 weeks for the treatment of moderate to severe plaque psoriasis or psoriatic arthritis
methotrexate (Subcutaneous) (Otrexup OR Rasuvo)	Subcutaneous folate analog metabolic inhibitor injected once weekly for the treatment of psoriasis and rheumatoid arthritis
Rituximab (Rituxan)	Intravenous infusion of CD20-directed cytolytic antibody for the treatment of moderate to severe rheumatoid arthritis
Sarilumab (Kevzara)	Subcutaneous IL-6 antagonist injected every 2 weeks for the treatment of moderate to severe rheumatoid arthritis
Secukinumab (Cosentyx)	Subcutaneous IL-17RA antagonist injected every 4 weeks for the treatment of moderate to severe plaque psoriasis
tildrakizumab-asmn (Ilumya)	Subcutaneous IL-23 antagonist injected every 12 weeks for the treatment of moderate to severe plaque psoriasis
Tocilizumab (Actemra)	Intravenous infusion of IL-6 antagonist administered every 4 weeks for the treatment of moderate to severe rheumatoid arthritis
Tofacitinib (Xeljanz)	Twice-daily oral JAK inhibitor for the treatment of moderate to severe rheumatoid arthritis
Ustekinumab (Stelara)	Subcutaneous IL-12 and IL-23 blocker injected every 12 weeks for the treatment of moderate to severe plaque psoriasis or psoriatic arthritis

PDE-4 = phosphodiesterase 4. JAK = Janus kinase. TNF-a = tumor necrosis factor alpha. IL-17RA = interleukin-17 receptor A. IL = interleukin.

swelling, pain, fatigue, and joint stiffness. People can develop psoriatic arthritis without first having psoriasis, but most commonly it starts about 10 years after psoriasis begins.[92]

TNF-a inhibitors used for rheumatoid arthritis are also indicated for psoriasis and psoriatic arthritis treatment, so the same adverse effects, storage requirements, and administration techniques should be communicated to psoriasis patients.

Another drug indicated for both conditions is subcutaneous methotrexate. Methotrexate is indicated for RA and for treatment-resistant psoriasis; it is also commonly used off-label for psoriatic arthritis. It acts as a folate analog metabolic inhibitor, which inhibits cytokine production and purine biosynthesis, leading to anti-inflammatory properties.[93] Subcutaneous methotrexate is dosed once weekly and injected into the abdomen or thigh. Using methotrexate subcutaneously bypasses the GI tract, leading to fewer GI side effects. While classic vial-and-syringe dosage is available in most pharmacies, single-dose auto-injectors are available via specialty-at-retail. The auto-injector formulation may be better suited for patients who have difficulty drawing up medication into a syringe, as it comes pre-filled and ready to use. Consult the package insert or manufacturer's web site for accurate administration information when patients require counseling.[80,94]

Pharmacists should also remind patients that subcutaneous methotrexate does **not** need to be refrigerated and should be kept at controlled room temperature. Common adverse effects of subcutaneous methotrexate are[80,94]:

- Nausea/vomiting/diarrhea
- Abdominal pain
- Stomatitis/mouth sores
- Rash
- Headache
- Bronchitis/nasopharyngitis
- Thrombocytopenia/leukopenia
- Alopecia (hair loss)
- Photosensitivity
- "Burning of skin lesions"
- Abnormal liver function tests

Although methotrexate is not metabolized by the CYP450 enzymes, it does interact with other medications. NSAIDs and PPIs should be used with caution in patients on high doses of methotrexate. These drug classes inhibit methotrexate's elimination, which can lead to elevated serum methotrexate levels and cause increased toxicity.[80,94] Pharmacy teams should encourage patients to avoid over-the-counter NSAIDs and PPIs and suggest suitable alternatives. Pharmacists should also be aware of the signs of methotrexate toxicity, and refer patients to seek medical attention if they experience nausea, vomiting, diarrhea, mucositis (inflammation and ulcers in the GI tract), tachycardia, hypotension, or neurologic dysfunction (seizures, motor dysfunction, stroke-like symptoms).[95]

Interleukin inhibitors are another common drug class used in psoriasis and psoriatic arthritis treatment. Interleukins (ILs) are cytokines involved in inflammatory and immune responses.[92]

Interleukin 17 is a pro-inflammatory which has been demonstrated to act synergistically with tumor necrosis factor and interleukin-1.

