Patient Safety
MEDICATION REFUSAL: UNDERSTANDING WHY “THEY JUST SAY NO”

ABSTRACT: Based on the principle of informed consent, competent patients always have the right to refuse medical treatment. Patients may refuse treatment for a variety of reasons, including dietary restrictions, religious reasons, medical misconceptions, a desire to avoid adverse effects, and mistrust of the medical team. Patient refusals can create serious dilemmas in the healthcare setting. On the one hand, clinicians have an ethical and legal obligation to honor patient autonomy. On the other hand, a patient’s refusal of treatment often leads to adverse medical outcomes, resulting in harm to the patient. Healthcare professionals should search for acceptable treatment alternatives that honor patients’ wishes while meeting their medical needs. Every institution—whether in the community, long-term care, or inpatient setting—should have a protocol to guide and standardize the approach to managing treatment refusals. In complex cases, it may be beneficial to use expert ethics consultations.

INTRODUCTION
“Drugs don’t work in patients who don’t take them,” remarked former U.S. Surgeon General C. Everett Koop. He spoke those words in 1985, but the problem persists 35 years later. Medication refusal and nonadherence remain prominent issues in many healthcare settings (see SIDEBAR, page 2). Patients fail to fill up to 30% of prescriptions, and simply don’t take 50% of chronic disease medications as prescribed. In addition to notably increasing morbidity and mortality rates, this nonadherence results in billions of dollars in U.S. healthcare costs.

To address this issue, it’s important for pharmacy staff to understand the reasons behind refusal. Many patients have misconceptions about their treatment, or fail to understand its importance. For example, patients taking preventive medications like statins may discontinue the medication since it does not provide externally evident benefits. Others may perceive prescription medications as unnatural, harmful chemicals and opt to self-treat with OTC products instead. Additional reasons for refusal include fear of adverse reactions, religious prohibition, dietary restrictions, desire for self-harm, or altered mental status.
Patients have the right to autonomy—that is, they have the final say as to whether they accept treatment. However, that doesn’t mean that a patient’s initial refusal closes the door to all subsequent treatment. Other patients may be open to alternatives—for example, a vegan may refuse a medication that contains animal products, but accept an animal-free option. It’s critical that pharmacists and technicians understand the reasons for refusal; only then can they identify alternative solutions that meet patients’ medical needs while staying true to their values.

**REASONS FOR REFUSAL**

**Dietary Restrictions**

Patients may refuse medications based on their personal beliefs, religions, or food sensitivities/allergies. Five percent of Americans consider themselves vegetarians, and 3% self-identify as vegans. Islam, Hinduism, and Sikhism—3 of the largest religions worldwide—do not approve of the use of certain animal-derived products. However, many widely-used medications contain ingredients that are sourced from animals, including gelatin (from pigs, cattle, or fish), lactose (from cattle), and magnesium stearate (from animal fat or vegetable matter). Additionally, the majority of drugs use animal testing in preclinical trials; the most commonly prescribed drugs were all tested on multiple animal models.

Patients with irritable bowel syndrome, lactose or gluten intolerance, or a peanut oil allergy—just to name a few—may need to avoid medications that contain even trace amounts of agitating ingredients. Unfortunately, 93% of oral medications contain at least one common potential allergen.

Pharmacists and pharmacy technicians should work with patients to identify medications compatible with dietary restrictions. It’s important to recognize that patients may wish to comply with their beliefs to the greatest extent possible, even if they can’t do so completely. For instance, it may be medically necessary for vegan patients to use animal-tested medications, but they still have the freedom of choosing between gelatin-containing vs. gelatin-free products, and should be informed accordingly. See Table 1 and the Tech Talk for common ingredients that prompt patients’ concerns.

**SIDEBAR: What’s in a Name? Non-Adherence vs. Refusal**

Medication adherence is the extent to which a patient follows treatment recommendations. Non-adherence occurs, for example, when patients forget to take their medications, take the wrong amount, take them at the wrong time, or discontinue medications. Other names for non-adherence include non-compliance, non-persistence, and non-concordance. Non-adherence may be intentional or unintentional:

- **Intentional non-adherence** is an active process in which the patient decides not to follow treatment recommendations. This may be caused by factors including skepticism about treatment efficacy, intolerable adverse effects, or medication-associated stigma.

