Medication Safety With Oral Chemotherapy – Not Just Any Ordinary Pill

Evelyn Handel, PharmD, BCOP
Clinical Pharmacist Specialist
Roswell Park Cancer Institute

CONFLICT OF INTEREST STATEMENT

I have no conflicts of interest related to the content of this presentation

OBJECTIVES

- Summarize major issues facing patients prescribed oral chemotherapy, their families and healthcare professionals caring for them
- Discuss areas of key vulnerability, including patient education about drug handling and adverse effects, prescription writing, patient self-administration and medication adherence, and failure to monitor and manage toxicities
- Identify guideline-based recommendations for safe handling of oral chemotherapy medications, including specialty pharmacy considerations
- Describe best practices for supporting patients taking oral chemotherapy using example patient experiences
Growing 15-20% per year:
- 30 new oral chemotherapy agents between 1953-2003
- 35 new agents between 2004-2014

Over 25% of the ~400 antineoplastics in development are oral

Currently 65 FDA-approved oral chemotherapy agents

Associated with considerable cost:
- Spending on oral chemotherapy more than doubled between 2002 and 2006, from 0.3% to 0.7% of total pharmacy benefit costs ($5 - 7 billion)
- Estimated yearly cost for one agent is often >$100,000

FDA APPROVED ORAL CHEMOTHERAPY

1. abiraterone (Zytiga)
2. acitretin (Soriatane)
3. afatinib (Gilotrif)
4. altretamine (Hexalen)
5. anastrozole (Arimidex)
6. anastrozole (Evista)
7. anastrozole (Femara)
8. anastrozole (Aromasin)
9. anastrozole (Arimidex)
10. anastrozole (Evista)
11. anastrozole (Femara)
12. anastrozole (Aromasin)
13. anastrozole (Arimidex)
14. anastrozole (Evista)
15. anastrozole (Femara)
16. anastrozole (Aromasin)
17. anastrozole (Arimidex)
18. anastrozole (Evista)
19. anastrozole (Femara)
20. anastrozole (Aromasin)
21. anastrozole (Arimidex)
22. anastrozole (Evista)
23. anastrozole (Femara)
24. anastrozole (Aromasin)
25. anastrozole (Arimidex)

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**ORAL CHEMOTHERAPY LANDSCAPE**

- Creates new areas of need
  - Develop new infrastructure to support comprehensive oral chemotherapy programs
  - Maintain clear flow of patient care
  - Define responsibilities for various health care provider roles
  - Define a standard for patient acquisition of oral chemotherapy agents
  - Provide support for financial needs surrounding treatment plan
  - Acknowledge requirements for safe handling and storage

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**PATIENT/CAREGIVER ADVANTAGES WITH ORAL CHEMOTHERAPY**

- Convenience of self-administration
- No need for infusion center wait time or chair time
- Elimination of IV access
- Potentially fewer clinic appointments
- Sense of empowerment

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**PATIENT/CAREGIVER CHALLENGES WITH ORAL CHEMOTHERAPY**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Caregiver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to swallow dosage form</td>
<td>Complicated regimen</td>
</tr>
<tr>
<td>Proper administration</td>
<td>May need to measure out liquids, open capsules, crush tablets</td>
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<tr>
<td>Safe handling at home</td>
<td>Proactive communication</td>
</tr>
<tr>
<td>Adherence</td>
<td>Care coordination (i.e., specialty pharmacy and clinic)</td>
</tr>
<tr>
<td>Reporting toxicities</td>
<td>Financial assessment</td>
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</tbody>
</table>
**Slide 10**

<table>
<thead>
<tr>
<th>Opportunities</th>
<th>Challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved quality of patient care</td>
<td>Patient selection</td>
</tr>
<tr>
<td>Setting up an in-house specialty pharmacy is a potential new revenue source</td>
<td>Monitoring outcomes and adherence</td>
</tr>
<tr>
<td>Defining standard operating procedure decreases errors and oversights</td>
<td>Coordinating with outside specialty pharmacies</td>
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<tr>
<td></td>
<td>Financial reimbursement and patient assistance</td>
</tr>
<tr>
<td></td>
<td>New communication and documentation needs</td>
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</tbody>
</table>

**PHYSICIAN/PRACTICE CONSIDERATIONS**

**Opportunities**
- Improved quality of patient care
- Setting up an in-house specialty pharmacy is a potential new revenue source
- Defining standard operating procedure decreases errors and oversights

**Challenges**
- Patient selection
- Monitoring outcomes and adherence
- Coordinating with outside specialty pharmacies
- Financial reimbursement and patient assistance
- New communication and documentation needs

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Which of the following is/are true about patient preference for oral therapy?

