台北醫學大學・雙和醫院
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EVALUATION OF DRUGS FOR FORMULARIES

新藥審查

P & T committee

- Develop and maintain a drug formulary system
- Formulary: promoting optimal pharmacotherapy because it contains only those drugs **judged by the P&T committee** to be in the best interest of the patient' health needs in terms of **efficacy and cost**

New Drug Request Procedure in TMUHs affiliated hospitals

聯合新藥申請作業程序

(一) 新進藥品申請原則:

1. 兩院每位專任主治醫師申請新進藥品每兩年僅限一項，新到任醫師或新設科別(以第一年為限)得另提專案處理。
2. 為管控兩院用藥總品項數，新藥申請要有取代品項。
3. 新藥理機轉或新臨床用途之新藥，經兩院新藥初審小組及藥劑部認定後，可特別申請，無需取代品項。
4. 各類新藥提案時程：

類別	提案時程
心血管及呼吸系統用藥	元月
止痛/消炎/消化/外用藥	三月
抗微生物製及疫苗	五月
神經及精神用藥	七月
荷爾蒙及代謝用藥	九月
血液腫瘤及免疫用藥	十一月

5. 新藥申請作業時程

作業預計時程	內 容	方 式
單月 1~15 日	1.新進藥品申請	兩院專科主治醫師填寫「新進藥品申請表」，送至兩院臨床各科部主任。
	2.各科部室初審(決定提案品項)	今年由萬芳各科(部)室主任召集提藥協調會議
單月 16 日~雙月 15 日	1.萬芳藥劑部彙整評估	1. 各科部室協調完畢後，將新藥提案及會議記錄送交萬芳藥劑部藥品管理組。 2. 臨床藥學組準備評估資料。
	2.新藥初審小組完成初審	1. 由六組新藥初審小組分案初審。 2. 提藥醫師需於初審會議報告藥品評估資料。
雙月 16 ~30 日	1.向藥委會正式提案審查	藥劑部整理新藥初審小組審查結果。
	2.藥委會完成新藥審查	1. 每月不定期召開聯合藥委會審查。 2. 提藥醫師需於藥委會報告藥品評估資料。 3. 藥委會決議進用之品項，經議價小組議價完成後執行。 4. 若有價格疑義者，則呈回藥委會再行討論，通過後才得正式進用。

Request for Formulary Consideration Form

- Date and time of request
- Name of product (e.g., generic, trade, chemical)
- Source of product (e.g., manufacturer, distributor)
- Specific information about drug product (e.g., class of drug, mechanism, adverse effects, clinical studies)
- Anticipated use of drug (e.g., what type of patient, how often)
- Comparable drugs already on the formulary
- Why the product is needed
- What drugs could be removed from the formulary
- What restrictions, policies, cautions, etc., are necessary
- How the drug fits into any clinical guidelines
- Action Requested (e.g, addition, deletion, restriction)

Request for Formulary Consideration Form

→ 實例

Types of drug reviews- 1.

- ***New drug monographs***
  - When FDA approves this new drug for marketing.
  - New chemical entities warrant a thorough evaluation and a written drug monograph.
  - A short (1 page) summary along with the full monograph. Or an executive summary format
  - A new drug that is therapeutically equivalent to agents already available on the formulary may use a abbreviated manner.

Types of drug reviews- 2.

- ***Addenda to original monographs used to reevaluate previous formulary decisions***
  - An addendum to the original monograph (new data on safety, efficacy, stability, methods of administration, cost, or pharmacoeconomics) warrants a reevaluation of the drug or dosage strengths or formulation stocked by the health system.

Types of drug reviews- 3.

- ***Therapeutic class reviews***
  - Should include all formulary & nonformulary meds within the class
  - & institutional utilization or outcomes data and newly published info.
  - May lead to formulary removal of therapeutically equivalent drugs or a change in restriction or guideline status for a drug.

Types of drug reviews- 4.

- ***Expedited reviews (速審)***
  - Rapid approval of a new chemical entity for a disease with no therapeutic alternative for patients who need it.
  - A new safety concern for addition of restrictions or removal from the formulary.