- **Unintentional non-adherence** is a passive process—an unplanned behavior that results in deviation from the recommended treatment regimen. For example, patients may forget to take a dose, misunderstand the directions, or confuse their medications.

Medication refusal occurs when patients reject the treatment and do not give their consent to receiving it. Refusal may be active or passive:

- **Active refusal** occurs when a patient directly refuses to accept treatment. Such behavior is apparent and easy to observe.

- **Passive refusal** occurs when a patient appears to accept treatment, but secretly takes measures to refuse it. For example, a patient may take the medication when offered, then later spit or vomit it out.

| **Table 1. Common Ingredients to Watch in Patients with Dietary Restrictions** |
|---|---|---|---|
| **Ingredient** | **Potential concern/s** | **% Occurrence in Medications** | **Common medications containing ingredient** |
| Magnesium stearate | Animal-derived product | 72% | Lisinopril (Mylan), metoprolol tartrate (Mylan) gabapentin (AvKARE), aripiprazole (Otsuka) |
| Lactose | Allergen, animal-derived product, exacerbation of IBS symptoms, lactose intolerance | 45% | Prednisone (ActiVase), anastazole (Teva), benazepril (Teva), warfarin (Exalan), losartan (Sandoz) |
| Gelatin | Allergen, animal-derived product | 17% | Tamsulosi (Teva), celecoxib (Teva), benzonate (Major), omeprazole (Mylan) |
| Peanut oil | Allergen | 0.10% | Valproic acid (Mylan), progesterone (Teva) |
Tech Talk: Your Insider Guide to Spotting Hidden Ingredients

At first glance, it can be hard to tell which medications are safe to use in patients with dietary restrictions. Many healthcare professionals don’t check ingredient lists before prescribing or dispensing. Even if they do, they may not recognize animal products and allergens referred to by scientific or alternate names. Here are some tips to make it easier to spot hidden ingredients.

- **Decode the label**—and show the patient how, too. OTC products have FDA-mandated Drug Facts labels that list both active and inactive ingredients. Prescription drug labels aren’t FDA-regulated and vary between pharmacies, but FDA-approved information is available online through sources like [Dailymed](https://dailymed.nlm.nih.gov/dailymed/).11

- **It’s all about the excipients.** Although health records often document patient allergies to active ingredients—like penicillin, aspirin, or ibuprofen—it’s the actually the inactive ingredients, or excipients, that cause the most problems. Manufacturers add excipients to improve the drug’s absorption, stability, taste, appearance, or accessibility, and they make up over 75% of the drug’s mass.9 Read the drug label carefully to identify which excipients are in the product.

- **Allergens have aliases;** they can go by many alternate names. For example, *magnesium stearate* is a salt of *stearic acid*; it may be referred to as one or the other in an ingredients list. Additionally, for lactose- or gluten-intolerant patients, it’s not always clear what products to avoid (besides the obvious lactose and gluten). Depending on their level of sensitivity, lactose-intolerant patients may need to avoid casein, whey, and other milk proteins, too. And gluten may be present in other wheat-based products like mannitol, sorbitol, xylitol, and hydrogenated starch hydrolysates.12 Be aware of these alternate names when reading the drug label and don’t hesitate to research unfamiliar names.

- **Not all formulations are created equal.** Just because one particular product doesn’t work doesn’t mean that active ingredient isn’t an option. Different manufacturers and dosage forms use different excipients. For example, amoxicillin capsules contain gelatin, while amoxicillin tablets do not.10 And one manufacturer’s product may use ingredients that another’s doesn’t. Do your due diligence to find alternatives, using resources like [Pillbox](https://pillbox.nlm.nih.gov/).

- **Know your sources.** There are plenty of valid sources available for healthcare workers and patients alike to find the right product:
  - [Pillbox](https://pillbox.nlm.nih.gov/): This National Institute of Health’s (NIH)-run database allows searching by drug name, ingredient, and appearance and offers information about physical appearance, active and inactive ingredients, manufacturers, and more.
  - [Dailymed](https://dailymed.nlm.nih.gov/dailymed/): This NIH-run database allows searching by drug name, class, NDC code, or Set ID. It provides FDA-approved drug label information.
  - [The Green Book](https://animaldrugsatfda.fda.gov/adafda/views/#/search): This list of FDA-approved animal drug products is updated monthly. Users can search by drug name, active ingredient, or application number.
  - [PETA’s animal-derived ingredients list](https://www.peta.org/living/food/animal-ingredients-list/): This list contains common animal-sourced products used in medications, cosmetics, and other products. It may be helpful for vegan, vegetarian, Muslim, Hindu, and Sikh patients.
  - [Medication manufacturers](https://www.peta.org/living/food/animal-ingredients-list/): Look for information on manufacturer websites or call them.