A. Oral chemotherapy has fewer side effects than parenteral chemotherapy
B. Oral chemotherapy regimens are simple for the patient to manage and do not require extensive education
C. Oral chemotherapy will shift some aspects of managing chemotherapy to the patient, and not all patients respond positively to this empowerment
D. Only A and C
E. All of the above

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**Setting up the Process**

1. Assess readiness
2. Develop new workflow
3. Training and credentialing
4. Ongoing experience-based improvement
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**ASSESSING PRACTICE READINESS FOR AN ORAL CHEMOTHERAPY PROGRAM**

- Communication and documentation plan
- Individual and practice beliefs
- Redefine patient and workflow patterns
- Proactively plan what will be needed for staff and patients
- Financial counseling/support
- Staff and patient education:
  - Monitoring and follow up
  - Staff in every role – credentialing process
  - Patient and family expectations
  - Physician role becomes more collaborative

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**PILLARS OF ORAL CHEMOTHERAPY MANAGEMENT PROGRAMS**

- **Education**
  - Staff in every role – credentialing process
  - Patient and family expectations
  - Physician role becomes more collaborative

- **Communication**
  - Discuss options with patient
  - Communicate plan with clinic team, pharmacy, and PCP

- **Follow Up**
  - Patient monitoring must be planned ahead
  - Follow up visits tailored to drug
  - Measuring quality outcomes

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**ORAL CHEMOTHERAPY WORKFLOW AND AREAS FOR PHARMACIST IMPACT**

- Review drug information and need for access
- Notification of physician of need for access
- Communication among other healthcare professionals
- Drug preparation and ordering
- Treatment outcomes
- Assessment of adherence
- Symptom diaries
- Pharmacists role

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SPECIALTY PHARMACY CONSIDERATIONS
- Designed to focus on medications with complex management issues, greater potential for harm, and higher expense
- Can be located within the practice/institution or external site
  - Contracted or not contracted
  - Consider patient convenience, continuity of care, financial impact
- Inventory management
  - Must stock specialized items and supportive care medications
  - Proper storage and handling
- Requirements by third party payers
  - May cover only specific pharmacies or require mail order
- Compliance with rules and regulations
  - Proper credentialing and oversight

SPECIALTY PHARMACY CHALLENGES
- Access to patient medical record and information sharing
- Maintaining current medication list to check for drug interactions
- Patients receive medications and information from multiple sources
- Insertion of an additional health care professional requires further coordination
- Services provided vary widely (dispensing only vs. close monitoring)

IDEAL ELEMENTS OF SPECIALTY PHARMACY SERVICES
- Access to specialty medications
- Drug information and patient education
- Drug and food interaction screening
- Side effect screening
- Adherence monitoring and dosing reminders
- 24/7 access to a pharmacist
- Insurance coverage/reimbursement assistance
- Home delivery services
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**SURVEY OF NCI-DESIGNATED CANCER CENTERS**

Does your institution have an outpatient retail/specialty pharmacy at which oncology patients can fill oral chemotherapy prescriptions? (n=16)

<table>
<thead>
<tr>
<th>Response</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, on-site and owned by the institution</td>
<td>8</td>
<td>50%</td>
</tr>
<tr>
<td>Yes, on-site and owned by an outside company</td>
<td>3 (18.8%)</td>
<td></td>
</tr>
<tr>
<td>No, but affiliated with an off-site retail/specialty pharmacy</td>
<td>4 (25%)</td>
<td></td>
</tr>
<tr>
<td>No, and not affiliated with an off-site retail/specialty pharmacy</td>
<td>3 (18.8%)</td>
<td></td>
</tr>
</tbody>
</table>


