

# Applied Pharmacoeconomic and Outcomes Research Forum Fall 2006

## REPORT

The second Southern California Applied Pharmacoeconomic and Outcomes Research Forum was held October 16<sup>th</sup> on the University of California San Diego campus. The event was hosted by the Skaggs School of Pharmacy and Pharmaceutical Sciences and supported by a grant from Allergan.

Attendees of the Forum represented Managed Care Organizations, Government Agencies, Medical Centers, Academia, and Pharmaceutical and Biotech companies in Southern California. Each attendee was invited because they had a demonstrated interest in expanding the practical application of pharmacoeconomic and outcomes research to enhance decision-making.

### Topic

“Biologics: Drawing (or Crossing) the line of Cost vs. Benefit? A Case in Oncology

The case, prepared by Margaret Stull, PharmD, Pharmacoeconomic Clinical Specialist at the VA San Diego Healthcare System, was for a hypothetical new biologic agent - Expenzumab (Vegitin™) - indicated for first-line treatment of metastatic colorectal carcinomas.

### Perspective Views

Three speakers commented from their institution’s perspective regarding issues they may face if evaluating and managing Expenzumab within their health care system.

- |                              |   |
|------------------------------|---|
| ❖ Government                 | US Navy - Ted Briski, PharmD, MBA, BCPS |
| ❖ For-profit Medical Group   | Sharp - Melissa Christopher, PharmD     |
| ❖ Integrated Delivery System | Kaiser – Doug Monroe, RPh, MS, FCSHP    |

### **Common views among speakers:**

- 1) Risks with Expenzumab usage were perceived as adverse drug reactions, economic, and political.
- 2) More evidence based data is needed earlier (beyond that required by FDA), nearer to the introduction of new drugs – perhaps more patients and longer term
- 3) Guidelines would be developed and used as mechanisms for ensuring appropriate use of Expenzumab - however...
- 4) Guidelines do not generally consider financial implications of recommendations

### **Speaker views differed based on their organization’s:**

- 1) Exposure as a direct payer and assumed risk of payment (e.g. IPA vs. Staff Model)
- 2) Financial structure and incentives (e.g. For-profit MD group vs. DoD)
- 3) Patient’s expectation of their healthcare system (e.g. HMO, PPO, VA)
- 4) Degree of patient input on decision making vs. system approach to assess the relative value of the product
- 5) Outpatient vs. inpatient environment and thus utilization sites and reimbursement source for Expenzumab
- 6) Legal obligations of the payer (e.g. legislation affecting the Department of Defense (DoD), contracting for For-profit MD group)

## Break-Out Group Opinions

Two questions were put to break-out groups for their consideration.

Considering the clinical, economic and humanistic aspects of the case, what ***advice*** could you give to *each perspective* that would **allow them to best afford or manage Expenzumab** as a covered and reimbursed benefit for their

### ***Recommendations***

Overall

- 1) Limit use of Expenzumab to labeled indications.
  - 2) Measure and monitor utilization and outcomes achieved with Expenzumab as possible within system - Patient Registry
  - 3) Use (continue or start) prior authorization for patients that meet only inclusion criteria for Expenzumab
  - 4) Need an individual - not just physician - to discuss risk vs. benefit of Expenzumab use as well as its associated cost so patients can make more informed decisions. This will assist physician as well.
  - 5) Cost share with patients
  - 6) Advice to one perspective may have negative influence on another perspective in the health care system
- ❖ Government should
    - a. use its buying power as much as possible to drive down cost of Expenzumab
    - b. try to decrease political influence in system to make decisions more evidence based
  - ❖ For-profit group medical group should remove the physician from the purchasing process of Expenzumab
  - ❖ Integrated Delivery system should wait for sufficient evidence regarding Expenzumab before making decisions (beyond the initial limited evidence the speaker deemed lacking)

