Isotretinoin, the drug that revolutionized acne treatment, is the only medication that can clear acne and produce long-term remissions. Since its introduction in 1982, it continues to be a vital and widely used acne medication worldwide. It is used mainly for severe, recalcitrant nodulocystic acne as well as recalcitrant moderate acne. Abroad, isotretinoin tends to be dispensed more liberally than in the US and with a trend toward lower doses. This article will not cover the well known pharmacology, dosing, and side effects of this medication. Instead, it will focus on all the other skills necessary for successful isotretinoin prescribing: patient education, common mistakes using iPLEDGE, and the challenges posed by isotretinoin’s bad reputation. The goal is to have the patient very well educated and for the provider to have all the tools and knowledge to guide the patient through a successful treatment.

PATIENT EDUCATION BASICS

Educating patients about isotretinoin and how it differs from other treatments is no easy task. Isotretinoin is a unique drug and is completely different than any other acne medication. Below are the topics that are essential to cover during the patient visit and information on how I explain them to patients. Much of this information is included in the Isotretinoin Fact Sheet (to be discussed later) that I routinely hand out.

Q: What is isotretinoin? Isotretinoin is a pill you take for four to five months. Your acne will start to improve in one to two months, and the vast majority of people are clear at the end of treatment. It is the only acne medication that permanently reduces acne an average of 80 percent—some people a little more and some a little less. It also makes our skin less oily long-term. Twenty percent of patients take the medication a second time if they still have significant acne. Some blood tests are required.

After hearing so much about how effective isotretinoin is, patients expect dramatic results the first month and need to have their expectations managed. I don’t think it is too early to mention the risk of relapse on the first visit, especially if the patient has risk factors for it.

Temporary improvement vs. permanent reduction: All other acne medications reduce your acne 50-75 percent at best and need to be taken for as long as you have acne, which for most people is at least into the late teens. Isotretinoin is the only medication to produce a substantial permanent reduction in acne after you stop taking it.

As I discussed in my previous article “Optimizing Acne Treatment” in the October 2014 issue, you have to assume that patients think that they will treat their acne for several months, they will be clear, and then they can stop. Isotretinoin is the only medication where these expectations can largely be met. For some people, it is quite a shock that at age 14 for example, without isotretinoin (and sometimes with it if they do not get full clearance) they will be treating their acne at least another five years. This stark contrast between isotretinoin and non-isotretinoin treatment should be made crystal clear.

How does it work? Isotretinoin works by shrinking your oil glands and normalizing the way your skin grows, which prevents pimples and clogged pores. Because your lips have a lot of oil glands they will become dry first, followed by your face and...
possibly other areas. Using lip balm frequently and moisturizing creams can manage these symptoms quite well. You will also sunburn faster.

I do not use the word “side effect” when discussing dry lips and dry skin because it is not a side effect in the classic sense (an unintended, possibly dangerous effect of a medication). We expect the medication to do this—this is how it works. Patients don’t need to be alarmed about this, and the fewer times the prescriber can say “side effect,” the better.

Isotretinoin does not make scars or PIH (post-inflammatory hyperpigmentation), or post-inflammatory erythema disappear. Some of the red marks and brown spots will clear up as your acne clears. The scars will not be affected by isotretinoin. A few months after you finish treatment, we can see what red marks and brown marks remain, assess your scarring, and review your treatment options for clearing those up.

Patients to some degree view scars, PIH, or post-inflammatory erythema as “acne,” and many believe everything will clear up with isotretinoin. Some treatments, like hydroquinone blend bleaching creams, can be initiated immediately after isotretinoin is finished or even during treatment if the skin can tolerate it. For some treatments (lasers, chemical peels, etc.) it is recommended to wait six months after treatment due to concerns about increased scarring.

Initial flare is not therapeutic! If your acne gets worse in the first month or two, let us know so we can treat it!