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### Slide 20

**SURVEY OF NCI-DESIGNATED CANCER CENTERS**

Has your institution developed a program or specific practices for managing oral chemotherapy medications? Please check all that apply. (n=16)

<table>
<thead>
<tr>
<th>Response</th>
<th>Count</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, pharmacist provide patient counseling</td>
<td>6 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Yes, pharmacists follow and make recommendations regarding side effects</td>
<td>5 (31.3%)</td>
<td></td>
</tr>
<tr>
<td>Yes, pharmacists review oral chemotherapy prescriptions for safety/accuracy</td>
<td>4 (25%)</td>
<td></td>
</tr>
<tr>
<td>No, but a program is in development</td>
<td>3 (18.8%)</td>
<td></td>
</tr>
<tr>
<td>No, another practitioner (RN, NP, PA) provides these services</td>
<td>2 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>No, there is no oral chemotherapy program</td>
<td>1 (6.3%)</td>
<td></td>
</tr>
</tbody>
</table>


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**What are the potential advantages of specialty pharmacies?**

A. The specialty pharmacist interacts directly with the patient, providing additional education and counseling
B. Specialty pharmacies are more suited to provide oral oncology management services and securing insurance coverage compared to retail pharmacies
C. Standard, convenient workflows have been established for communicating patient-related information between prescribing physicians and specialty pharmacies
D. A and B above
E. All of the above

### Key Areas of Vulnerability

1. Patient selection and education
2. Prescription writing
3. Self-administration and adherence
4. Monitoring/managing toxicities

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### Staff roles for oncology team

- **Physician:** patient selection/consent, treatment plan development, oversight of clinical outcomes
- **Clinic staff (RPh, RN):** education, triage, monitoring
- **Patient:** consent to treatment, symptom reporting, adherence
- **Pharmacy:** dispensing, interaction screening, reinforce counseling, communication back to oncology clinic
- **Financial:** reimbursement, patient assistance

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### AREAS OF KEY VULNERABILITY: PATIENT SELECTION AND EDUCATION

- Staff roles for oncology team
  - **Physician:** patient selection/consent, treatment plan development, oversight of clinical outcomes
  - **Clinic staff:** education, triage, monitoring
  - **Patient:** consent to treatment, symptom reporting, adherence
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### AREAS OF KEY VULNERABILITY: PATIENT SELECTION FACTORS

- **Physical**
  - Can the patient swallow the medication?
  - Are they able to open the vial?
  - Do they have allergies?
- **Cognitive**
  - Do they understand the importance, dosing, side effects?
  - Can the patient identify the medication?
  - Will they understand how to make changes if needed?
  - Can they perform basic daily activities?
- **Support & Communication**
  - Do they have social support?
  - Are they willing to comply with instructions?
  - Does the patient have communication skills?
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**AREAS OF KEY VULNERABILITY: PATIENT EDUCATION**

- Who provides it and when?
- What content is included?
- What handouts/resources will be provided?
- How and when is the process evaluated?
- How will education be documented?
- How will it be reinforced, how often, and by whom?
- What type of staff training and development is required?

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**AREAS OF KEY VULNERABILITY: PATIENT EDUCATION**

- Drug information
  - Dosage
  - Frequency and schedule, what to do if a dose is missed
  - Adverse effects
  - Interactions with other medications or food
  - Monitoring and follow up plan
  - When to call the physician/care
  - How to contact the clinic during and after business hours
- Drug handling
  - Storage
  - Protective methods (e.g., gloves, handwashing) required
  - How to administer
  - Disposal

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**AREAS OF KEY VULNERABILITY: PRESCRIPTION WRITING**

- Concerns regarding prescribing and dispensing
  - Inappropriate prescribing by non-oncology trained providers
  - Drug dispensing by pharmacies with little or no experience
  - Unintended negative consequences for patients in rural/remote areas
- Develop appropriate credentialing process
  - Prescribers
  - Clinic staff providing patient education
  - Specialty pharmacies
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**ELEMENTS OF A COMPLETE ORAL CHEMOTHERAPY PRESCRIPTION**

