Oral Cancer Therapies: Important Prescribing Considerations

Introduction

Do you know the prescribing laws in your state, especially regarding generic versus branded oral cancer therapies? What are your state's laws regarding Dispense as Written (DAW)? When prescribing generics, do you know the difference between bioavailability and bioequivalence? How confident are you that instructions for taking oral cancer therapies are being followed by patients, especially if generics are used? This brief article will provide some insights and resources for these common challenges.

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Regulatory Approval Processes

There are considerable differences between the FDA approval processes for branded versus generic drugs. The journey to approval for new drugs is a long and rigorous process that can take many years. As the first step, research institutions and pharmaceutical companies present results of preclinical animal testing to the FDA. Following approval by the FDA and a local institutional review board, the therapy can move on to human testing that is conducted in 3 phases. Phase 1 studies determine dose and safety of the new drug and are usually performed in healthy subjects. Phase 2 studies investigate efficacy in affected patients. Phase 3 studies are larger scale and compare the new drug to the current standard of treatment or placebo.[1] When studies are complete, all trial data are presented to the FDA for official approval to market the drug.

The approval process for generic formulations is much less stringent because these drugs are not required to establish safety and efficacy via preclinical and clinical data. Instead, generic drugs must demonstrate bioequivalence to the approved drug (**Table 1**). This means that the generic products must demonstrate the equivalent amount of the active ingredient in systemic circulation as the approved drug.[2] To gain FDA approval, the generic drug must be bioequivalent between 80% and 125% of the original patented drug.

There are sometimes concerns that bioequivalence does not equate to comparable clinical efficacy and tolerability. Current bioequivalence requirements are based on a measure of average bioequivalence, but this may not be suitable for drugs with a narrow or wide therapeutic range, or drugs with high intrasubject or intersubject variability.[3]

TABLE 1

Definitions of Bioavailability and Bioequivalent

- **Bioavailability:** the rate and extent to which the active ingredient is absorbed from a drug product and is available at the site of action.
- **Bioequivalent:** a drug product that shows comparable bioavailability under similar test conditions.

Branded versus Generic State Laws

If oral medication is part of the treatment plan, consideration is usually given to branded versus generic options. The oncologist needs to know whether the generic option is appropriate for the patient, and also needs to know and understand state regulations for each. Web links with this information are provided in **Table 2**.

TABLE 2

Web Resources for Generic Substitution and E-Prescribing

HealthIT.gov: Requirements for Specifying "Brand Necessary" by State
www.healthit.gov/sites/default/files/appb-1.1.pdf

HealthIT.gov: Report on State Prescribing Laws: Implications for e-Prescribing, 2009
(Information regarding prescribing DAW starts in section 3.4)
www.healthit.gov/sites/default/files/290-05-0015-state-rx-law-report-2.pdf

National Association of Boards of Pharmacy, 2010 Survey of Pharmacy Law
(Information on drug product selection laws, including DAW, starts on page 61)
Available for purchase at www.nabp.net/publications/survey-of-pharmacy-law

Prescribing services can be of great assistance. Prescribers can instantly assess the patient's accompanying online computerized medical records systems profile and check for compliance with the patient's health plan. The system also automatically screens each prescription for possible interactions, patient allergies, health problems, or previously prescribed medications in the computerized medical record.

Prescriptions route immediately to the patient's pharmacy of choice. The system also provides a list of cost-effective generic alternatives to the prescriber.

While all states have laws designed to encourage use of generic drugs, physicians are allowed to override these by transmitting, along with the e-prescription, a message that the brand name is medically necessary ie, DAW. Federal law used to require that "brand necessary" needed to be handwritten on a prescription printout, but this law has been amended to permit this to be electronically transmitted.[4] However, state laws may differ.

Drug substitution laws vary by state, so it is important to know your state's rules. Some states follow the Orange Book, but others have specific mandatory or permissive substitution rules. Some states require patient consent or notification, and others require cost savings to be achieved.

Patient Information and Adherence

Health care professionals (HCPs) have serious responsibilities in prescribing drug products with care and providing appropriate information to each patient. Patients need to be educated on the differences between branded and generic so they can fill their prescription appropriately and take the medication correctly (**Table 3**). For example, HCPs should instruct patients to look at their oral medication to ensure that it matches the shape, color, and writing on the tablet that they expected to receive.

TABLE 3

Information Patients Need About Prescriptions

- Why is this medication prescribed?
- How should this medicine be used?
- What special precautions should be followed?
- Does this medication interact with other medications the patient is taking?
- What special dietary instructions should be followed?
- What should the patient do if a dose is forgotten?
- What side effects can this medication cause?
- What should the patient know about storage and disposal of this medication?
- In case of emergency/overdose
- What other information is important?
- Brand name(s) of the medication
- Should the patient accept a generic substitution for this medicine?

Patient adherence to medication is a critical issue for cancer treatment. Factors that can affect adherence include oral versus IV route of administration, understanding the dosing requirements, management of side effects, rapport with oncologist, oncologist explanations of treatment, and understanding the consequences of missing a dose.[5]

There are many ways that generic drugs differ from branded ones. Some may not affect the action of the therapy, such as shape, scoring configuration, and packaging. But others may have direct effects on therapeutic action, such as expiration date and stability under various storage conditions. The amount of active ingredient may have an impact on efficacy, even if it is within acceptable variances from the branded drug. In addition, the drug label can have differences, and some differences in coloring, flavoring, fillers or preservative ingredients can lead to potential allergic reactions.[6]

Due to these many variables, the characteristics of a specific product, other than the active ingredient, may be important in the therapeutic plan for specific patients.

Conclusion

It is important for HCPs to be aware of their state's DAW regulations, and to understand exactly what therapy patients will receive when writing the prescription. Educating patients about what the pill should look like and how it is administered are also very important.

References

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