Initial flare is a common but preventable side effect. The more severe, inflammatory, widespread and cystic the acne is, the more common initial flare is. Strategies to prevent initial flare include lower initial dose and concurrent use of prednisone the first month. Many patients don’t contact their provider thinking that initial flare is therapeutic and that “the acne is coming to the surface.” Not treating an initial flare results in unnecessary breakouts and scars. Acne can also get worse the first month simply because all other acne medications have been discontinued and isotretinoin may take a month or two to begin working, causing a treatment gap. Keep in mind that non-drying topical medications can be continued as can spironolactone (for female patients) and any antibiotic except tetracyclines (due to the increased risk of Pseudotumor Cerebri).

Take with food: Isotretinoin absorbs twice as well if you take it with meals.

Isotretinoin is a lipophilic medication. One study showed 1.5-2 times greater absorption in the fed (large breakfast with 28 grams of fat) versus a fasting state. This difference in absorption is not a trivial concern. For the first few monthly follow-ups, I reinforce this important message of taking the medication with food.

The easiest way to assess if the patient is a candidate for bid dosing is to ask if they have breakfast most days. If they do, ask what they eat. If it is a light meal or they do not regularly eat breakfast, stick with QD dosing. Although the pharmacokinetics do favor twice daily dosing, if that causes more medication to be taken in the fasting state with poor absorption, it is counterproductive.

In 2012 isotretinoin-Lidose (Absorica) came on the market promising higher absorption both in the fed and fasting states. While it does have a marginal edge in the fed state vs generic isotretinoin (keep in mind this was tested with the 1,005 calorie high fat meal, which very few people eat) its real advantage is in the fasting state. Its fasting absorption is 68 percent versus the fed state. This was much better than standard isotretinoin, which only reached 39.6 percent absorption versus the fed state. Over the course of treatment, poor absorption could lead to lower actual cumulative doses and higher relapse rates. Patients with low fat diets or those who have irregular meal schedules benefit most from isotretinoin-Lidose.

Birth defects: This medication can cause birth defects only while you are taking it (and a month after, which is explained at the last visit) but does not affect long-term fertility. What this means is that if you become pregnant while taking it there are very strong odds of losing the baby or of serious birth defects. For this reason every female who is biologically capable of becoming pregnant must take monthly pregnancy tests and have a pregnancy prevention plan.

Especially with younger patients I never say, “You are required to use two forms of birth control,” which is inaccurate, as abstinence is an option. For patients who don’t volunteer any information about birth control or sexual history, I have them pick their primary and second forms of pregnancy prevention from a form (form described below) and use that as a starting point for counseling.

Isotretinoin’s Reputation

Your colleagues will almost certainly offer positive feedback and praise for this drug. Many have even prescribed it to their own children. However, when you discuss it with patients, a significant number have a negative opinion. How did this huge disconnect happen? Lawyers and high-profile lawsuits, very visible dry lips and dry skin, teratogenic properties and the belief in the public that acne doesn’t need a strong medication to treat it all played a role. It would take an entire article to detail the history of the bad press isotretinoin has received. This creates significant challenges reconciling our views with what the patient has heard from non-expert sources.

Introducing Isotretinoin as a Treatment Option

Great care must be taken when discussing isotretinoin as a treatment option, as it has a potential to alienate patients
We cannot and should not hold it against patients or look will not return or will return wanting to try something else. that this is the best treatment choice, and they agree, many and are fearful of the medication. Even if we convince them drug worth considering; they already have a strong opinion our profession’s view that isotretinoin is a safe and effective side effects horrible?” or “Isn’t it hard on your liver?” It will that the drug that causes massive depression?” “Aren’t the thing, which usually indicates they have not heard of it at all medications can be helpful. Accutane is also a good option.”

A new acne patient questionnaire is a great starting point. This questionnaire is detailed in my previous article “Optimizing Acne Treatment.” One specific question asks the patient to circle the treatment options they are interested in. Isotretinoin is on that list (listed as Accutane so patients recognize it). Some people circle it and some cross it out (this does not necessarily mean they will never consider it, but expect resistance). The other useful question asks, “I will need to achieve a minimum ______% improvement to consider my acne treatment a success.” Almost everyone circles 70–100 percent. This level is very difficult to achieve for severe acne patients without isotretinoin and patients need to be educated to that reality. Many believe that there has to be something else that will get them these results, therefore, a breakdown of available treatments and expected results is often needed. If not, the patient may believe that you are just pushing one treatment option on them.