- Patient-specific information
  - Name
  - Date of birth
  - Height, weight
  - Calculated body surface area (if applicable)
  - Known drug allergies
- Drug-specific information
  - Generic drug name
  - Indication for use or diagnosis
  - Dose (if applicable, the dose expressed on the basis of weight or body surface area as well as the calculated dose)
  - Route of administration
  - Dosing frequency, interval, or specific date(s) of administration
  - Cycle number and duration of therapy/time limit
  - Quantity to be dispensed (including refills if allowed)

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**AREAS OF KEY VULNERABILITY: SELF-ADMINISTRATION AND ADHERENCE**

- Patients play a significantly more active role
  - Success depends on effective education
  - Active engagement can lead to quality improvement
- What can be done to enhance patient adherence?
  - Provide education regularly
  - Reinforce key points often
  - Share resources that are relevant
  - Create an expectation that adherence will be monitored
  - Direct to product-specific compliance programs
  - Create log sheets or online self-reporting for patient documentation
  - Drug medication hotline for clients, perform pill counts
  - Track with pharmacy via specialty pharmacies
  - Ask patient to describe how they take their medication each day

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**FACTORS ASSOCIATED WITH NONADHERENCE TO ORAL REGIMENS**

- **Patient**
  - Substantial behavior change required
  - Physical limitations
  - Cognitive limitations
  - Expectations about the effectiveness of the regimen
- **Social**
  - Family/friend support
  - Financial support
  - Beliefs and satisfaction surrounding treatment
- **Therapeutic**
  - Complex treatment regimen, dose changes
  - Side effects
  - Medication administered outside a controlled setting
  - Unforeseen or unusual adverse events
- **Education**
  - Don’t understand consequences of poor adherence
  - Poor communication with health care providers
  - Emotional or financial stress
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COMMON SCENARIOS IN NONADHERENCE

- Confusing dose instructions
- Over or under administration
- Reduced direct supervision
- Insufficient patient education
- Side effects not observed early enough
- Interventions not made until severe symptoms
- Insufficient patient education
- Misunderstood effect on disease state
- Stop taking medication if they feel better

COMMON SCENARIOS IN NONADHERENCE

- ↑ toxicities
- ↑ clinic/ER visits
- ↓ efficacy

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AREAS OF KEY VULNERABILITY: TOXICITY MONITORING/MANAGEMENT

- Oral chemotherapy medications are not less toxic than IV medications
- Maintain regular proactive contact with the patient
  - Clinic visits, phone calls, email reminders
  - Tailor monitoring plan for each medication
    - When will it occur
    - Correlate with when refills or lab checks are due
    - Who will meet or speak with the patient
    - What will be monitored/discussed
    - How will changes be made if needed
    - Consider feasibility of online patient-reported symptom tracking
  - Standardize workflow and documentation
    - Directing information to those who need it
    - Coordinate with specialty pharmacy

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Which of the following is/are true about adherence to oral chemotherapy?

A. Adherence is an important factor that can not be easily assessed with a questionnaire
B. No completely reliable method of monitoring adherence is currently available
C. Nonadherence and improper administration of oral chemotherapy could result in increased toxicities, increased clinic and ED visits, and/or decreased efficacy
D. Successful treatment with oral chemotherapy depends on effective education and active engagement of the patient and their family members
E. All of the above
Safe Handling of Oral Chemotherapy Agents

2013 ASCO/ONS Chemotherapy Administration Safety Standards

2011 Safe Handling of Oral Chemotherapeutic Agents in Clinical Practice: Recommendations from an International Pharmacy Panel

Staffing-related standards
- 1A. Oral chemo order must be written/signed by qualified practitioner
- 1D. Comprehensive educational program for staff in place

Chemotherapy planning: chart documentation standards
- 2H. Frequency of office visits and monitoring is included in plan
- 2I. Assessment of patient’s ability to obtain and administer drug

General chemotherapy practice standards
- 8. On-site pharmacy should have a policy for drug storage/handling