新藥申請，須同時提出院內比較品項

- 取代藥品：院內相似藥理作用品項
- 比價藥品：院內同成分同劑型品項
- 特別申請案：無院內相似藥理作用品項
  - 新藥：新藥理機轉、或新臨床用途

- 理由

(二) 新進藥品申請之審查流程：

1. 專任主治醫師提藥後，將申請表及新藥審查相關資料於院方規定期限內送交各臨床科部主任，由兩院之該醫療科部主任進行初審。
2. 科內初審通過後，由兩院藥劑部成員進行文獻查證及經濟效益比較，經兩院藥委會新藥初審小組(共六組)詳細討論，作成初審意見。
3. 初審意見為通過之藥品，提藥醫師需於兩院聯合藥委會以投影片說明，其報告內容必需包括本院同類及同療效藥品之療效、安全性及經濟效益之比較。報告內容必須使用無偏見之文獻證據，不得直接使用廠商之資料。
4. 兩院聯合藥委會根據初審意見、提藥醫師報告及藥委之意見，作成結論。

(三) 新進藥品申請之審查原則：

1. 兩院藥劑部依臨床及經濟之考量，排定審查之優先順序及時程。
2. 提出申請之新藥必需於療效、安全性及經濟效益上優於擬取代品項，才可通過。
3. 兩院藥劑部須進行 Financial Impact Analysis(FIA)，充分探討經濟面之影響。
4. 為避免後線新藥之過度使用，使病患之治療符合實證醫學之治療準則，後線新藥之採用建議以非處方集品項為原則。若臨床有特殊案例，循緊急採購以個案審查方式通過。必要時需提出限制性使用條件，以降低後線新藥個案審查之困難及爭議。

新藥審查原則教戰

- 了解流程→ 藥委會新藥提藥時程
- 審查方式→ 單月15日藥庫將廠商資料給各主審藥師、分配品項、評讀文獻、寫-「新藥審查評估單」、作比較表、跑平均月用量、問相關醫師意見、問議價會議是否開完
- 初審小組開會前準備→ 統整三院平均月用量及醫師意見、新藥審查評估單email三院、連絡三院醫師時間、確定會議時間、發三院開會通知、借會議室、向事務組訂便當
- 初審小組(subcommittee)→ 帶開會簽到單、錄音筆、便當、新藥審查評估單影本
- 初審小組開會後 →會議記錄及決議 寄給藥庫
- 藥委會(P&T)→ 報告初審決議

Drug-evaluation document

- A written document with a standard format (eg., a drug monograph, drug review, drug-evaluation document) should be developed by the pharmacy and provided to the P&T committee.

新進藥品評估表

1. 作用類似之藥品
2. FDA核准
3. SCI文獻證實其療效
4. 醫學中心使用
5. 嚴重副作用/交互作用
6. 給藥方便性/病患依從性
7. 臨床上可適用之病人
8. 與同類藥品相比，此藥之每日(或療程)藥費
9. 藥品外觀或名稱與現有品項相似
10. 提藥時有無 取代 / 比價藥品
11. 三院有無緊急採購使用之經驗

雙和醫院・台北醫學大學附設醫院・萬芳醫院

聯合藥事委員會

新進藥品評估表

商品名	學名	劑量/劑型	臨床用途	健保價/ 每日藥費
提藥醫師				
申請理由				

評估項目			備註
1.作用類似之藥品(請註明)	無	有	
2.FDA 核准(若填否時，請註明核准上市國家)	是	否	
3.SCI 文獻證實其療效 (若為學名藥時請註明有無臨床試驗 data)	有	無	
4.醫學中心使用(請註明)	有	無	
5.嚴重副作用/交互作用(若有,請說明) 與同類藥品相比有無不同	無	有	
6.給藥方便性/病患依從性(若高,請說明)	高	低	
7.臨床上可適用之病人(若多,請說明)	多	少	
8.與同類藥品相比，此藥之每日(或療程)藥費(see FIA)	較低	較高	
9.藥品外觀或名稱與現有品項相似(若有,請說明)	無	有	
10.提藥時有無 取代 / 比價藥品	有	無	
11. 兩院有無緊急採購使用之經驗(若有,請說明)	有	無	

評估意見:

新進藥品評估表

- Efficacy
- Safety
- Financial Impact Analysis (FIA)
- Reference

→實例

初審小組意見：
Efficacy(Outcome Indicators)
Safety (Toxicity Profile with Incidence rates)
Financial Impact Analysis (FIA)
References

評估藥物的重點：

- 新藥在使用上是否安全
- 新藥與原本品項比較是否有療效或安全上的優越性
- 其他考慮
- 若在安全上與療效上，新藥都與原本品項相似，則可考慮是否有經濟上的優越性

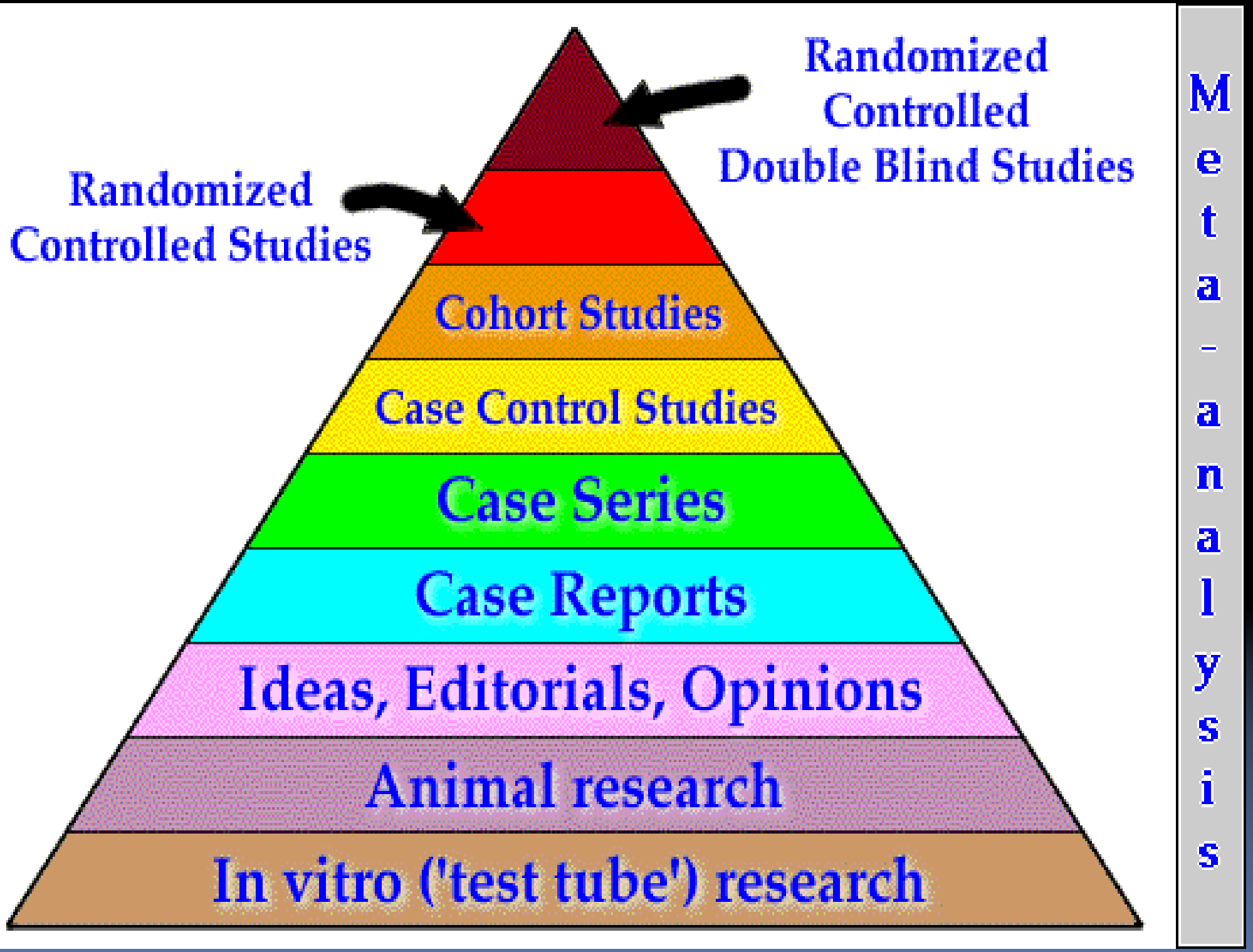
Evaluating medications for inclusion in the formulary

