Evidence-Based Formulary Decision-Making

Doris J Kao, PharmD, BCPS
Supervisor, Drug Information Services
Coordinator, TPMG Regional P&T Committee
Kaiser Permanente – CA Regions

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Objectives

- Be able to differentiate between a *formulary* and a *formulary system.*
- Explain the role of the P&T Committee in a Formulary system.
- Identify resources used to support evidence-based decision-making.
- Describe current trends in FDA approvals.
- Understand the value of comparative effectiveness and outcomes research.

Kaiser Permanente

- Not-for-profit integrated health care system
  - Kaiser Foundation Health Plan Inc.,
  - Kaiser Foundation Hospitals
  - Permanente Medical Groups (in NCAL: TPMG)
- 7 regions
- 10 million members
- 38 hospitals
- 618 medical offices
- >17,000 physicians

Drug Information Services

- Part of CA Pharmacy Care Support Services
  - Staff in Oakland and Downey
- Supports a multitude of information needs for KP health care providers, members and the medical care program.
- Various services provided nationally.
- All products shared nationally.

Scope of Services

Evidence-based Medicine

"The conscientious, explicit, and judicious use of the best current evidence in making clinical decisions about the care of individual patients."

Eddy D. Evidence-based medicine. What it is, why use it, and how to incorporate it into decision-making. Formulary 2002; 525-6, 529-30.

Evidence-based Medicine

"Evidence-based medicine is a systematic approach to the evaluation of biomedical literature and application to clinical practice and should be applied to formulary decision-making….

"Evidence-based decision-making standardizes and improves the quality of patient care and promotes cost-effective prescribing."

American Society of Health-System Pharmacists. ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. Am J Health-Syst Pharm. 2008; 65:1272–83.

Formulary

"A **formulary** is a continually updated list of medications and related information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis, prophylaxis, or treatment of disease and promotion of health.

…includes, but is not limited to, a list of medications and medication-associated products or devices, medication-use policies, important ancillary drug information, decision-support tools, and organizational guidelines."

American Society of Health-System Pharmacists. ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. Am J Health-Syst Pharm. 2008; 65:1272–83.

KP Formularies

Commercial	Medicare Part D	ACA Exchange
▪ Medications provided or administered to commercial plan members in KP patient care settings (clinic, inpatient, outpatient) ▪ Maintained under authority of the Regional P&T Committee	▪ National - Outpatient Medicare Prescription Drug Benefit ▪ Maintained by the KP Interregional Medicare Part D P&T Committee (iMPacT) ▪ Subject to CMS regulations	▪ New - Jan. 1, 2014 ▪ Affordable Care Act (ACA) Exchange Formulary ▪ Maintained under authority of TPMG and SCPMG Regional P&T Committees ▪ Subject to federal and statewide regulations for QHPs
Regional	National	Statewide

NCAL Region Sub-Formularies

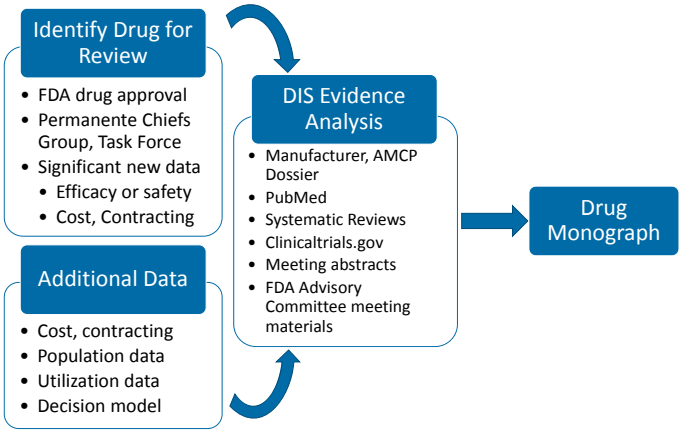
Optometry	Compounding
▪ List of Formulary agents approved for use by TPMG Therapeutic Pharmaceutical Agent (TPA) certified Optometrists	▪ Evidence-based formulations recommended by the appropriate Chiefs of Service groups & approved by Regional P&T. ▪ Purpose is to reduce variation in product RXs, identify & eliminate problem practices, reduce costs, & improve patient care

"A **formulary system** is the ongoing process through which a health care organization establishes policies regarding the use of drugs, therapies, and drug-related products and identifies those that are most medically appropriate and cost-effective to best serve the health interests of a given patient population.

"The **Pharmacy & Therapeutics (P&T) committee** is responsible for managing the formulary system."