Specifically, IL-12, IL-17, and IL-23 are associated with psoriatic inflammation, and **Table 2** lists drugs that target these ILs and block them. All interleukin inhibitors used for psoriatic conditions are administered subcutaneously. Possible adverse reactions to interleukin inhibitors include[77-79,83,84,87]:

- Injection site reactions
- Arthralgia (joint pain), myalgia (muscle pain)
- Headache
- Fatigue
- Nausea, diarrhea
- Infections (herpes simplex, tinea, influenza, upper respiratory)
- Neutropenia

Brodalumab, an IL-17 receptor antagonist, also has a Boxed Warning for suicidal ideation and behavior. Pharmacists should encourage patients experiencing mood changes after starting brodalumab to seek medical attention promptly.[77]

All interleukin inhibitors should be kept refrigerated at 36°F to 46°F (2°C to 8°C) in the original carton to protect from light and physical damage. They should never be frozen or shaken.[77,79,83,84,87] When necessary, brodalumab can be stored at a maximum temperature of 77°F/25°C for up to 14 days, but should not be returned to the refrigerator (patients should discard unused brodalumab).[77] Tildrakizumab-asmn can be stored at room temperature (maximum 77°F/25°C) for up to 30 days. Once brought to room temperature, it should not be returned to the refrigerator and any unused portion should be discarded after 30 days.[84]

Table 3. Treatment Guidelines and Patient Information for Selected Specialty Conditions		
Condition	**Organization**	**Where to Find?**
Acute Myeloid Leukemia	*National Comprehensive Cancer Network*	https://jnccn.org/view/journals/jnccn/15/7/article-p926.xml
NSCLC	*National Comprehensive Cancer Network*	https://jnccn.org/view/journals/jnccn/15/4/article-p504.xml
Psoriasis	*American Academy of Dermatology*	https://www.aad.org/practicecenter/quality/clinical-guidelines/psoriasis
Psoriatic Arthritis	*American College of Rheumatology*	https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Psoriatic-Arthritis
Rheumatoid Arthritis	*American College of Rheumatology*	https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Rheumatoid-Arthritis
Oral Chemotherapy (Patient Information)	*Dana Farber Cancer Institute*	https://www.dana-farber.org/chemotherapy/oral-chemotherapy/ https://www.dana-farber.org/health-library/articles/oral-chemotherapy-fact-sheet/
Psoriasis (Patient Information)	*National Psoriasis Foundation*	https://www.psoriasis.org/
Rheumatoid Arthritis (Patient Information)	*Arthritis Foundation*	https://www.arthritis.org/about-arthritis/types/rheumatoid-arthritis/
Cancer (Patient Information)	*NCCN Patient and Caregiver Resources*	https://www.nccn.org/patients/

TREATMENT APPROACHES

Specialty pharmacy providers, oncologists, rheumatologists, and dermatologists have specialized training in the aforementioned conditions and their respective fields. However, it is still important for community pharmacy teams to stay up-to-date on guidelines and treatments for these conditions. Specialty-at-retail programs provide an additional opportunity for coordinated patient care, and pharmacists should be well-versed in all drugs passing through their pharmacy, however briefly. **Table 3** summarizes guidelines for treatment of NSCLC, leukemia, RA, psoriasis, and psoriatic arthritis**.** Pharmacists who have questions about medication dosing and treatment escalation for these conditions should consult these guidelines and consult with a patient's healthcare providers as necessary.

Pharmacists should consult with specialty providers when patients are intolerant of their current treatment or when treatment escalation appears necessary. Pharmacy teams are also in a position to recognize challenges that other specialty providers may not, like OTC drug interactions, issues with storage requirements, or administration difficulties.