- The P& T committee should use a structured, evidence-based process in the evaluation.
- P& T should provide information that reflects a thorough, accurate, and unbiased review and analysis of the evidence available in the scientific literature.
- Pharmacists should play an integral part in the preparation and presentation of the drug review document to the P&T committee.
  - Expertise and training of pharmacists (drug information specialists in particular)

Evidence-based evaluation

- Stronger evidence (meta-analyses, RCT) should drive decisions; other types (case-control, cohort, case reports, consensus opinions) may be appropriate when stronger evidence is not available.
- May incorporate expert opinion when published data are not available. (expert sometimes access to unpublished data).
  - Should clearly identified in the review if adopted.
- Internal data and prescribing & outcome information.
- Use formulary packets and dossiers prepared by pharmaceutical manufacturers.

RCT: randomized controlled trials


Randomized Controlled Double Blind Studies
Randomized Controlled Studies
Cohort Studies
Case Control Studies
Case Series
Case Reports
Ideas, Editorials, Opinions
Animal research
In vitro ('test tube') research
Meta-analysis

選擇studies的方法：

- 若有與取代品項比較之實驗，則可選用。
- 若有與治療該項疾病的gold standard比較之實驗，則可選用。
- 若無上兩類實驗，但有與其他治療該項疾病的藥物比較之實驗，則可選用。
- 若無以上類似實驗，則可以與placebo比較之實驗來評估。

評讀studies時需注意

- 實驗組與對照組使用的劑量是否在功效上是相似的
- 病人族群大小, follow up的時間長短
- 病人族群與本院病人族群相似度
- 實驗設計是否客觀

參考各國HTA (Health Technology Assessment)評估建議

- The International Network of Agencies for Health Technology Assessment (INAHTA): http://www.inahta.org/
- The Canadian Agency for Drugs and Technologies in Health (CADTH): http://www.cadth.ca/index.php/en/home
- The Pharmaceutical Benefits Advisory Committee of Australia (PBAC): http://www.health.gov.au/internet/main/publishing.nsf/content/health-pbs-general-listing-committee3.htm
- Cochran Review

→實例

Pharmacoeconomic assessments

- When new meds having equivalent efficacy and safety to existing alternatives, then the cost-minimization approach is appropriate.
  - Cost-effectiveness analysis (clinical outcome)
  - Cost-utility evaluations (QOL adjusted clinical outcome)
- Consider costs associated with drug and non-drug related costs (costs of administration, monitoring, prolonged hospital stay, lab test monitoring)
- Incorporating local data when published data are limited or unavailable
  - Institution-specific costs are often different from the costs used in published studies.

Recommended by UHS or ASHP

P&T MONOGRAPHS TEMPLATE – ELEMENTS OF A DRUG EVALUATION DOCUMENT

Elements of a drug-evaluation document__ASHP

- **Brand and generic names and synonyms**
- FDA approval information, including date and FDA rating
- Pharmacology and mechanism of action
- **FDA-approved indications**
- Potential non-FDA-approved (offlabel) uses
- **Dosage forms and storage**
- **Recommended dosage regimens**
- Pharmacokinetic considerations
- Use in special populations (e.g., children, elderly, patients with renal or liver failure)
- Pregnancy category and use during breast-feeding**,**
- **Comparisons of the drug's efficacy, safety, convenience, and costs with those of therapeutic alternatives (with evidence tables when feasible)**
- **If information on comparative efficacy is minimal or lacking, data on absolute efficacy (i.e., efficacy versus placebo)**
- Clinical trial analysis and critique
- **Medication safety assessment and recommendations** (adverse drug reactions; drug–drug and drug–food interactions; specific therapy monitoring requirements; unusual administration, storage, or stability issues; and potential for medication errors, such as look-alike or sound-alike issues)
- **Financial analysis,** including pharmacoeconomic assessments

P&T Monographs Template

A.	**Header Elements**
	•Hospital name •Pharmacy and Therapeutics Committee •Date •Generic and proprietary names of monograph •Name of clinician sponsoring request •Name of person preparing monograph