Religious Refusal

Seventy-five percent of Americans consider religion very important or fairly important in their lives.13 Religious beliefs may influence what treatment options a patient chooses and adheres to. Sometimes, a patient’s beliefs conflict with medical advice, causing the patient to refuse treatment. For example, Jehovah’s Witnesses and Christian Scientists may choose prayer and faith healing over conventional treatment. Many Jehovah’s Witnesses also prohibit blood transfusions. Some religions view health issues as the outcome of immoral, sinful behavior.14 Or, as previously discussed, patients who practice religions such as Islam, Hinduism, and Sikhism may have dietary restrictions that would be violated by certain products.6

In emergency, life-threatening situations, some religions may allow a little leeway and permit otherwise unacceptable treatment options.6 However, depending on the patient and religion, this is not always the case. Things get especially complicated when it comes to the care of children, whose medical decisions are largely determined by their parents. In complicated situations, healthcare professionals can request ethics consultations, legal counsel, and religious advice, where appropriate.

Medical Misconceptions

Often, insufficient or inaccurate knowledge prevents a patient from accepting treatment. In the hectic healthcare setting, providers may not have time to explain treatments fully or correct patient misconceptions. Additionally, in today’s digital world, it’s easy for false information to propagate rapidly.

A prime example is the anti-vaccination movement. Vaccines are a critical part of preventive healthcare and have significantly decreased the rate of many deadly infectious diseases. Unfortunately, there has been a recent rise in anti-vaccination sentiment, which has spread into mainstream culture. Most opposition comes from the false belief that vaccines cause autism and other severe adverse effects. Correspondingly, immunization rates have dropped, and there have been outbreaks of previously eliminated diseases, such as measles.15
Patients may also refuse vaccinations due to misconceptions about who can and should be immunized. Society tends to place a higher emphasis on vaccinating children, so many patients may not realize that adults, too, need certain vaccines. For example, though an annual flu shot is recommended for everyone six months and older without contraindications, only 45% of adults are vaccinated, compared to 63% of children. Consequently, the prevalence of vaccine-preventable illnesses is higher among adults than children.

Some patients may reject medically recommended treatments in favor of self-treating with OTC products or using complementary/alternative approaches. While these treatment options are useful in certain situations, they lack a strong evidence base. Patients who rely solely on alternative approaches may have worsened health outcomes, especially for severe diseases that warrant immediate, heavy-hitting treatment. For instance, disease-modifying therapies (DMTs) delay the progression of multiple sclerosis (MS) and prevent relapses. However, up to 31% of MS patients refuse DMT recommendations; one of the most common causes for refusal is a preference for a complementary medicine approach.

Healthcare professionals should identify and address patient misconceptions regarding treatment and counsel patients accordingly. Even a few minutes of patient education may have a long-lasting positive impact. The case study (on the right) demonstrates this principle.

**PAUSE AND PONDER:** What medical misconceptions do your patients have? How can you address and resolve their misconceptions?

**Mental Status Refusals in Long-Term Care**

More than 8.3 million Americans use long-term care—supportive services for patients with a limited capacity for self-care due to elderly age, mental disability, chronic illnesses, or other health-related conditions. Due to their comorbidities, these patients often need to receive multiple medications, making treatment refusal and nonadherence an ongoing issue. Some residents refuse medications because they are difficult to swallow or unpleasant-tasting (see Table 2, next page). Others may reject medications due to schedule conflicts—administration times sometimes interfere with their planned activities or rest schedules.

