The Essential Drugs Programme

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On behalf of: The Essential Drugs Programme, NDoH

FUNDISA: PHARMACOECONOMIC WORKSHOP
Health Technology Assessment for Medicines in South Africa
Current Situation and International Trends

October 2019

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Medicine Value Chain Framework

Essential Drugs Programme (EDP)

CORE FUNCIONS

Selection

Contracting

Supply Chain

Contract Management

Product Use

Accessibility and Availability

Governance

Workforce Management

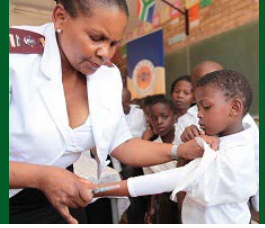
Information Systems & Management

Financial Management

Education & Research

ENABLING FUNCTIONS

Essential medicines Concept



Why Standard Treatment Guidelines and Essential Medicine List?

"For the rational and equitable use of medicines in South Africa in accordance with the WHO Essential Medicines concept"

What is the Essential Medicines List?

- Developed to satisfy the priority health care needs of the population
- Selected according to disease prevalence, evidence on efficacy and safety, and affordability.
- Determined by the ministerially appointed National Essential Medicines List Committee (NEMLC) that has technical sub-Committees (Expert Review Committees)

What are the Standard Treatment Guidelines?

- Implementation mechanism of the EML providing guidance on how to use medicines which appear on the EML

Review process is continuous –
As health needs, evidence and healthcare costs are dynamic.

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* Ref: http://www.health.gov.za/index.php/essential-drugs-programme-edp

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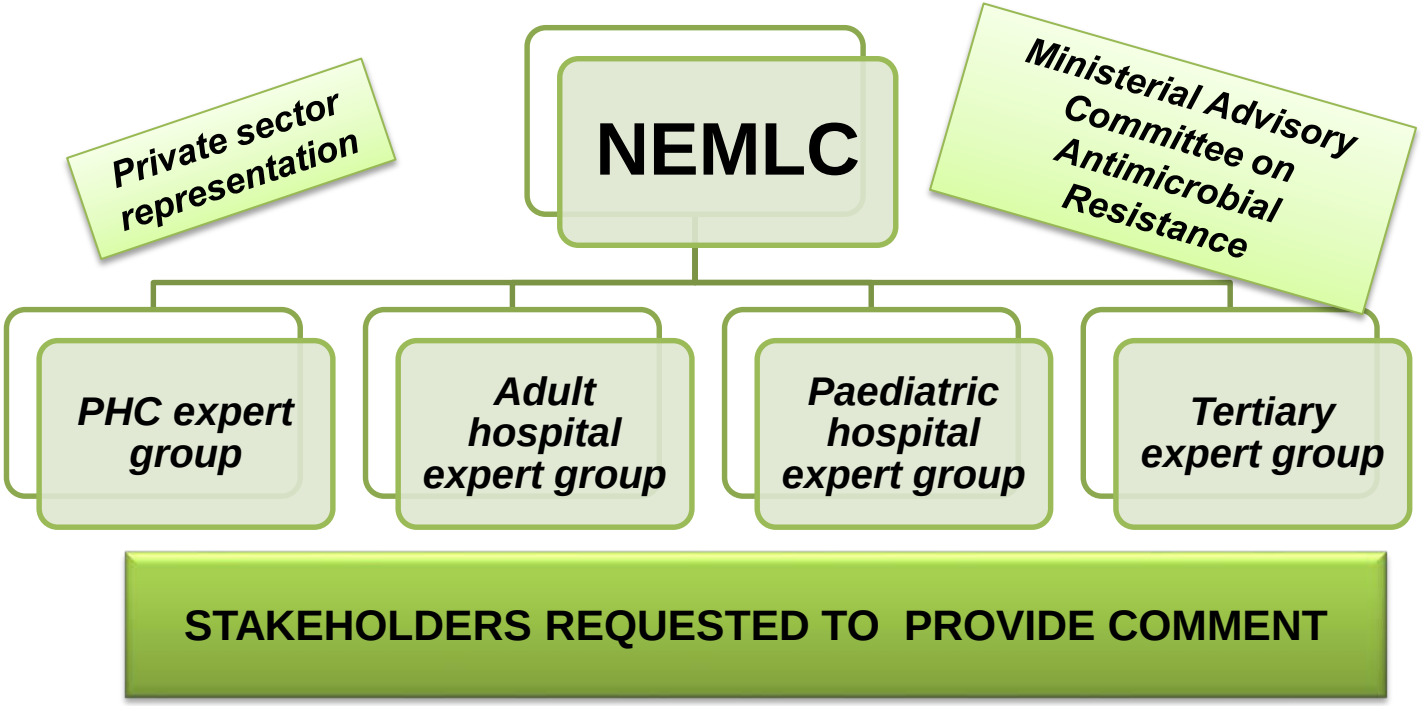
Process to decision making



MULTIDISCIPLINARY PROCESS

NEMLC comprises of Specialists, medical practitioners; nurse practitioners; pharmacists; pharmacologists; public health specialists; economists; private sector Medical Schemes; bioethics experts; academia

Principles and review criteria

AIM

*…..to inform the formulation of **safe, effective,** health policies that are patient focused and seek to achieve **best value.***

What are the principles of selection?