UHC (University Hospitals Consortium)
ASHP

B. Monograph Sections

1. Executive Summary

- Summary of main therapeutic and clinical considerations
- Patients safety assessment summary
- Ranking of overall potential for errors to happen as a result of adding drug to the formulary
- Summary of therapeutic arguments for/against formulary addition
- Summary of safety-related arguments for/against formulary addition
- Recommendation regarding addition to the formulary addition
- Recommendations regarding follow-up review (eg., 6 month minireview focused on to-date usage, economic impact, institution-reported ADRs/errors, and literature-based summary assessment of safety trends related to drug)

1. Executive Summary Cont's

- Bulleted list of actions/decisions needed prior to initial use

  a. Considerations for safe prescribing (eg, education of prescribers)

  b. Considerations for safe handling by pharmacy (purchasing, pharmacy storage, dosage form preparation and labeling, dispensing [eg, education of pharmacy staff about expected use, precautions, admixture, special handling, etc.])

  c. Considerations for safe handling by nursing (storage, administration, and assessment of response [eg, education of nurses about drug storage and administration; development of patient teaching materials])

2.	Drug Name Consideration
	•Generic name and pronunciation guide •Proprietary name and manufacturer •Other relevant synonyms or abbreviations •Names and formulary status of drugs with **similar sounding (or similarly spelled)** •Other patient safety considerations related to drug name
A S H P	Generic name: • List the officially approved name of all chemical entities in the drug product. Trade name(s): • List the most common trade name(s) of the drug product.

3. Clinical Indications and Expected Use

- Therapeutic classification
- FDA-approved indications(s)
- Names of drugs already on formulary for the same or similar indications, including their main limitations and/or advantages
- Inclusion current practice guidelines (or likelihood of inclusion in future)
- Non-FDA-approved uses
- Assessment of the relative importance of non-FDA-approved uses
- Patient safety considerations related to off-label uses of this drug (eg., need to obtain patient consent)

3.	Clinical Indications and Expected Use Cont's
ASHP	Therapeutic indications: • State the uses of the drug as approved by the FDA; indicate whether the use is prophylactic, therapeutic, palliative,curative, adjunctive, or supportive. • Evaluate uses of the drug in comparison with other established forms of therapy, using, if possible, human studies for comparison. Comparisons should emphasize therapeutics (efficacy,incidence of treatment success, remission, sensitivity, ease of monitoring, and treatment periods required) and include a critical analysis of clinical studies in such areas as patient population, methodology, statistics, and conclusions. • Identify non-FDA-labeled uses for the drug and those uses that show promise in investigational studies.

4.	Chemical and Pharmacologic Classifications
	• Chemical name and structure • Pharmacological classification • Mechanism of action • Names and formulary status of drugs with similar chemical structures • Known safety concerns with other members of this pharmacological drug class •Evidence regarding comparative safety of this drug relative to other members of this pharmacological drug class
A S H P	Pharmacologic Considerations: • State the pharmacologic class to which the drug belongs and any similar properties it possesses compared with existing drugs. • State the mechanism of action; if the mechanism of action is unknown, state this. If applicable, the mechanism of action may be compared with that of another drug or class of drugs.

5.	Pharmacokinetic Considerations
	• Absorption • Distribution Implications for breastfeeding • Metabolism Prodrug implications Cytochrome P450 considerations • Excretion • Patient safety considerations related to the pharmacokinetic profile of drug

5.	Pharmacokinetic Consideartions
A S H P	•List bioavailability data for the most common route of administration and dosage of the drug.Other bioavailability data should be available on request by the P&T committee. • List pharmacokinetic data for absorption, distribution,metabolism, and excretion of the drug. For absorption, include information on the extent and rate of absorption of the drug by the usual routes of administration; the factors that might affect the rate or extent of absorption; the therapeutic, toxic, and lethal blood levels; the period of time required for onset, peak, and duration of therapeutic effect; and the half-life and factors affecting it. For distribution,include information on the usual distribution of the drug in body tissues and fluids, the drug's propensity to cross the blood–brain barrier or placenta or to appear in human milk, the drug's propensity for protein binding, and the drug's volume of distribution.For metabolism, include information on sites of metabolism, extent of biotransformation, and metabolic products and their activity. For excretion,include information on routes of elimination from the body, factors affecting elimination, and the form in which the drug is eliminated.