THE PHARMACY TEAM'S ROLE

Pharmacy teams participating in specialty-at-retail programs hold a unique role in the process. While it is easy for pharmacists to be complacent and passively hand-off specialty medications, patients engaging with specialty pharmacy services are some of the most vulnerable. Pharmacists can make a big difference. Pharmacy teams can help patients enrolled in specialty-at-retail in the pharmacy by:

1. Establishing a relationship: Know how to contact your specialty pharmacy counterparts and understand their workflow. Appreciating how the specialty pharmacy operates and the services they provide will help to coordinate care better and ensure therapy is not delayed or interrupted.

2. Inviting discussion: Make it a point to introduce yourself to specialty-at-retail patients the first time they use your pharmacy, and to follow-up with them upon refill trips. Actively opening the lines of communication will help patients to feel more comfortable reporting therapy changes or adverse effects, and let them ask questions they may not have addressed with the specialty pharmacy team.

3. Screening for drug interactions: Drug utilization review (DUR) is an important step in the pharmacy process that cannot be ignored. Rather than simply handing-off specialty medications, check patient profiles for possible interactions or contraindications when the medication arrives at the pharmacy. Additionally, pharmacists should ensure patients are aware of OTC interactions, and technicians at point-of-sale should refer patients picking up specialty medications and OTC items to the pharmacist for review. Pharmacists should also inquire about complementary and alternative medicines, as patients often don't consider them as risky as conventional medicine.

4. Helping patients to step-up care: Opening the lines of communication with specialty-at-retail patients will make them more likely to be comfortable coming to the community pharmacy team with questions. You are in a position to act as a patient advocate when treatment appears to be inadequate. Offer to contact a patient's provider for them when step-up appears necessary.

5. Reinforcing counseling: Specialty pharmacy providers are adequately trained to explain administration techniques for specialty medications. However, a patient may never actually see a device until picking it up at your pharmacy and important counseling points can be missed when delivering a large quantity of information at once. Offer additional counseling on correct use of specialty-at-pharmacy products and reinforce major counseling points using the teach-back method. Also, consider finding videos that show how to use specific devices; ensure that patients know how to access them. Manufacturer web sites are the best source for teaching aids and videos.

CONCLUSION

Specialty-at-retail programs provide a unique opportunity for pharmacy teams to impact patient care positively for vulnerable populations (see **Figure 2**). Rather than simply serving as a middle-man in the process, pharmacists should be actively involved in patient counseling for specialty conditions and prepared to answer questions or seek out accurate information for specialty patients.

Figure 2. Advancing Pharmacists and Pharmacy Technicians Role in Specialty-at-Pharmacy

Best

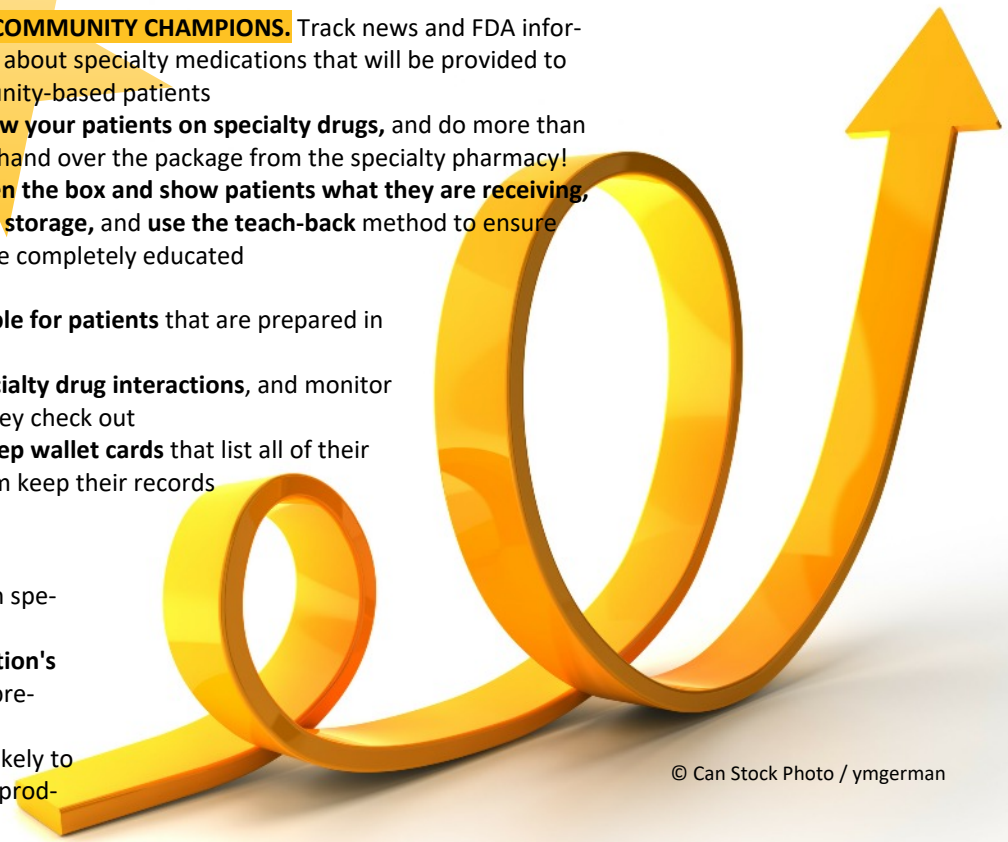
1. **Be COMMUNITY CHAMPIONS.** Track news and FDA information about specialty medications that will be provided to community-based patients
2. **Know your patients on specialty drugs,** and do more than simply hand over the package from the specialty pharmacy!
3. **Open the box and show patients what they are receiving, discuss storage,** and **use the teach-back** method to ensure they are completely educated