Additionally, many long-term care patients suffer from altered mental status due to psychiatric illnesses or diseases that are more common with aging, such as dementia. In these situations, navigating medication refusal becomes a challenge. Like informed consent, informed refusal requires the patient to be competent, sufficiently informed, and acting voluntarily. It can be difficult, however, to determine whether long-term care patients are mentally competent enough to make their own healthcare decisions. And mental status isn’t static; a patient with dementia may become incompetent as the disease course progresses, or a patient with bipolar disorder may end a manic cycle and regain competency.

**Brain disorders**

There are multiple reasons why patients suffering from brain disorders may be unwilling to receive treatment. Illness-associated stigma is a major barrier to treatment, as it makes patients ashamed to seek out or accept care. Stigmatization has many sources, including patients themselves (self-stigma), healthcare
Dementia

Behavioral and psychological symptoms of dementia (BPSD) occur in 90% of dementia patients; resulting cognitive and functional impairments complicate treatment. Notable BPSD include agitation and irritability, which is compounded in patients who feel they have lost their independence. These patients may resent long-term care staff and therefore refuse treatment. Other symptoms (e.g., delusions, hallucinations, and anxiety) may make patients suspicious of and nonreceptive to treatment.

One particularly concerning BPSD is depression, which is exacerbated by the patient’s loss of health, self-esteem, and independence. Patients suffering from depression may refuse medication out of self-destructive intent, using medication refusal as a form of self-harm. Long-term care workers must be particularly vigilant for this behavior, especially since dementia patients may have an increased risk for suicidal behavior.

Regardless of its challenges, proper treatment is critical for long-term care patients. Medication refusal increases morbidity, mortality, and healthcare costs. Healthcare workers should strive to identify and address barriers to treatment for these vulnerable populations.

Refusal of Cancer Treatment

Up to 19% of cancer patients partially or completely refuse chemotherapy, and some patients refuse conventional treatment entirely. In these situations, it’s critical to understand and address the patient’s emotional and cognitive status. Often, refusal is a rational, carefully-considered decision. However, some patients may be cognitively compromised, pressured by external factors, or misinformed about the treatment. Each patient’s unique situation requires him or her to balance many factors.

Chemotherapy is notorious for its side effects, which include hair loss, nausea and vomiting, fatigue, mood changes, urinary and bladder changes, and neuromuscular problems. While it may somewhat extend a patient’s life span, it significantly decreases quality of life. It’s not so surprising, then, that many patients refuse treatment to avoid severe adverse effects, maintain their quality and control of life, and preserve their dignity. Interpersonal relationships also affect the choice to refuse. Family and friends have a major influence; they may pressure the patient into making certain decisions, or patients may refuse treatment to avoid burdening their loved ones. The treatment team’s relationship with the patient is also a major determinant of care. Patients who are misinformed or resentful from previous medical experiences may reject treatment out of distrust for the system.

Some patients may not be mentally competent, making treatment refusal complex. A quarter of cancer patients suffer from major depression, which can cause sporadic mood swings, feelings of worthlessness, and suicidal ideation or attempts. Most cancer patients also have multiple risk factors for delirium, which affects judgment and behavior. In situations like these, a
patient’s rational decision-making ability is compromised, and family members may need to make difficult treatment decisions. However, this is something that must be carefully assessed; clinicians should not automatically assume incompetence when a patient refuses treatment against medical advice.

Ultimately, healthcare professionals must respect and honor a competent patient’s decision, regardless of whether they personally agree. Many patients who refuse care feel that their providers do not respect their decision and consider it irrational, which discourages patients from communicating their values, emotions, and reasons for refusal.27,32 It’s especially important to maintain an open, respectful dialogue with cancer patients, who are looking for a trusted professional that will support them throughout their painful journey.27 Additionally, patients may be open to altering their management plan as the disease progresses, new treatment options emerge, or personal factors change.

DEALING WITH MEDICATION REFUSAL

Patient Autonomy and Informed Consent

Medication refusal is associated with many ethical and legal principles, the foremost of which is patient autonomy. Based on this ethical principle, patients have the right to their own thoughts, choices, and actions regarding their medical care.33 Therefore, competent patients always have the right to refuse treatment. Autonomy is preserved through informed consent—the process by which patients are educated about, and consent to, a treatment’s risks, benefits, and alternatives.