6.	Efficacy Assessment
	• Assessment of the overall quantity and quality of data regarding the efficacy of drug • Summary of evidence for efficacy form the FDA-approved product labeling • Summary of evidence for efficacy form published clinical trials not included in the product labeling • Summary of evidence for efficacy form all other information sources

7.	Toxicity Assessment
	• Approximate extent of patient exposures to the is drug to date (number of patients and duration of exposure) • Summary of adverse drug reactions described in the FDA-approved product labeling •Summary of adverse drug reactions described outside of the FDA-approved product labeling •Assessment of the ADR and toxicity profile of drug compared with other members of its drug class or other drugs used for similar indications
A S H P	•Discuss adverse effects of the drug and their frequency of occurrence from research data of human studies. • Discuss means or methods of preventing or treating adverse effects and toxicities. Benefits of disease treatment and risks of adverse effects should be emphasized.

8.	Drug-Drug Interaction Considerations
	• Assessment of the adequacy of the data relating to the detection of potential drug-drug interaction • CytochromeP450 considerations predictive of the potential for drug interactions with drug • Other pharmacokinetic or pharmacodynamic considerations predictive of the potential for drug interactions • Summary of drug interactions described in the FDA-approved product labeling for drug • Assessment of the drug interaction potential of drug compared with other members of its drug class or the drugs used for similar indications

9.	Labeled Contraindications, Warnings, and precautions
	• Summary of the labeled contraindications, warnings, and precautions described in the FDA-approved product labeling for this drug • Assessment of the drug interaction potential of drug compared with other members of its drug class or other drugs used for similar indications
ASHP	• List precautions and contraindications for certain disease states or other conditions. • Compare all of the preceding data with existing similar agents, where applicable. • List potential drug interactions if deemed clinically important.

10. Implications for Special Populations

- Pediatric considerations
- Geriatric considerations
- Pregnancy considerations: Pregnancy risk category
- Breast feeding recommendations
- Concomitant disease state considerations:

  Liver dysfunction, Cardiac dysfunction, Lung dysfunction, Renal dysfunction, Mental impairment, Considerations for diabetics, Visual impairment, Hearing impairment, Other concomitant disease state considerations
- Assessment of the comparative safety of drug for special populations compared with similar drugs

11.	Dosage Considerations:
	• Minimum and maximum dose by indication and age-specific parameters (ie, usual, pediatric, and geriatric) • Minimum and maximum dosage level that should trigger communication with the prescriber • Summary of patient safety issues related to drug administration, dosing, or duration of therapy • Evaluation of administration schedule/regarding number of times per day administered
ASHP	• List the dosage range for different routes of administration of the drug. • List initial, maintenance, maximal, geriatric, and pediatric doses for the drug.

12.	Monitoring Necessary to Assess Efficacy and Avoid Toxicity
	• Assessment of the comparative ease of monitoring drug compared with similar drugs

13.	Preparation of Dosage Form for Administration and Other Physical Considerations
	• Classification, strength, and physical description of commercially available dosage forms •Physical description of packaging • Names and physical description of formulary drugs with similar-looking dosage forms or packaging •Assessment of patient safety considerations related to similarities with the dosage forms, packaging, labeling, or physical storage locations of other formulary drugs • Assessment of special safety considerations related to preparation of dosage form for administration to the patient

13.	Preparation of Dosage Form for Administration and Other Physical Considerations Cont's
	• Assessment of special safety consideration related to the administration of the dosage form to the patient a. Assessment of necessity to check dosage calculation prior to dispensing or adminsitration b. Assessment of necessity to control rate of administration via a pump or other administration device c. Assessment of necessity to require special documentation by health care practitioners prior to dispensing or administering the dosage form d. Assessment of necessity to require supplementary educational materials prior to dispensing of administration e. Assessment of safety considerations related to disposal of unused or expired medication f. Assessment of the label for potential consufion
ASHP	• List all dosage forms available as approved by FDA; list unit cost.