Better

1. **Have resources available for patients** that are prepared in patient-friendly language
2. **Make note of OTC-specialty drug interactions**, and monitor what patients buy when they check out
3. **Educate patients to keep wallet cards** that list all of their medications, and help them keep their records current

Good

1. **Know your colleagues** who work in specialty pharmacies
2. **Be familiar with your practice location's policies** and how to process specialty prescriptions
3. **Know which conditions** are most likely to require specialty drugs and why these products are considered unique



REFERENCES

1. Medicare Prescription Drug Benefit Manual: Chapter 6 – Part D Drugs and Formulary Requirements. Available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf. Accessed April 1, 2019.
2. Hagerman J, Freed S, Rice G. Specialty Pharmacy: A Unique and Growing Industry. American Pharmacists Association. Published July 2013. http://www.pharmacist.com/specialty-pharmacy-unique-and-growing-industry. Accessed January 14, 2019.
3. National Association of Specialty Pharmacy. NASP Definitions of Specialty Pharmacy and Specialty Medications. Published February 24, 2016. http://naspnet.org/wp-content/uploads/2017/02/NASP-Defintions-final-2.16.pdf. Accessed January 14, 2019.
4. Drug Channels: Expert Insights on Pharmaceutical Economic and the Drug Distribution System. Exclusive Update: The State of Specialty Pharmacy Accreditation in 2017. Published April 13, 2017. https://www.drugchannels.net/2017/04/exclusive-update-state-of-specialty.html. Accessed January 14, 2019.
5. Drug Channels: Expert Insights on Pharmaceutical Economic and the Drug Distribution System. The Specialty Pharmacy Accreditation Boom Continues. Published March 10, 2016. https://www.drugchannels.net/2016/03/the-specialty-pharmacy-accreditation.html. Accessed January 14, 2019.
6. U.S. Food & Drug Administration. Novel Drug Approvals for 2017. Updated February 2018. https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm537040.htm. Accessed January 14, 2019.
7. Pharmaceutical Executive. 2016 Pharm Science Strategic Outlook – – An Industry in Flux: 2015-–2016 Market Trends. Published February 2016. http://files.pharmtech.com/alfresco_images/pharma/2016/02/25/3d9096e7-6975-457b-be99-2867668f3844/PharmaScienceStrategicOutlook2016.pdf. Accessed January 14, 2019.
8. United Health Center for Health Reform & Modernization. The Growth of Specialty Pharmacy: Current Trends and Future Opportunities. Published April 2014. http://www.unitedhealthgroup.com/~/media/UHG/PDF/2014/UNH-The-Growth-Of-Specialty-Pharmacy.ashx. Accessed January 14, 2019.
9. CVS Specialty Pharmacy Distribution Drug List: Effective April 2019. Available at: https://www.cvsspecialty.com/education-center/downloads/SpecialtyDrugs.pdf. Accessed May 1, 2019.
10. AllianceRx (Walgreens specialty) pharmacy list of specialty medications: Effective March 2019. Available at: https://www.messa.org/pdf/walgreens_specialty_meds.pdf. Accessed May 1, 2019.
11. Advisory Board. Specialty pharmacy, explained. Published February 22, 2018. https://www.advisory.com/research/care-transformation-center/care-transformation-center-blog/2018/03/specialty-pharmacy. Accessed May 1, 2019.
12. U.S. Cancer Statistics Working Group. U.S. Cancer Statistics Data Visualizations Tool, based on November 2017 submission data (1999 2015): U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; www.cdc.gov/cancer/dataviz, June 2018.