Chemotherapy order/prescription standards
- 9. Verbal orders not permitted except to hold chemo administration
- 12. Components of a complete prescription for oral chemotherapy
- 13. Orders should have a time limitation to ensure proper evaluation
- 14. Procedure for communicating oral chemo treatment plan changes, including alerting the dispensing pharmacy

Drug preparation standards
- 15. Two people independently verify each order for chemotherapy

Patient consent and education standards
- 20. Provide written information about diagnosis, goals, treatment plan, adverse effects, emergency contact information, monitoring plan, potential drug interactions, and document patient’s understanding and engagement

Monitoring and assessment standards
- 25. Assess patient adherence to oral chemo, include plan for any issues
- 26. Update current med list at every visit and screen for interactions
- 31A. Provide 24/7 triage to a practitioner for care of toxicities
- 31B. Consistent documentation: communication of toxicities/changes
- 35. Ongoing plan for regimen-specific assessment of oral chemotherapy

ASCO/ONS 2013: SELECTED ORAL CHEMO ADMINISTRATION STANDARDS

2011 GUIDELINE: SELECTED ORAL CHEMO SAFE HANDLING STANDARDS

Storage
- Keep cytotoxic agents separate from non-cytotoxic agents
- Follow manufacturer recommendations for light/air/moisture

Handling
- Do not dispense oral chemo agents using automated counting machines
- Use gloves when handling, wash hands before and after
- Cutting, crushing, or compounding should be done in a biological safety cabinet using personal protective equipment
- To minimize further handling, liquid medications should be unit dosed

Disposal
- Any materials in contact with oral chemo is considered cytotoxic waste

Training
- Ensure comprehensive education and competencies

2011 GUIDELINE: SELECTED ORAL CHEMO SAFE HANDLING STANDARDS

Which of the following is/are true about ensuring safety with oral chemotherapy?
A. The same workflow that is used for parenteral chemotherapy has also been implemented for oral chemotherapy, thus reducing the risk of medication errors
B. It is acceptable to verbally call in oral chemotherapy prescriptions to a specialty pharmacy
C. When cytotoxic or hazardous medications are administered, patients and caregivers should use gloves and wash hands thoroughly before and after glove application
D. Unused oral chemotherapy medications can be disposed of with regular household trash or flushed down the toilet
Your clinic has recently initiated a comprehensive oral chemotherapy pilot program. A standard operating procedure was developed which includes:
- Copy of the workflow and outline of staff roles
- Patient drug information sheet
- Chemo consent form
- Patient schedule
- Adherence and symptom monitoring log
- Monitoring and toxicity management plan
- Letter for the specialty pharmacy and general practitioner

As a pharmacist, your role is to provide the initial education session about the medication and assess if the patient is an appropriate candidate for the drug.

You complete the patient assessment and education including:
- Overview of treatment plan, goals, and follow up
- Questions to ensure understanding of how to self-administer oral chemotherapy and the importance of adherence
- Potential complications, how to recognize these and what action to take

The following were identified as possible barriers:
- Denies side effects will occur
- Views oral chemotherapy as a milder form of treatment
- Not always able to call in to report side effects

Possible solutions:
- Speak to experienced patients
- Reinforce realistic expectations and offer practical tips for adherence
- Provide 24-hour contact information including phone number and email, and proactively contact the patient at regular intervals during the cycle

Which of the following are scenarios that could lead to medication errors with oral chemotherapy?
A. Lack of reinforcement when the clinician instructs the patient to change the dose
B. Patient not counseled about taking with respect to food, bedtime, and other medications
C. Person handling chemotherapy at home has not been told to wear gloves and does not do so
D. One home caregiver administers the medication when unaware that someone else has already given the medication
E. All of the above
The oral oncology pipeline is growing, and 25% of antineoplastics in development are oral agents.

Oncology practices should consider implementing a structured oral chemotherapy management program.

Various specialty pharmacy services can be provided to meet patient needs with oral agents.

Key areas of vulnerability surrounding the safe use of oral chemotherapy include patient selection, education about drug handling and adverse effects, prescription writing, adherence, and toxicity monitoring/management.

Guidelines that address safe handling of oral chemotherapy medications are available.

Patients require frequent, individualized monitoring and support throughout treatment in order to maximize success.

REFERENCES