When a person is a candidate for isotretinoin and there are still other options that will yield some improvement, I first see what the patient knows about the medication by saying, “Since you have severe acne with scarring, there are many options to consider: combined topical and oral medications can be helpful. Accutane is also a good option.”

The patient may then offer up what they have heard about Accutane, negative or positive. Many will not say anything, which usually indicates they have not heard of it at all and need to know the basics. Some ask questions like, “Isn’t that the drug that causes massive depression?” “Aren’t the side effects horrible?” or “Isn’t it hard on your liver?” It will be an uphill battle to get these patients to come around to our profession’s view that isotretinoin is a safe and effective drug worth considering; they already have a strong opinion and are fearful of the medication. Even if we convince them that this is the best treatment choice, and they agree, many will not return or will return wanting to try something else. We cannot and should not hold it against patients or look down on them that they have been exposed to misinformation that they accept it as fact. There are not experts.

The best way to educate those who have strong negative opinions about isotretinoin is by giving them a few simple facts: “Accutane has been FDA approved for 32 years and has been used all over the world by millions of people. It is considered safe, very effective, and has never been withdrawn from the market in any country for safety concerns. Within the dermatology community, it is not considered a controversial medication. Dermatologists are very comfortable with its use, so much so that many prescribe it to their own children or relatives (I usually add here that my brother took it on my recommendation). But the most important thing is that you have to be comfortable with it.” I then give them an Isotretinoin Fact Sheet handout and explain that we have more than 30 years of facts and safety data that they can research for themselves.

If the patient wants to consider it as an option right then and there they will pursue that conversation, if not I pivot to other treatments. If the patient chooses other treatments, at least you have set the stage for more informative discussion down the road if they are not getting the results they want. We have become very comfortable with using isotretinoin but must remember that for a patient, parent or teen, to consider taking a medication that is teratogenic and needs monitoring may just be too scary to consider, even if it is the only thing that will help.

**NAVIGATING iPLEDGE**

iPLEDGE is often frustrating and confusing. Often times our failure to navigate it and guide patients through it prevents patients from getting their medication. Prescribers should not delegate iPLEDGE responsibilities to medical assistants without first mastering the system ourselves. For me this required several months of clearing people and making multiple calls to iPLEDGE, but it was a worthwhile investment. Going through this process, I concluded that it is unrealistic to expect a person with a medical assistant level education to master iPLEDGE on their own. We can eventually delegate this task after we have mastered iPLEDGE and have the expertise to properly train and supervise our MAs. If a pregnancy does occur, our interaction
with iPLEDGE will be put under a microscope, so it is essential that we are the iPLEDGE experts in our practice. Below are some facts that can greatly increase your success using iPLEDGE.

1. Male patients and females of non-child bearing potential never need to call iPLEDGE or go on the website. We have to register them and clear them every month but they do absolutely nothing. Whether these patients had blood tests is not a criteria for clearing them. How often we monitor their labs is up to the provider’s discretion. They have a 30-day window to pick up their medication.

2. For a female of child-bearing potential, the 30-day window opens the day she is registered with iPLEDGE. Registration cannot take place without a pregnancy test and even if the pregnancy test date precedes the registration date, the 30-day window starts on the registration date. This is why it is important to register patients the day the pregnancy test results come in to avoid delays.

3. Schedule a four and a half to five week follow-up rather than four weeks follow-up for the second visit. Two pregnancy tests must be taken more than 30 days apart. This means that if you schedule your female patient back for a one month follow up, they return 28 days later (4 weeks) with their labs in hand that they took a few days beforehand, this is too early, and they have to re-take the pregnancy test after the 30 days window. A four and a half to five week follow-up is ideal as it gives the patient enough time to get their next pregnancy test and labs.

4. If female patients miss the seven day window to pick up their medication when they are getting their first prescription they have to wait at least 19 days to get another pregnancy test and pick up their prescription (look at the patients calendar on iPLEDGE for the first date they can get another pregnancy test again). For any prescription other than the first, if the seven day window is missed, all the patient has to do is take another pregnancy test, which immediately opens up another seven day window to get their medication.