13. Lash S. Learning to love your specialty pharmacy: perspective on a new business relationship. Biotechnol Healthc. 2007;4(5):45-48.
14. Specialty pharmacy improves cancer outcomes. Express Scripts web site. http://lab.express-scripts.com/insights/specialty-medications/specialty-pharmacy-improves-cancer-outcomes. Published December 19, 2013. Accessed January 16, 2019.
15. "What is Non-Small Cell Lung Cancer?" American Cancer Society. Revised May 16, 2016. https://www.cancer.org/cancer/non-small-cell-lung-cancer/about/what-is-non-small-cell-lung-cancer.html. Accessed April 1, 2019.
16. American Society of Hematology. Blood Cancers. https://www.hematology.org/Patients/Cancers/. Accessed May, 02, 2019.
17. Chaar M, Kamta J, Ait-Oudhia S. Mechanisms, monitoring, and management of tyrosine kinase inhibitors–associated cardiovascular toxicities. Onco Targets Ther. 2018 Sep 25;11:6227-6237
18. Hartmann JT, Haap M, Hopp H, Lipp H. Tyrosine Kinase Inhibitors – A Review on Pharmacology, Metabolism, and Side Effects. Curr Drug Metab. 2009 Jun;10(5):470-81.
19. Nerlynx (neratinib) package insert. Los Angeles, CA: Puma Biotechnology, Inc.; 2017.
20. Alecensa (alectinib) package insert. South San Francisco, CA: Genentech USA, Inc.; 2015.
21. Inlyta (axitinib) package insert. New York, NY: Pfizer Labs; 2012.
22. Bosulif (bosutinib) package insert. New York, NY: Pfizer Labs; 2012.
23. Alunbrig (brigatinib) package insert. Cambridge, MA: Ariad Pharmaceuticals, Inc.; 2017.
24. Cabometyx (cabozantinib) package insert. South San Francisco, CA: Exelixis, Inc.; 2012.
25. Zykadia (ceritinib) package insert. East Hanover, NJ: Novartis Pharmaceuticals Coroporation; 2014.
26. Xalkori (crizotinib) package insert. New York, NY: Pfizer Labs; 2011.
27. Vizimpro (dacomitinib) package insert. New York, NY: Pfizer Labs; 2018.
28. Sprycel (dasatinib) package insert. Princeton, NJ: Bristol-Myers Squibb Company; 2006.
29. Tarceva (erlotinib) package insert. Northbrook, IL: OSI Pharmaceuticals, LLC; 2016.
30. Iressa (gefitinib) package insert. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2018.
31. Gleevec (imatinib) package insert. East Hanover, NJ: Novartis Pharmaceuticals Coroporation; 2017.
32. Tykerb (lapatinib) package insert. East Hanover, NJ: Novartis Pharmaceuticals Coroporation; 2018.
33. Lorbrena (lorlatinib) package insert. New York, NY: Pfizer Labs; 2018.
34. Tasigna (nilotinib) package insert. East Hanover, NJ: Novartis Pharmaceuticals Coroporation; 2018.
35. Tagrisso (osimertinib) package insert. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2015.
36. Jakafi (ruxolitinib) package insert. Wilmington, DE: Incyte Corporation; 2016.
37. Sutent (sunitinib) package insert. New York, NY: Pfizer Labs; 2017.
38. Mekinist (trametinib) package insert. East Hanover, NJ: Novartis Pharmaceuticals Coroporation; 2018.
39. Pharmacy Times. Get to Know an Enzyme: CYP3A4. Published September 1, 2008. https://www.pharmacytimes.com/publications/issue/2008/2008-09/2008-09-8687. Accessed May, 1 2019.
40. Sherbet GV. Therapeutic Potential of Thalidomide and Its Analogues in the Treatment of Cancer. Anticancer Res. 2015 Nov;35(11):5767-72.
41. Thalomid (thalidomide) package insert. Summit, NJ: Celgene Corporation; 2017.
42. Revlimid (lenalidomide) package insert. Summit, NJ: Celgene Corporation; 2019.
43. Pomalyst (pomalidomide) package insert. Summit, NJ: Celgene Corporation; 2018.
44. Dana Farber Cancer Institute. Oral Chemotherapy. https://www.dana-farber.org/chemotherapy/oral-chemotherapy/. Accessed May 1, 2019.