American Society of Health-System Pharmacists. ASHP guidelines on the pharmacy and therapeutics committee and the formulary system. Am J Health-Syst Pharm. 2008; 65:1272–83.

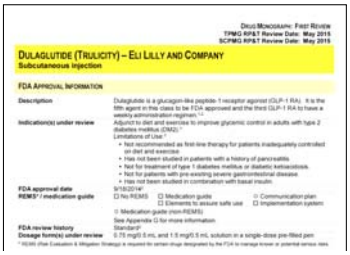
KP Formulary Process



Elements of a KP Drug Monograph

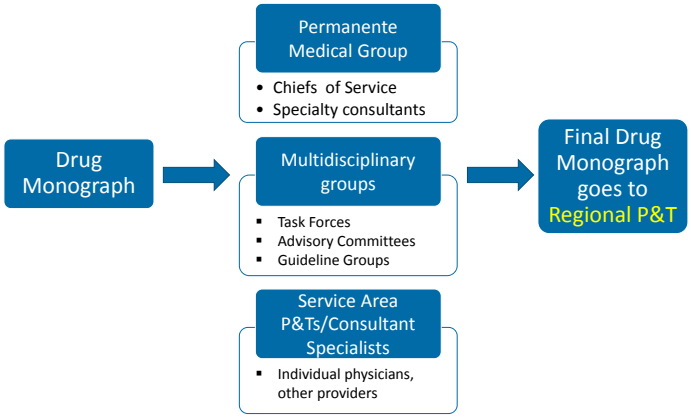
Monograph (selected)
- FDA Approval Information
- Issues to be Determined
- Efficacy Summary
- Safety
- Other Considerations
- Special Populations
- Potential Off-Label Uses
- Pharmacology, MOA, dosing, storage
- Comparative Cost of Therapy
- Projected Role in Therapy

Monograph Appendices (selected)
- Clinical Trial Analysis
- Current Therapeutic Modalities
- Disease State Review
- FDA Review History
- REMS Summary


DULAGLUTIDE (TRULICITY) – ELI LILLY AND COMPANY
Subcutaneous injection

FDA APPROVAL INFORMATION

KP Formulary Process



TPMG Regional P&T Committee

Physician Members TPMG

TPMG Executive Liaison Associate Executive Director, TPMG

Pharmacy Liaison VP, Pharmacy Programs and Services, NCAL Region

- **Voting Membership**
  - Local P&T Chiefs, KPNC Medical Centers
  - TPMG Physician Lead – Pharmacy, CA Regions
  - VP, Pharmacy Strategy and Operations
- **Committee Officers**
  - Elected Physician Chair
  - Secretary of Record (RPh)
  - Subcommittee Physician Chairs
    - Formulary Subcommittee
    - Pharmacy Education Subcommittee
    - MUE Subcommittee
    - BEPTAC (Biotechnology and Emerging Pharmaceutical Technology Assessment Committee) Subcommittee
  - Nursing Services (non-voting)
    - Chair, Nurse Practitioner Regional Committee

- **Assistant Pharmacy Ops Leaders**
- **Regional Inpatient Pharmacy Director**
- **Pharmacy Mgr Peer Group Liaisons**
  - Area Pharmacy Director
  - Inpatient Pharmacy Director
  - COM and DEC
  - Outpatient Pharmacy Director

Drug Use Management Leader, NCAL

Director, Drug Information Services

Director, Pharmaceutical Contracting and Strategic Purchasing

Pharmacist Evidence Analysis and Strategy (PEAS) Team Drug Information Services

KP Formulary Process

- Permanente Medical Group P&T decisions

Final Drug Monograph goes to Regional P&T

Formulary Status
- Formulary
- Non-Formulary
- Tiers (MPD)

Additional Stipulations
- Restrictions
- Guidelines
- Limited quantities

Electronic Health Record
- Decision support

Other recommendations
- MUE
- Re-review date
- Utilization data
- CER

Challenges of an Evidence-based Process

- Time and resource intensive
- Skills required to perform critical clinical data analysis
- Flaws in evidence available
- Lack of definitive evidence
- Funding and sponsorship of research
- Conflicts of interest (COI)

Challenges of an Evidence-based Process

- Room for expert opinion and consensus recommendations
- Ghost-writing
- Selective outcome reporting
- Suppression and “spinning” of negative data
- Incomplete disclosure
- Pharma’s influence of academia, both faculty and institutions
- “Thought-leaders” promotion of off-label uses