Providers are legally and ethically obligated to obtain informed consent,33 but a patient’s refusal to consent can create ethical dilemmas. Primum non nocere—that is, “first, do no harm”—is one of healthcare’s fundamental tenets. This is also known as the principle of non-maleficence. Another ethical principle, beneficence, describes the act of promoting good and ensuring that actions are beneficial to patients. Autonomy conflicts with beneficence and non-maleficence when a patient’s refusal causes harm to the patient.34

One exception to the requirement for informed consent occurs when a patient is incapacitated.35 Such patients are physically or mentally incapacitated of making fully informed decisions due to conditions such as unconsciousness, delirium, or brain disorders. Instead, a designated healthcare proxy, family members, or provider may make medical decisions. In situations of mental incapacitation, it can be challenging to determine whether a patient is competent. Since capacity can fluctuate, providers should assess mental status every time a healthcare decision must be made.34

Covert Medications, Surreptitious Prescribing

Repeated medication refusal and nonadherence are common in patients with brain disorders, which may cause frustrated healthcare staff and caregivers to employ questionable administration practices. Covert medication is the practice of concealing medications in the patient’s food or drink. Surreptitious prescribing occurs when clinicians supply medications to a patient’s caregiver, knowing that the patient will likely be medicated without his/her knowledge or consent.33

Are either of these practices ever warranted? Many healthcare workers think so. Up to 57% of long-term care nurses report practicing covert medication,36 and 96% of clinicians who work with vulnerable patients feel that it’s justified on some occasions.37 The general consensus is that this behavior is not ethically justifiable for mentally competent patients, but what about for patients who are incapacitated?

Serious risks and costs can occur when brain disorders go untreated, including increased morbidity, prolonged suffering, and self-destructive behavior. In cases where treatment is necessary, covert medication is a less disruptive and upsetting approach than aggressive methods like restraints and forced injections. Additionally, although covert medication may violate patient autonomy, some medications are actually intended to restore mental capacity, which has the ultimate result of restoring patient autonomy.33
On the other hand, covert medication may be perceived as an abuse of power and a breach of trust. Patients who discover the truth may feel angry, betrayed, and paranoid regarding future treatment. Patients who remain unaware may attribute medication-derived benefits to other factors, or use their improved condition as proof that they are not ill and do not require treatment. Covert medication also raises safety concerns, as patients may consume other products that interact dangerously with the medication.33

Ultimately, the decision to practice covert administration must be carefully balanced with other treatment factors. Clinicians should carefully consider a patient’s condition, history, and loved ones before making a choice. It’s also important to assess the patient’s mental status regularly for any changes in capacity.33

Establishing an Institutional Protocol

It can be difficult to make optimal treatment decisions in the chaotic, fast-moving healthcare environment. Things only get more complicated when ethical dilemmas come into play. Establishing an institution-specific protocol helps guide decision-making, resulting in more streamlined, fair, and consistent healthcare delivery. Adhering to standardized guidelines also makes it easier for multiple healthcare workers to coordinate their care for a patient.38

Ideally, a medication refusal protocol should integrate patient-clinician communication and allow for external consultants as necessary. An effective guideline would include the following steps4,12,39:

- **Verify that refusal or nonadherence is occurring.** In the long-term care setting, patients may practice passive refusal, which requires close observation to detect. In the outpatient and community settings, patients may be hesitant to admit nonadherence.
- **Identify the reason for refusal.**4,12,39
  - Assess your patients’ lifestyles and beliefs. Are they limited by any dietary or religious restrictions? Do they have medical misconceptions? Does the treatment administration interfere with their schedules?
  - Assess your patients’ perceptions of the treatment. Do they understand the purpose of the treatment, and the results of refusing it? Does the medication cause unpleasant side effects? Is it difficult to take the medication? Is the treatment too costly?
- **Consider an ethics consultation for complicated cases.**12
  - Many healthcare institutions employ ethics counselors, who help navigate and clarify complex situations without dictating a final decision.12,40
  - Most ethics counselors are trained by the American Society for Bioethics and Humanities in core competencies (situational assessment, moral reasoning, communication facilitation, legal and institutional policy, etc.)12,41
  - Exact protocols vary by institution, but in most cases, consultations are free, and anyone involved in the case (patients, families, legal representatives, doctors, nurses, social workers, etc.) can request help.40,42-44
- **Identify and implement solutions.**4,12,39
  - Consult the provider to discontinue unneeded medications, or change them from scheduled to as-needed administration.
  - Consider alternate dosage forms (smaller pills, chewable dosage forms, liquids) for patients who have difficulty swallowing.
  - Collaborate with the patient to identify alternative options, depending on the patient’s objections. For example, find products without gelatin for vegetarian patients.
  - Change the time of administration if it is inconvenient for the patient, interfering with planned activities or sleep. For example, if a patient skips breakfast, give a medication that must be taken with food at dinnertime instead.
  - Adapt to patients’ disease state behavior. Some dementia patients may respond favorably to repeated attempts—even after initially refusing, they may accept after a few more queries. Other patients may prefer certain staff members and only accept medications from these workers.