45. Dana Farber Cancer Institute. Oral chemotherapy fact sheet. https://www.dana-farber.org/health-library/articles/oral-chemotherapy-fact-sheet/. Accessed May 1, 2019.
46. Beleodaq (belinostat) package insert. Irvine, CA: Spectrum Pharmaceuticals, Inc.; 2014.
47. Dacogen (decitabine) package insert. Dublin, CA: Astex Pharmaceuticals, Inc.; 2018.
48. Evomela (melphalan) package insert. Irvine, CA: Spectrum Pharmaceuticals, Inc.; 2016.
49. Fusilev (levoleucovorin) package insert. Irvine, CA: Spectrum Pharmaceuticals, Inc.; 2011.
50. Halaven (eribulin mesylate) package insert. Woodcliff Lake, NJ: Eisai, Inc.; 2016.
51. Istodax (romidepsin) package insert. Summit, NJ: Celgene Corporation; 2014.
52. Jevtana (cabazitaxel) package insert. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2010.
53. Lupron Depot (leuprolide acetate) package insert. North Chicago, IL: AbbVie Inc.; 2019.
54. Sylatron (peginterferon alfa-2b) package insert. Whitehouse Station, NJ: Merck & Co., Inc.; 2015.
55. Treanda (bendamustine) package insert. Frazer, PA: Cephalon, Inc.; 2008.
56. Trelstar (triptorelin) package insert. Parsippany, NJ: Actavis Pharma, Inc.; 2014.
57. Velcade (bortezomib) package insert. Cambridge, MA: Millennium Pharmaceuticals, Inc.; 2008.
58. Vidaza (azacitidine) package insert. Summit, NJ: Celgene Corporation; 2018.
59. Zoladex (goserelin) package insert. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2009.
60. Tai E, Guy GP, Dunbar A, Richardson LC. Cost of cancer-related neutropenia or fever hospitalizations, United States, 2012. Journal of Oncology Practice 2017;13(6):e552–e561.
61. Cancer.Net: Doctor-Approved Patient Information from ASCO (American Society of Clinical Oncology). Neutropenia. Published February 2018. https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/neutropenia. Accessed May 1, 2019.
62. Neopogen (filgrastim) package insert. Thousand Oaks, CA: Amgen Inc.; 2016.
63. Neulasta (pegfilgrastim) package insert. Thousand Oaks, CA: Amgen Inc.; 2016.
64. Leukine (sargramostim) package insert. Bridgewater, NJ: Sanofi Aventis U.S. LLC; 2018.
65. American College of Rheumatology. Prevalence Statistics. https://www.rheumatology.org/Learning-Center/Statistics/Prevalence-Statistics. Accessed May 1, 2019.
66. Gibofsky A. Overview of epidemiology, pathophysiology, and diagnosis of rheumatoid arthritis. Am J Manag Care. 2012 Dec;18(13 Suppl):S295-302.
67. Centers for Disease Control and Prevention. Rheumatoid Arthritis (RA). Reviewed March 5, 2019. https://www.cdc.gov/arthritis/basics/rheumatoid-arthritis.html. Accessed May 1, 2019.
68. National Rheumatoid Arthritis Society (UK). Anti-TNFa Treatment in Rheumatoid Arthritis. Reviewed January 14, 2019. https://www.nras.org.uk/anti-tnfa-treatment-in-rheumatoid-arthritis. Accessed May 1, 2019.
68. National Rheumatoid Arthritis Society (UK). Anti-TNFa Treatment in Rheumatoid Arthritis. Reviewed January 14, 2019. https://www.nras.org.uk/anti-tnfa-treatment-in-rheumatoid-arthritis. Accessed May 1, 2019.