FDA Approval Trends/Challenges

- FDA meets or exceeds Prescription Drug User Fee Act (PDUFA) goals
- Greater first cycle approvals, less "complete response letters"
- Risk Evaluation and Mitigation Strategy (REMS) & Elements To Assure Safe Use (ETASU) - High risk drugs with significant safety concerns
- Post-marketing study requirements, some leading to approval withdrawal
- More accelerated approvals and breakthrough designations

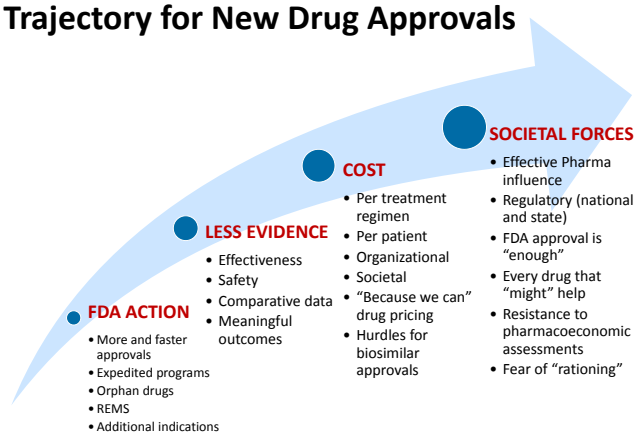
FDA Safety and Innovation Act (FDASIA)
July 9, 2012

- Provision for "Breakthrough Therapy" designation
  - "helps FDA assist drug developers to expedite the development and review of new drugs with preliminary clinical evidence that indicates the drug may offer a substantial improvement over available therapies for patients with serious or life-threatening diseases"
- 2014 Guidance "Expedited Programs for Serious Conditions – Drugs and Biologics"
  - Defines (expands) "unmet medical need"
  - Surrogate endpoints or an intermediate clinical endpoint

Fast Track	Breakthrough Therapy
Accelerated Approval	Priority Review

http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDASIA/#innovation

Trajectory for New Drug Approvals



When published data are not available or the evidence is not strong…

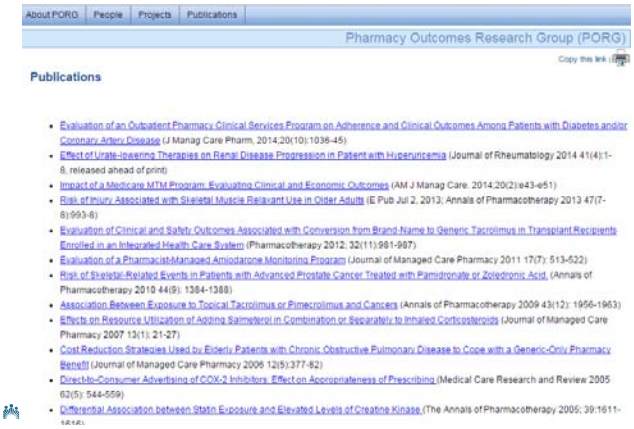
- Consensus-based recommendations/opinion
- Expert panels
- Internal prescribing and utilization data
- Internal outcomes research
- External benchmarking programs

Scope of Services

Pharmacy Outcomes Research Group (PORG)

- Provides research support throughout California
  - Support CFS, consultation with pharmacy researchers
- Addresses key questions in the areas of
  - Impact of pharmaceuticals on health care resource utilization and clinical outcomes
  - Cost effectiveness of pharmaceuticals
  - Medication safety
  - Evaluation of intervention tools
- Supports Drug Use Management initiatives for California and ICPSS (interregional)
- Collaborations with DOR, R&E, and outside researchers

Pharmacy Outcomes Research Group (PORG)



Comparative Effectiveness Research (CER)

"…compares the results of one approach for managing a disease to the results of other approaches

"…designed to inform health-care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options. The evidence is generated from research studies that compare drugs… to deliver health care."

AHRQ

KP Formulary Process
Post P&T Review – CER, Utilization

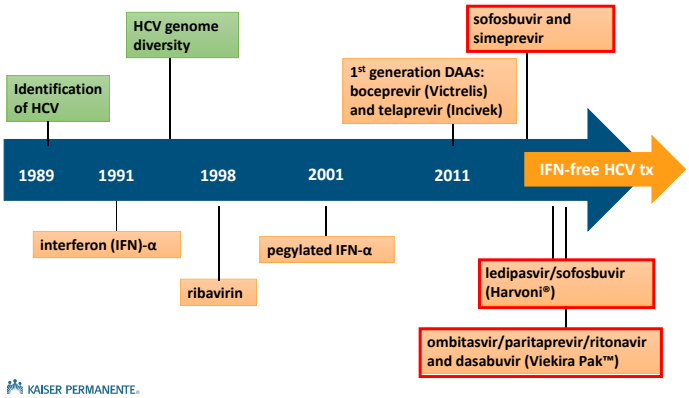
- Integrated health care system and EHR provide opportunity to gather real world outcomes data in our population.
- In addition to comparative efficacy, CER can provide institution-specific data on
  - Medication adherence and persistence
  - Adverse events
  - Subpopulations
  - Resource utilization
  - Total health care cost

