New TB Drugs Approval in Thailand

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Outlines

- TB Drugs in National List of Essential Drugs
- Approved TB Drugs
- Regulation concerning New TB drug Registration in Thailand
  - New Drugs
  - Process of New Drug Registration
  - Requirements for New Drug Registration
- ASEAN Pharmaceutical Harmonization
  - Implementation
  - ACTR for NCE
# TB Drugs in National List of Essential Drugs

- **Ethambutol HCl**  
  Tab

- **Isoniazid**  
  Tab

- **Pyrazinamide**  
  Tab

- **Rifampicin**  
  Cap, Tab,  
  Dry syr, Syr

- **Streptomycin sulfate**  
  Sterile powder

- **Standard drug sublist**
TB Drugs in National List of Essential Drugs

- Amikacin sulfate Sterile sol
- Cycloserine Cap
- Ethionamide Tab
- Isoniazid + Rifampicin Cap/Tab
  (100+150mg/150+300 mg)

Specialist sublist where monitoring of prescribing is required.
TB Drugs in National List of Essential Drugs

- Isoniazid + Rifampicin + Tab
  Pyrazinamide +
  Ethambutol HCl
  (75 + 150 + 400 + 275 mg)
- Kanamycin sulfate Sterile powder
- Ofloxacin Tab
- Para-aminosalicylic acid EC Tab
  (PAS)

Specialist sublist where monitoring of prescribing is required.
Approved TB Drugs

- Ethambutol HCl Tab
- Isoniazid Tab, sterile sol
- Pyrazinamide Tab
- Rifampicin Cap, Tab, Dry syr, Susp
- Streptomycin sulfate Sterile powder
- Cycloserine Cap
- Ethionamide Tab
- Sodium aminosalicylate EC tab
Approved TB Drugs

- Isoniazid + Rifampicin \( \text{Cap, Tab} \)
- Isoniazid + Rifampicin + Pyrazinamide + Ethambutol HCl \( \text{Tab} \)
- Isoniazid + Rifampicin + Pyrazinamide \( \text{Tab} \)
- Isoniazid + Ethambutol HCl + Pyridoxine HCl \( \text{Tab} \)
- Isoniazid + Pyridoxine HCl \( \text{Tab} \)
## Approved TB Drugs

- **Number of Approved TB Drugs**: 152
- **Single drug products**: 124
- **Combination drug products**: 28
- **Local manufacturing drugs**: 131 (86%)
- **Imported drugs**: 21 (14%)
Regulation concerning New TB drug Registration in Thailand
New Drugs

- New Chemical Entities (NCE)
- New combination
- New indication
- New delivery system
Process of New Drug Registration

**NORMAL**
- NCE: 210-280 days
- New Generic: 110 days

**FAST TRACK**
- NCE: 110-130 days
- New Generic: 70 days
Process of New Drug Registration in Thailand

Track 1 : Standard Review  
(Normal Track)  
210 - 280 working days

Track 2 : Accelerated or Priority Review  
(Fast Track)  
Drugs for public health problems/ for life-threatening diseases  
100-130 working days
Requirements for New Drug Registration

• Chemical and Pharmaceutical data
• Preclinical data
• Clinical data
• Current status of drug approval or registration in foreign countries
• Patent status
• Sample of the product, Label and Package insert
• Certificate of Pharmaceutical Products / Certificate of Free Sale etc.
Requirements for New Drug Registration

• Comparative data between new drugs and approved drugs in the same therapeutic group on the following scopes are required for antimicrobials.

  • Antimicrobial spectrum
  • Pharmacokinetic properties
  • Pharmacodynamic properties
  • Efficacy
  • Safety
  • Resistance mechanism
  • Price
Chemical and Pharmaceutical Data

- Complete formulation per unit dose
- Master formulation
- Manufacturing process
- Route of synthesis of active ingredients
- References of each raw material
- Raw material specification and control method
Chemical and Pharmaceutical Data

- In-process control and specification
- Finished product specification and control method
- Certificate of analysis of active ingredient raw material
- Certificate of analysis of finished product
- Packaging
- Stability studies of finished products
- Stability studies of active ingredients (NCE)
Preclinical data
Pharmacological data

• Comprehensive Summary of Pharmacological data
• Pharmacodynamics
  • Mode of action
  • Undesirable effects
• Pharmacokinetics
  • Absorption
  • Distribution
  • Biotransformation
  • Excretion
Preclinical data
Toxicological data