5. If the patient chooses abstinence as their primary form of birth control, the secondary form should be “none”. If the patient wants to choose abstinence as their primary form of birth control and condoms as the secondary form this is a red flag. It may indicate they plan to occasionally have sex and use condoms with no primary form of birth control.

6. Tubal ligation is not considered a sterilization procedure by iPLEDGE and therefore the woman is still considered to be of child bearing potential. If the patient chooses to be abstinent and has a tubal ligation, tubal ligation should be listed as their secondary form of birth control and abstinence their first. If they are sexually active then tubal ligation is their primary form of birth control and they must declare a secondary form of contraception as well.

HELPFUL FORMS

The following four forms can help make the complex task of prescribing isotretinoin a little easier.

1. For females of childbearing potential, the schedule during the first month can be confusing. A form that lists the date after which they can get their blood tests (after 30 day window), and the earliest date their next follow up is very helpful.

2. Before the patient signs iPLEDGE forms, I discuss pregnancy prevention. This is a sensitive subject and many patients don’t volunteer any information. When this happens I give them a form to fill out along with their iPLEDGE book. This is simply a list where they select their primary and secondary forms of contraception. When you return their answers are used as the starting point for counseling.

3. Isotretinoin Fact Sheet: With so much misinformation out there I make sure to give patients a handout so they start learning about isotretinoin from me rather than the internet. The introduction stresses the safety and efficacy of isotretinoin. Then there is a FAQ section. On the back are a half dozen article citations that can be viewed online, with a brief summary of the findings.

4. Effects of Isotretinoin: This handout covers the mucocutaneous effects and systemic side effects. The first two things listed are dry skin and dry lips with recommendations on specific products used to treat them and a list of other side effects arranged from most common to least common. The last thing listed are rare side effects that if experienced should prompt the patient to discontinue their treatment like worsening headache and decreased night vision.

AVOIDING PHARMACY FAILURES

The final step is for the patient to obtain their medication at the pharmacy. With an average cash price of more than $300 for a 30-day supply, there is potential for problems. Prior authorizations are commonly needed. If the patient has a prescription drug deductible, they may have to pay a large sum out of pocket until the deductible is met. Also, isotretinoin has the rare distinction of having four branded generics. This sometimes causes confusion in the pharmacy, where they do not understand that any branded generic isotretinoin is inter-
The Medicare Program is expensive. It provides medical care to millions of Americans over age 65, and their ranks are only going to grow in coming years. In efforts to control the growing costs of the Medicare program, US legislators focused on physician fees. Their logic was simple: cut the amount paid to care providers, and you cut the costs of care overall. However, business is not always logical. When Medicare began implementing physician fee schedules in the 1980s, total payments to physicians actually increased. Not surprisingly, physicians began ordering more tests and providing more services to patients in order to obtain reasonable payments. They did more work, but they got paid.

In the 1990s, Congress attempted to limit the overall rate in growth of Medicare expenditures with the Volume Performance Standards Set, allowing for reductions of fee schedules by 2-3% annually. The system didn’t work, leading Congress to introduce the SGR, as part of the Balanced Budget Act of 1997. Per CMS, “The use of SGR targets is intended to control the growth in aggregate Medicare expenditures for physicians’ services.

The SGR targets are not direct limits on expenditures...the fee schedule update, as specified in section 1848(d) (4) of the Act, is adjusted to reflect the comparison of actual expenditures to target expenditures. If expenditures exceed the target, the update is reduced. If expenditures are less than the target, the update is increased.” To read more about the specific formula, see the handout at PracticalDermatology.com.

Since 2003, Congress has passed legislation to prevent the SGR from taking effect in each given year, and avoiding its substantial cuts to physician payments. Implementation of the SGR this year would result in essentially a 21 percent cut in physician payments. It’s not just Medicare participating physicians who worry. Private insurers base their payments on Medicare’s fee schedules, so they could begin dropping reimbursements as well.