KP Formulary Process
Post P&T Review – CER, Utilization

- CER data can be used to
  - Support, repeal, or modify formulary status
  - Inform contracting
  - Identify subpopulations
  - Identify safety issues
  - Inform prescribing

KP CER Example:
Hepatitis C Treatments

Hepatitis C Virus (HCV) Treatment Milestones



KP CER Example: Boceprevir and Telaprevir

- Approved late 2011
- RCTs vs best available therapy; no boceprevir vs telaprevir CER
- Contracting potential
- KP IR Hepatitis Workgroup
  - Guideline development
  - PORG CER Study
- Formulary status with implementation date pending future recommendations
- Drug Use Management

BOCEPREVIR VS. TELAPREVIR IN HEPATITIS C INFECTIONS

Jim Chan, PharmD, PhD
Rita Hui, PharmD, MS
Michele Spence, PhD
Mirta Millares, PharmD
Pharmacy Outcomes Research Group
Drug Information Services

Study Purpose

- To evaluate the relative effectiveness of boceprevir and telaprevir in genotype 1 hepatitis C infection in KP California
  - Phase 1 : early indicators of comparative effectiveness and safety
  - Phase 2: SVR and development of a predictive model based on patient characteristics and treatment selection

Study Design and Setting

- Concurrent data collection
- Retrospective cohort analysis
- Population
  - all patients initiated on boceprevir or telaprevir
- Data sources
  - KPNC and KPSC
  - Legacy data and HealthConnect

Outcome Measures for Early Interim Analysis

- Primary
  - Proportion of patients who reached early undetectable viral load
- Secondary
  - Proportion of patients with an initial 2 log drop in viral load
  - Proportion who discontinued treatment
  - Proportion who initiated treatment with erythropoietin

Early Interim Analysis

- Proportion of patients reaching early undetectable viral load not significantly different
  - TEL earlier with BOC catch-up with treatment completion
  - Greater difference was between regions, not drug
- Proportion of patients with an initial 2 log drop in viral load
  - Trend for TEL, NS
- Proportion who discontinued treatment
  - NS
- Proportion who initiated treatment with erythropoietin
  - Significantly higher for BOC
- Consequences:
  - Evaluation of care management differences
  - Guideline endorsement
  - Coordinated care management

KP CER Example: ledipasvir/sofosbuvir and sofosbuvir

Study Objectives

1. Explain the comparative effectiveness and safety of the second-generation direct-acting antivirals (DAAs)

Sofosbuvir	LDV/SOF (Harvoni)

2. Estimate the cost effectiveness of the second-generation DAAs compared with the first-generation DAAs

2nd generation DAAs	Sofosbuvir
	LDV/SOF (Harvoni)
1st generation DAAs	Telaprevir
	Boceprevir

Methodology

- **Data**
  - Pharmacy information management system
  - Laboratory utilization review results
  - Electronic medical records
- **Effectiveness Endpoints**
  - Primary: composite of SVR12/EOT
    - Sustained Viral Response (SVR)12: 12 weeks after the completion of therapy or,
    - End of therapy (EOT) virologic response
      - Undetectable ≤25 IU/mL
  - Secondary:
    - Rapid virologic response (RVR): within 35 days of therapy initiation
    - Time to first undetectable viral load
- **Safety Endpoints**
  - Primary: Premature discontinuation
- **Pharmacoeconomic Analysis**
  - Estimated cost effectiveness of sofosbuvir and LDV/SOF (Harvoni)

Conclusions

- There was significant difference in EOT/SVR12 achieved between LDV/SOF (Harvoni) and sofosbuvir (OR=20.8, 95% CI 4.78 – 90.6, p<0.001).
- There was no significant difference in RVR achieved between LDV/SOF (Harvoni) and sofosbuvir.
- Baseline viral load affects both RVR achieved and time to first undetectable viral load.
- Discontinuation rate was low for both LDV/SOF (Harvoni) and sofosbuvir with no statistically significant difference but favors Harvoni.

Recap

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