- Comprehensive Summary of Toxicological data
- General Toxicological data
  - Acute
  - Subacute
  - Chronic
- Reproductive toxicology
  - Fertility and general reproductive performance
  - Teratogenicity
  - Pre-natal and Post-natal study
Preclinical data
Toxicological data

- Mutagenicity (if relevant)
- Carcinogenicity (if relevant)
- Antigenicity (if relevant)
- Dependence (if relevant)
- Local toxicity (if relevant)
Clinical data

- Comprehensive Summary on Clinical Data
- Phase I
  - Pharmacokinetics
    - Absorption
    - Distribution
    - Biotransformation
    - Excretion
    - Bioavailability
Clinical data

- Phase I
  - Pharmacodynamics
    - Therapeutic effects
    - Mechanism of action
- Phase II
- Phase III
- Phase IV (if any)
New Drug Registration Scheme in Thailand

New drug applications

Step I
- Conditional approval
  - Experts/Subcommittee Approval
  - Safety Monitoring Program & Limited distribution (2 yrs)

Step II
- Unconditional approval
  - Voluntary Spontaneous ADR Reporting System
Conditional Approval

- Safety Monitoring Program (SMP) will be conducted for approx. 2 years.
- Drug packages must bear labeling to show conditional approval status.
  - Triangle shows monitoring status.
  - Specially-control drug
  - Registration No. (NC)
    1C 10/51 (NC), 1A 10/51 (NC)
  - Limited distribution only through medical institutes or hospitals

ใช้เฉพาะสถานพยาบาล / ใช้เฉพาะโรงพยาบาล
ASEAN Pharmaceutical Harmonization

Implementation:

- **ASEAN deadline:**
  
  End of 2008

- **Trial period (voluntary):**
  
  Started in June 2004

- **Official announcement for full implementation:**
  
  January 2008
ASEAN Pharmaceutical Harmonization

ASEAN Harmonized Products

- ASEAN Common Technical Requirements (ACTR)
- ASEAN Common Technical Dossiers (ACTD)
- 4 Technical Guidelines
  - Process Validation
  - BA/BE
  - Analytical Validation
  - Stability
ACTR on Nonclinical Data for NCE

- **Pharmacology**
  - Primary Pharmacodynamics
  - Secondary Pharmacodynamics
  - Safety Pharmacology
  - Pharmacodynamics Drug Interactions

- **Pharmacokinetics**
  - Absorption
  - Distribution
  - Metabolism
  - Excretion
  - Pharmacokinetics Drug Interaction (non-clinical)
  - Other Pharmacokinetics Studies
ACTR on Nonclinical Data for NCE

- **Toxicology**
  - Single dose toxicity
  - Repeat dose toxicity
  - Genotoxicity
  - Carcinogenicity
  - Reproductive and developmental toxicity
  - Local tolerance when applicable
  - Other toxicity studies when applicable
ACTR on Clinical Data for NCE

- **Bioavailability (BA) and Bioequivalence (BE) Studies**
  - BA Studies
  - Comparative BA or BE Studies

- **Studies Pertinent to Pharmacokinetics Using Human Biomaterials**
  - Plasma Protein Binding Studies
  - Hepatic Metabolism and Drug Interaction Studies
  - Studies Using Other Human Biomaterials
ACTR on Clinical Data for NCE

- **Human Pharmacokinetic (PK) Studies**
  - Healthy Subject PK and Initial Tolerability studies
  - Patient PK and Initial Tolerability Studies
  - Intrinsic Factor PK Studies
  - Extrinsic Factor PK Studies

- **Human Pharmacodynamic (PD) Studies**
  - Healthy Subject PD and PK/PD studies
  - Patient PD and PK/PD studies

- **Efficacy and Safety**
  - Controlled Clinical Studies Pertinent to the Claimed Indication
  - Uncontrolled Clinical Studies

- **Post Marketing Data** (If available)
ACTR on Quality

S DRUG SUBSTANCE

S1 General Information
S2 Manufacture
S3 Characterisation
S4 Control of Drug Substance
S5 Reference Standards or Materials
S6 Container Closure System
S7 Stability
ACTR on Quality

P DRUG PRODUCT

P1 Description and Composition
P2 Pharmaceutical Development
P3 Manufacture
P4 Control of excipients
P5 Control of Finished Product
P6 Reference Standards or Materials
P7 Container Closure System
P8 Stability
P9 Product Interchangeability Equivalence evidence (for generic)
THANK YOU FOR YOUR ATTENTION