Has Expenzumab **crossed the line of cost vs. benefit?**

- ❖ One group clearly said Yes “if it exceeds an “acceptable” dollar value per Quality Adjusted Life Year (QALY)” which was data not available in the case.
- ❖ Two groups were unsure saying the answer would “depend on your perspective” and “not sure... need to know Number Needed to Treat for benefit as well as would like to have Quality of Life data”
- ❖ One group questioned the question. “What line are we referring to? Cost/QALY? What Dollar/QALY is the line? Oncologists do not consider even \$200,000/QALY as inappropriate”

## Next Forum

Our next Applied Pharmacoeconomic and Outcomes Research Forum will be held on **Monday May 14<sup>th</sup> 2007**. The topic will be related to **Quality Adjusted Life Years (QALY's)** as voted on by attendees at the October Forum. Final date and time are to be determined.

With the success of our first two Forums, we are on our way to accomplishing the Forum's second goal of fostering the creation of a broad, multi-perspective Pharmacoeconomic and Outcomes Research Interest Group in our region.

## Purpose of the Forum

The number of individuals in the Southern California region with interest in pharmacoeconomics (PE) is growing rapidly across the healthcare system - from those involved with creation of PE data within pharmaceutical and biotech companies to those incorporating results into decision making within a plethora of managed care organizations. The region provides an excellent opportunity to gather individuals to debate issues, and propose solutions that are vetted from multiple perspectives – not just individual silos defined by employer.

The Applied Pharmacoeconomic and Outcomes Research Forum was created to facilitate this cross perspective communication. The goals of the forum are to:

1. Discuss commonly encountered obstacles to conducting or utilizing results of applied pharmacoeconomic studies and explore solutions from various perspectives of the health care system.
2. Create an environment and foundation to foster the creation of a Southern California Pharmacoeconomic and Outcomes Research Interest Group

Our committee members representing major perspectives of the healthcare system are:

Charles Daniels, R.Ph., Ph.D.  
UCSD Healthcare Department of Pharmacy

Jan D. Hirsch, R.Ph., Ph.D.  
UCSD, Skaggs School of Pharmacy  
& Pharmaceutical Sciences

Anthony P. Morreale, Pharm.D., MBA, BCPS  
VA San Diego Healthcare System

Robert Schoenhaus, Pharm.D.  
UCSD Healthcare Department of Pharmacy

Ted Ganiats, MD  
UCSD School of Medicine

Mirta Millares, Pharm.D., FCSHP, FASHP  
Kaiser Permanente – CA Regions

Frank J. Papatheofanis, MD, MPH, PhD  
Aequitas

Ray Townsend, Pharm.D.  
Elan Pharmaceuticals, Inc.

The Forum is only one of the activities in our larger effort to promote the application of pharmacoeconomic and outcomes analyses to provide timely, actionable data for enhanced decision-making regarding the value of pharmaceuticals and medication related services for key across stakeholders in the U.S. health care system. Other activities include education, training, research, and dissemination activities, including Continuing Education Programs to support this goal.

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**The Case of Expenzumab (Vegitin™)**

**FDA-approved indication:**

Expenzumab is a genetically engineered murine/humanized monoclonal antibody that binds to circulating Vascular Endothelial Growth Factor (VEGF) inhibiting angiogenesis. Expenzumab is approved for use in combination with intravenous 5-fluorouracil-based chemotherapy for first-line treatment of metastatic colorectal carcinomas.

**Dosing and Administration:**

Expenzumab is infused intravenously. Infusions are given in an outpatient setting. The dose of expenzumab is 5-10 mg/kg. The dose is repeated every 14 days until disease progression or toxicity. Studies show that expenzumab can halt progression of disease up to one year. Patients could potentially be on this regimen for up to one year.