PROBLEMS WITH THE SGR

Problems with the SGR are numerous. Many critics, including the Heritage Foundation’s Chris Jacobs, note that the decision to tie physician payments to the GDP via the SGR was ill-conceived. As Mr. Jacobs writes, “Congress established a fiscal target bearing little resemblance to the actual cost of medical goods and services. Other targets, such as the consumer price index (CPI) or the medical economic index, provide a clearer link to price inflation and general health cost growth.”

Implementing the SGR “fixes” or freezes is costly to the
National Health Expenditure was $2.9T in 2013. Physician and Clinical Services Expenditure was $586.7B.

Medicare system. The Congressional Budget Office (CBO) says permanently freezing SGR target levels would cost $139.1 billion over 10 years.3

Consider this, as pointed out by the American Association of Physician and Surgeons’ Richard Amerling, MD: From 2002-2012 Medicare spending on physician services per beneficiary increased by 72%. “A 9% increase in rates during this period was dwarfed by the growth in volume of physician services, including lab tests (91% increase), imaging (79% increase), and other procedures (up 68%).”4 (Table 1)

Pay cuts and freezes may be forcing physicians out of private practice and into costlier hospital systems; From 2002-2012, Medicare fee-for-service rates increased 9%, while the cost of operating a practice increased 27%.4

Numbers crunchers focus on the problems with the SGR formula and its implementation. But many overlook a key element of the equation: physician payments represent just a small proportion of overall Medicare program costs. (Tables 2,3) Congress is targeting the low-hanging fruit, but the larger, riper targets continue to swell. (Table 3)

WHAT NOW

The House of Representatives passed the Medicare and CHIP Reauthorization Act (MACRA) in March to repeal the SGR, but as of press time the Senate had not acted on it. The merits of any new system will need to be assessed, but the reality is that the SGR does not and cannot work. As physicians, we should actively educate our peers and our patients about the flawed SGR, as well as our overall place in the Medicare program. We provide important patient services, and our reimbursement for those services represents just a small proportion of the total costs of the Medicare program. An appropriate reimbursement model will value our diagnostic and clinical skill, encourage us to treat each individual patient as we see fit rather than to comply with government standards, and reward efficiency rather than incentivize the use of unnecessary tests and treatments. We don’t make treatment decisions based on the GDP, why should we get paid based on it? ■

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changeable. They may call you to ask if, for example, Claravis can be substituted for Zenatane. These problems can be avoided by simply writing isotretinoin instead of the branded generic name if you have no preference.

I detailed in my previously published series “Prescribing Pitfalls” (both parts available on www.practicaldermatology.com) that when a prescription is expensive and complicated to fill, partnering with a knowledgeable independent pharmacy with dermatology experience can be very helpful. I explain to patients that this is a specialty medication and while I can send it to their regular pharmacy, a pharmacy that specializes in dermatology is better equipped to make sure everything goes smoothly. Most patients are happy with this option. In addition, both Zenatane and now Absorica have partnered with mail order pharmacies to streamline isotretinoin prescribing. They offer “concierge services” that include applying discount coupons, sending patients reminders to get labs, and monitoring iPLEDGE dates to help patients avoid missing windows. Zenatane even has a patient assistance program for patients who cannot afford the medication.

A REWARDING EXPERIENCE

Following the suggestions outlined in this article, the often-frustrating experience of prescribing isotretinoin can be converted into the manageable and rewarding experience it should be. It is a tragedy for any patient not to be able to obtain this life-changing medication because of our inability to navigate the prescribing process. This requires the prescriber to take the lead and become an expert in all aspects of isotretinoin prescribing and patient education. The predictably dramatic improvements in patients’ acne and reduction in frustration and problems make it well worth the extra effort. ■


Online First:
Expert Perspectives on Isotretinoin Prescribing

Go to PracticalDermatology.com for a sneak peek at interviews with acne experts who discuss their approaches to patient counseling. Read the full report in the May edition of Practical Dermatology® magazine.

index.php/article/missing_from_the_debate_over_the_medicare_sustainable_growth_rate_sanity/