Oral Specialty Cancer Medicines: Benefits and Challenges

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The Important Considerations

• The most important question
  – What drug is best for my cancer?
• Drug toxicity
• Dosing
• Compliance
• Reimbursement
• Distribution channels
Toxicity Doesn’t Go Away with Orals

Diseases desperate grown
By desperate appliance are relieved,
Or not at all

Shakespeare W. Hamlet, Act 4, Scene 3
Toxicity Doesn’t Go Away with Orals

- Cardiovascular: Hypertension (15% to 34%; grade 3: 4% to 13%), peripheral edema (24%), decreased left ventricular ejection fraction (11% to 16%; grades 3/4: 1% to 3%), heart failure (≤15%), chest pain (13%)
- Central nervous system: Fatigue (33% to 62%), headache (≤23%), insomnia (15% to 18%), chills (14%), mouth pain (6% to 14%), depression (11%), dizziness (11%), glossalgia (11%)
- Dermatologic: Skin discoloration (25% to 30%), skin rash (14% to 29%), palmar-plantar erythrodysesthesia (14% to 29%; grades 3/4: 4% to 8%), hair discoloration (7% to 29%), xeroderma (≤23%), alopecia (5% to 14%), erythema (12%), pruritus (12%)
- Endocrine & metabolic: Hyperglycemia (23% to 71%), hyperuricemia (≤46%), hypocalcemia (34% to 42%), hypoalbuminemia (28% to 41%), hypophosphatemia (≤36%), hyponatremia (≤29%), hypoglycemia (17% to 22%), hypokalemia (12% to 21%), hypomagnesemia (≤19%), hyperkalemia (≤18%), hypothyroidism (4% to 16%; grades 3/4: ≤2%), hypercalcemia (13%), hypernatremia (10% to 13%)
- Gastrointestinal: Diarrhea (40% to 66%), nausea (45% to 58%), increased serum lipase (17% to 56%), anorexia (33% to 48%), mucositis (29% to 48%), dysgeusia (21% to 47%), abdominal pain (39%), vomiting (34% to 39%), increased serum amylase (17% to 35%), dyspepsia (15% to 34%), constipation (20% to 23%), weight loss (16%), flatulence (14%), xerostomia (13%), gastroesophageal reflux disease (12%)
- Hematologic & oncologic: Anemia (26% to 79%; grades 3/4: ≤8%), leukopenia (78%; grades 3/4: 8%), neutropenia (53% to 77%; grades 3/4: 10% to 17%), lymphocytopenia (38% to 68%; grades 3/4: ≤18%), thrombocytopenia (38% to 68%; grades 3/4: 5% to 9%), hemorrhage (18% to 37%)
- Hepatic: Increased serum AST (39% to 72%; grades 3/4: 2% to 5%), increased serum alkaline phosphatase (24% to 63%; grades 3/4: 2% to 10%), increased serum ALT (39% to 61%; grades 3/4: 2% to 4%), hyperbilirubinemia (10% to 37%; grades 3/4 ≤1%)
- Neuromuscular & skeletal: Increased creatine kinase (49%), limb pain (14% to 40%), weakness (22% to 34%), arthralgia (15% to 30%), back pain (≤28%), myalgia (14%)
- Renal: Increased serum creatinine (12% to 70%)
- Respiratory: Cough (27%), dyspnea (26%), epistaxis (21%), nasopharyngitis (14%), upper respiratory tract infection (11%)
- Miscellaneous: Fever (≤22%)
Toxicity Doesn’t Go Away with Orals

- Cardiovascular: Edema (25% to 27%), hypertension (9% to 22%; grades 3/4: 1% to 4%)
- Central nervous system: Fatigue (39%), insomnia (14%)
- Dermatologic: Bruise (13%)
- Endocrine & metabolic: Increased serum triglycerides (63%), hyperglycemia (57%), hypernatremia (33%), hypokalemia (17% to 28%; grades 3/4: 3% to 5%), hypophosphatemia (24%; grades 3/4: 7%), hot flash (19% to 22%)
- Gastrointestinal: Constipation (23%), diarrhea (18% to 22%), dyspepsia (6% to 11%)
- Genitourinary: Urinary tract infection (12%)
- Hematologic: Lymphocytopenia (38%; grades 3/4: 9%)
- Hepatic: Increased serum ALT (11% to 42%; grades 3/4: 1% to 6%), increased serum AST (31% to 37%; grades 3/4: 2% to 3%)
- Neuromuscular & skeletal: Joint swelling (30%, including joint discomfort), myalgia (26%)
- Respiratory: Cough (11% to 17%), upper respiratory infection (5% to 13%), dyspnea (12%), nasopharyngitis (11%)
Length of Therapy

- Average duration of therapy is 7 months for Nexavar and Sutent but days supplied indicate it is about 5 months for Nexavar and 6 months for Sutent.
- Average duration of therapy for Votrient is 5.6 months but is 4.5 months based on days supplied.

UnitedHealthcare data, 2012. Renal cell carcinoma patient analysis

Compliance for all oral specialty medications is 58%
Dosing

- Poor tolerability
- Fixed, arbitrary adjustments due to pill size
- Unbalanced clinical trials

Benefit Differentials

- Pharmacy benefit is different than the medical benefit
- Parity laws passed in 30 states
  - 12 states considering
- Operational issues
  - Different systems
  - Costs
- Medicare does NOT have parity provision
Distribution Systems

• Specialty pharmacy
• Retail pharmacy
• Physician distribution
• Compliance studies
  – Improved patient compliance with specialty pharmacy.
    • Possession ratios of 0.66 versus 0.58
    • Copayment was $50 per month
  – Lower medical costs with specialty pharmacy
    • $84,000 versus $97,000

Tschida SJ. Am J Pharm Benefits 2012;4: 165-174
When Do Preferences Count?

A comparison between a equivalent oral and intravenous regimens

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<td>Leucovorin</td>
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Consumers Look at Their Checkbooks

- Consumers buy the plan; patients use the plan
  - The Oregon farmer
  - The Town Car driver in Houston
- Oral specialty drugs*
  - Mean compliance 58% with $50 monthly co-payment

* Tschida SJ. Am J Pharm Benefits 2012;4: 165-174
Summary

- Orals are neither superior or inferior to intravenous medications
  - What’s best for the cancer?
  - What are the trade-offs for equal therapies?
- Dosing change effects are still unknown
- Specialty pharmacies are preferred distribution
- Cost is an issue regardless of administration method