**Efficacy - Metastatic colorectal carcinoma studies:**

1. A multicenter, prospective, randomized, phase III study compared IFL (irinotecan, 5-fluorouracil, lecovorin) with standard dosing to IFL at identical dosing + expenzumab in metastatic colorectal cancer. Time to progression in the IFL + placebo arm was 7.2 months compared to 12.6 months ( $p < 0.001$ ) in the IFL + expenzumab arm. Median survival was 15.6 months in IFL + placebo and 21.3 months ( $p < 0.001$ ) with addition of expenzumab.
2. A multicenter, randomized, phase III trial of 5FU/LV (5-fluorouracil, lecovorin) dosed with Roswell Park protocol to 5FU/LV at identical dosing + expenzumab in metastatic colorectal cancer. Time to progression in the 5FU/LV + placebo arm was 5.2 months compared to 10 months in the 5FU/LV+ expenzumab 5mg/kg arm and 12.2 months in 5FU/LV + expenzumab 10mg/kg ( $p < 0.001$ ). Median survival was 13.8 months in 5FU/LV + placebo and 19.5 months with addition of expenzumab 5mg/kg and 20.1 with addition of expenzumab 10mg/kg ( $p < 0.001$ ).

**Safety:**

Phase III studies showed an increase in side effects with expenzumab therapy as compared to standard chemotherapy regimen. Serious events were more common in expenzumab therapy and include GI perforations and arterial thromboembolic events. Recently, the manufacturer announced warnings of an increased risk of GI perforations and arterial thromboembolic events, some fatal, during expenzumab therapy.

**Payer:**

As with all cancer injectables and biologics expenzumab is covered under Medicare part B. Patients will be required to pay 20% of the Medicare approved amount.

**Conclusion:**

Expenzumab has been shown to halt progression of disease by up to 6 months longer when added to standard therapy and to increase median survival by up to one year with addition to first line 5-fluorouracil based chemotherapy. There are increased risks associated with expenzumab. Risks of GI perforation and arterial thromboembolic events are increased by 60% with addition of expenzumab therapy. While risks are very rare they have been fatal in half of the patients affected. Expenzumab therapy is five times more costly than standard therapy. Medicare will require patients to pay 20% of both drugs which with addition of expenzumab could increase costs for patients up to thousands of dollars a month.

### Acquisition Costs:

Drug	Daily Dose	FSS Cost/Week (\$)*	FSS 6 week Cost (\$)*	AWP Cost/Week (\$)*	AWP 6 Week Cost (\$)*	6 Week Medicare Cost of Drug to Patient (20%)
IFL	Irinotecan 125 mg/m2 IV qweek LV 20mg/m2 5FU 500mg/m2 qweek x 4 of every 6 weeks	\$1086.51	\$4346.04	\$1923.82	\$7695.28	\$1539.06
IFL + Expenzumab (5mg/kg)	Irinotecan 125 mg/m2 IV qweek LV 20mg/m2 5FU 500mg/m2 qweek x 4 of every 6 weeks Exp 5mg/kg q 14 days	\$3648.86	\$9470.74	\$6459.18	\$25,836.72	\$5167.34
5FU/LV (Roswell Park)	LV 500mg/m2 5FU 500mg/m2 qweek x 6 of every 8 weeks	\$43.09	\$258.54	\$91.38	\$548.28	\$109.66
5FU/LV (Roswell Park) + Expenzumab (5mg/kg)	LV 500mg/m2 5FU 500mg/m2 qweek x 6 of every 8 weeks Exp 5mg/kg q 14 days	\$2605.44	\$5383.24	\$4626.74	\$9619.00	\$1923.8
5FU/LV (Roswell Park) + Expenzumab (10mg/kg)	LV 500mg/m2 5FU 500mg/m2 qweek x 6 of every 8 weeks Exp 10mg/kg q 14 days	\$5167.79	\$10,507.94	\$9162.10	\$18,689.72	\$3737.94

\*Cost based on 80kg/ BMI 1.7  
 FSS = Federal Supply Schedule  
 AWP = Average Wholesale Price

Drug	AWP Price	FSS Price
Expenzumab 100mg vial (25mg/ml):	\$868.36	\$490.60
Expenzumab 400mg vial (25mg/ml):	\$4535.36	\$2562.35
Fluorouracil 500mg vial (50mg/ml):	\$30.73	\$17.82
Leucovorin 500mg vial (10mg/ml):	\$14.96	\$8.45
Irinotecan 40mg (20mg/ml):	\$308.02	\$174.02
Irinotecan 100mg (20mg/ml):	\$769.42	\$434.70