- **Document, document, document**4,12,39
  - Note incidences of refusal and nonadherence, what interventions and strategies were employed, how the patient responded, and what the current regimen is.
  - Documentation greatly facilitates shared patient care and transition of care.

All healthcare settings in which medication refusal or significant nonadherence are prominent should implement a protocol to address these incidents effectively.

**PAUSE AND PONDER:** Who is responsible for implementing a medication refusal protocol in your workplace? Where can you document the relevant information?
Implementing the Protocol, Maintaining Patient Trust

Even after establishing a set of guidelines, things might not be smooth sailing. Before implementing the protocol, healthcare workers need to build trust and cultivate a respectful relationship with patients. The patient-provider relationship strongly influences a patient’s acceptance of and adherence to treatment, especially in vulnerable populations.

 Patients who trust their physicians are more likely to believe that their medication is necessary, resulting in adherence rates that are up to three times higher. Additionally, an increased level of trust results in safer medication management. Conversely, when patients feel that a provider does not respect their decisions, they may stop communicating and terminate their relationship with that provider.

It may take some time and repeated interactions before patients trust the provider enough to divulge and explain their refusal or nonadherence. Clinicians need to be patient, nonjudgmental, and empathetic, as well as utilizing techniques such as motivational interviewing (see Table 3 for the interviewing RULEs of thumb). Once they understand the patient’s motivations, they can implement and tailor the protocol accordingly.

CONCLUSION

Medication refusal is an ongoing healthcare issue that continually frustrates clinicians and caregivers. Although it may be tempting to override a patient’s refusal, healthcare workers are obligated ethically and legally to honor patient autonomy. There are no easy solutions, but institutional protocols can help by streamlining and standardizing the healthcare response. Ideally, implementing a protocol will shed light on patient motivations for refusal, guiding the selection of acceptable alternatives.

Table 3. Interviewing RULEs

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<td>Resist the righting reflex</td>
<td>Avoid directly telling patients what to do, or where they’re wrong. Behavioral change is more effective when it’s self-articulated and self-motivated.</td>
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<tr>
<td>Understand the patient’s motivations</td>
<td>Don’t assume that you already know patients’ motivations. Allow patients to set the pace and divulge their reasoning, motivations, and barriers.</td>
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<tr>
<td>Listen with empathy</td>
<td>Try to understand the patient’s position and avoid judgment. Ask open-ended questions for clarification.</td>
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<tr>
<td>Empower the patient</td>
<td>Encourage the patient to set achievable goals. Collaborate with the patients’ healthcare provider to develop techniques to overcome barriers.</td>
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Figure 1. Helping Patients Understand the Need to Take Medication as Recommended

Best

1. **BE COMMUNITY CHAMPIONS.** Volunteer to work with or on a local ethics committee or find training so you are a subject matter expert!

2. **Pledge to empower patients** by helping them set realistic, achievable goals.

3. **Mind privacy issues!** Discussion about medication refusal is a sensitive issue and should be conducted in a calm, quiet environment.

Better

1. **Refine your communication skills,** and pay particular to patients at high risk for medication refusal.

2. **Establish a quick reference library** so you can answer questions quickly.

3. **Be alert for situations in which caregivers may be medicating covertly** and offer alternatives.

Good

1. **Always ask patients** why they refuse medications

2. **Know which religions or diets** may create challenges with specific excipients

3. **Leave all prejudices at home** and accept patients’ beliefs and preferences.
REFERENCES

7. Tatham KC, Patel KP. Suitability of common drugs for patients who avoid animal products. BMJ. 2014;348:g401. doi:10.1136/bmj.g401