14.	Patient Education and Prescriber Considerations
	• Summary of special competencies necessary for health care practitioners to ensure safe prescribing, dispensing, and administration or this drug to patients •Summary of special education necessary to ensure safe medication use by patients •Assessment of need for prescribing restriction, preprinted orders, or computer entry standards, to ensure safe medication prescribing

15.	Cost, Expected Extent of Use, and Pharmacoeconomic Impact
	• Drug cost • Assessment of drug const compared with cost of similar formulary drugs • Insurance coverage (state medication assistance plan and other major insurance plans) • Usage trends to date • Assessment of to-date usage relative to other similar formulary drugs • Budgetary considerations a. Projected annual use and cost (based on current usage, the estimate of requestor, and/or a best-guess factor for growth in usage during the first year on formulary) b. Assessment of annual drug costs compared with the annual cost associated with simiar formulary drugs

16.	Other Issues Related to Drug Safety, Efficacy , Benefits, or Significant Limitations

- Guidelines ofr use and/or plans

a. Assessment of need to incorporate into existing guidelines or patient care plans

b. Assessment of need to develop new guidelines or patient care plans

- Assessment of need for a standardized order form
- Assessment of need for establishing a check system to verify that prescribing follow guidelines or other aspects that require verification
- Assessment of need for reminder system
- Assessment of need for limits on prescribing
- Assessment of need for administration guidelines
- Assessment of need for auxiliary warnings or other label enhancements
- Assessment of need for special computer entry codes
- Assessment of need for special drug storage conditions to avoid errors due to look-alike names/packages falling together alphabetically in storage areas
- Assessment of need for special education plans for practitioner (pharmacists, nurses, physicians)
- Assessment of need to monitor the published literature for evidence of evolving safety concerns related to this drug, including a plan for reporting findings back to the P & T Committee

17.	Supply Issues
	• Drug availability •Currently available form more than one source? •Currently available form wholesaler? •Currently available form manufacturer(s)? More than one manufacturer? •Alternative sources if shortages occur (eg, Canada)
ASHP	• Identify the pharmaceutical vendors from which the drug product can be procured. • For a generic drug product, identify the actual manufacturer; if applicable, identify the vendors distributing the product.

Comparisons	
ASHP	• List therapeutic comparisons with other drugs or treatment regimens. • List cost comparison data of a standard treatment regimen with the new drug versus currently used drugs. • List unusual monitoring or drug administration requirements for the drug.
Other Recommendations	
ASHP	• Formulate recommendations from analysis of all of the preceding data and consideration of other factors such as medical staff preference, distribution problems, and availability of the drug.

本院

- 商品名/學名
- 劑量/劑型
- 臨床用途
- 每日藥費
- 提藥醫師及申請理由
  - 1.作用類似之藥品
  - 2.FDA核准
  - 3.SCI文獻證實其療效
  - 4.醫學中心使用
  - 5.嚴重副作用/交互作用
  - 6.給藥方便性/病患依從性
  - 7.臨床上可適用之病人
  - 8.與同類藥品相比，此藥之每日藥費
  - 9.藥品外觀或名稱與現有品項相似
  - 10.取代/比價藥品
- Efficacy(Outcome Indicators)
- Safety (Toxicity Profile with Incidence rates)
- Financial Impact Analysis (FIA)
- 評估意見

→實例

Final Decision of Formulary Status

- Drug's Formulary Status
  - **Add, delete**
  - **Uncontrolled, monitored, restricted, conditional**
- Formulary exceptions process: (緊急採購)
  - Provides prescribers and patients with timely access to meds that are not on the formulary
  - Criteria for approval of nonformulary meds (eg, allergy, therapeutic failure to formulary drug, or not treatable)
  - P&T evaluate trends in such use

References

1. *ASHP Guidelines on the P&T and the Formulary System*
   - *AJHP 2008;65:1272-83*
2. *ASHP Guidelines-- Formulary System Management: Technical Assistance Bulletin on the Evaluation of Drugs for Formularies*
   - *AJHP 1988;45:386-7*
3. *UHC (University Hospitals Consortium) A Safety-Focused Drug Monograph Template for P&T Monographs*
   - *Murri NA, Ploetz P. University of Washington Academic Medical Centers and University Hospitals Consortium Medication Management/Quality Improvement Committee; 2002.*