69. Humira (adalimumab) package insert. North Chicago, IL: AbbVie Inc.; 2019.
70. Cimzia (certolizumab pegol) package insert. Smyrna, GA: UCB, Inc.; 2016.
71. Enbrel (etanercept) package insert. Thousand Oaks, CA: Amgen Inc.; 2017.
72. Simponi (golimumab) package insert. Horsham, PA: Janssen Biotech, Inc.; 2011.
73. Remicade (infliximab) package insert. Horsham, PA: Janssen Biotech, Inc.; 2013.
74. Orencia (abatacept) package insert. Princeton, NJ: Bristol-Myers Squibb Company; 2017.
75. Otezla (apremilast) package insert. Summit, NJ: Celgene Corporation; 2017.
76. Olumiant (baricitinib) package insert. Indianapolis, IN: Eli Lilly and Company; 2018.
77. Siliq (brodalumab) package insert. Bridgewater, NJ: Valeant Pharmaceuticals LLC; 2017.
78. Tremfya (guselkumab) package insert. Horsham, PA: Janssen Biotech, Inc.; 2017.
79. Taltz (ixekizumab) package insert. Indianapolis, IN: Eli Lilly and Company; 2016.
80. Otrexup (methotrexate) package insert. Ewing, NJ: Antares Pharma, Inc.; 2018.
81. Rituxan (rituximab) package insert. South San Francisco, CA: Genentech USA, Inc.; 2019.
82. Kevzara (sarilumab) package insert. Bridgewater, NJ: Sanofi-Aventis U.S. LLC; 2017.
83. Cosentyx (secukinumab) package insert. East Hanover, NJ: Novartis Pharmaceuticals Coroporation; 2016.
84. Ilumya (tildrakizumab-asmn) package insert. Whitehouse Station, NJ: Merck & Co., Inc.; 2018.
85. Actemra (tocilizumab) package insert. South San Francisco, CA: Genentech USA, Inc.; 2013.
86. Xeljanz (tofacitinib) package insert. New York, NY: Pfizer Labs; 2018.
87. Stelara (ustekinumab) package insert. Horsham, PA: Janssen Biotech, Inc.; 2012.
88. Abbvie, Inc. "HUMIRA CITRATE FREE ADULT SELF-INJECTION PEN" TRANSCRIPT. https://www.humira.com/humira complete/transcript_adultPen. Accessed May 15, 2019.
89. Cimzia prefilled syringe – step-by-step instructions for use. Available at: https://www.cimzia.com/sites/default/files/inline-files/IFU_Brochure.pdf
90. Enbrel dosing and administration. Available at: https://www.enbrel.com/hcp/dosing-and-administration
91. Schwartz DM, Kanno Y, Villarino A, et al. JAK inhibition as a therapeutic strategy for immune and inflammatory diseases. Nat Rev Drug Discov. 2017 Dec 28;17(1):78.
92. National Psoriasis Foundation. About Psoriasis/Statistics. Reviewed October 23, 2018. https://www.psoriasis.org/about-psoriasis. Accessed May 15, 2019.
93. DiPiro, Joseph T. Pharmacotherapy: A Pathophysiologic Approach. New York: McGraw-Hill Medical, 2008.
94. Rasuvo (methotrexate) package insert. Chicago, IL: Medac Pharma Inc.; 2018.
95. Maryland Poison Center: University of Maryland School of Pharmacy. Tox Tidbits: Methotrexate Toxicity. Published January 2009. https://mdpoison.com/media/SOP/mdpoisoncom/ToxTidbits/2009/January%202009%20toxtidbits.pdf. Accessed May 1, 2019.