What are the criteria for selection?

Need: Public Health Relevance

- Priority health diseases and conditions contribute significantly to burden of illness and injury
- Local epidemiology

Quality, Safety & Efficacy & Effectiveness

- Product is registered in terms of the Medicines Act
- Evidence of efficacy, safety and effectiveness.

Cost & Affordability

- Affordability of medicine, compared to current standard of care and within budgets of providers of health care services.

Implications for Practice

- Pragmatic considerations
- Feasibility (e.g. adherence)
- Acceptability
- Monitoring & evaluation to further inform decision-making

Process Map for Revision, Dissemination and Implementation of STGs and EML

1 Planning

- List of conditions
- Review of National ABC Analysis (Expenditure and Volume)
- Departmental Guidelines
- Call Up Notice to Pharmaceutical and Therapeutics Committee (PTC)

2 1st Review

- PTC Submissions
- External Consultation
- Reviewer compiles chapter
- External Comment
- Literature Review
- Meta-analyses
- Health Technology Assessments
- Randomised Controlled trials
- Market Intelligence (Availability & Price)
- Pharmacoeconomic Analyses
- Technical Expert Committee Peer Review

3 2nd Review

- National Essential Medicines List Committee (NEMLC)
- External Comment
- Comments compiled and investigated
- Peer Review by Technical Expert Committee
- NEMLC approves amendments

4 Editorial

- Editing – Essential Medicines List extracted from Standard Treatment Guidelines

5 Measure and Evaluate

- Provincial ABC Analysis and Drug Utilisation Review

Good governance in decision making

Conflict of interest: ***Preserving selection decisions against undue influence is of paramount importance***

'There is no such thing as a free lunch'

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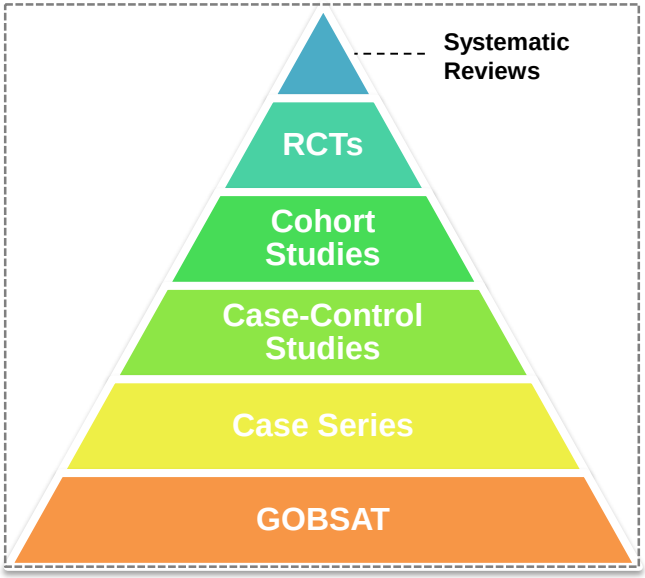
Progress of decision making

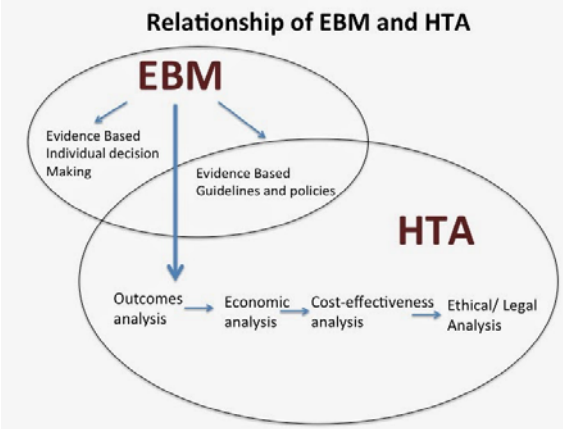
GOBSAT

Good Old Boys Sat Around a Table

EBM
(Evidence-based Medicine)



HTA
(Health Technology Assessment)



Template for medicine reviews developed in collaboration with Cochrane SA

Motivating for a Medicine on the EML

National Essential Medicine List
***Indicate the Level of Care* Medication Review Process**
Component:

MEDICINE MOTIVATION:

1. **Executive Summary**

Date:
Medicine (INN):
Medicine (ATC): *http://www.whocc.no/atc_ddd_index/*
Indication (ICD10 code): *http://apps.who.int/classifications/icd10/browse/2016/en*
Patient population:
Prevalence of condition: [article citation AND hyperlinked]
Level of Care:
Prescriber Level:
Current standard of Care:
Efficacy estimates: (preferably NNT)
Motivator/reviewer name(s):
PTC affiliation:

2. **Name of author(s)/motivator(s)**

3. **Author affiliation and conflict of interest details** *[Organisation, Involvement/receipts] http://www.health.gov.za/index.php/component/phocadownload/category/194*

4. **Introduction/ Background**
Contextualisation – why we need it and why alternatives already on EDL are not suitable.

5. **Purpose/Objective i.e. PICO question** [comparison to current standard of care for a specific indication]:
-P *(patient/population):*
-I *(intervention):*
-C *(comparator):*
-O *(outcome):*

6. **Methods:**
   a. **Data sources** *e.g. Medline, EMBASE, Pubmed, etc.*
   b. **Search strategy** *Cut and past your search strategy – the idea being that if an update is required at a later stage, the same strategy can be used. Describe briefly what you ended up with – e.g. 14 RCTs, of which 3 were duplicate publications, two observational studies, etc.*
   c. **Excluded studies:** *Describes briefly which you have rejected and why*

Author, date	*Type of study*	*Reason for exclusion*

   d. **Evidence synthesis** –[article citation AND hyperlinked] *Brief (don't get carried away!) critical appraisal of included studies, including key drawbacks (e.g. underpowered, control medication dose too low, etc) Include key objective endpoints effect sizes with their confidence intervals and p values. Doesn't need to be too detailed, but should reference the appropriate study, which should ideally be available in full text (a pdf is easiest.)*

Author, date	*Type of study*	n	Population	Comparators	Primary outcome	Effect sizes	Comments

   e. **Evidence quality:** *You may have said it all under evidence synthesis, but just a line or so on the quality of the whole evidence 'package'.*

7. **Alternative agents:** *List therapeutic alternatives, if they exist, with supporting evidence for comparable dose for this specific indication.*

EVIDENCE TO DECISION FRAMEWORK

	JUDGEMENT	SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS
QUALITY OF EVIDENCE	**What is the overall confidence in the evidence of effectiveness?** Confident ☐ Not confident ☐ Uncertain ☐	
BENEFITS & HARMS	**Do the desirable effects outweigh the undesirable effects?** Benefits outweigh harms ☐ Harms outweigh benefits ☐ Benefits = harms or Uncertain ☐	
THERAPEUTIC INTERCHANGE	Therapeutic alternatives available: Yes ☐ No ☐ List the members of the group. List specific exclusion from the group:	Rationale for therapeutic alternatives included: References: Rationale for exclusion from the group: References:

NDoH_EML_Motivation_Technical Review Form_v5.0_2016Oct28

Motivating for a Medicine on the EML

VALUES & PREFERENCES / ACCEPTABILITY	**Is there important uncertainty or variability about how much people value the options?** Minor ☐ Major ☐ Uncertain ☐ **Is the option acceptable to key stakeholders?** Yes ☐ No ☐ Uncertain ☐	
RESOURCE USE	**How large are the resource requirements?** More intensive ☐ Less intensive ☐ Uncertain ☐	Cost of medicines/ month: **Medicine** | **Cost (ZAR)** **Additional resources:**
EQUITY	**Would there be an impact on health inequity?** Yes ☐ No ☐ Uncertain ☐	
FEASIBILITY	**Is the implementation of this recommendation feasible?** Yes ☐ No ☐ Uncertain ☐	

Type of recommendation	We recommend against the option and for the alternative	We suggest not to use the option or to use the alternative	We suggest using either the option or the alternative	We suggest using the option	We recommend the option
	☐	☐	☐	☐	☐

Recommendation

Rationale:

Level of Evidence:

Review indicator:

Evidence of efficacy ☐ Evidence of harm ☐ Price reduction ☐

VEN status:

Vital ☐ Essential ☐ Necessary ☐

Monitoring and evaluation considerations

Research priorities

References: *Remember to reference the excluded studies.Vancouver style format.*

National Department of Health: Affordable Medicines - Essential Drugs Programme in collaboration with Cochrane South Africa, South African Medical Research Council
Medicine review/motivation form template: May 2016_draft_v1.0

NDoH_EML_Motivation_Technical Review Form_v5.0_2016Oct28

Example

Evidence review – *Primary Health Care EML*

Question: Amongst adult patients on first-line combination ART, is the integrase inhibitor dolutegravir more efficacious and/or better tolerated than the non-nucleoside reverse transcriptase inhibitor (NNRTI) efavirenz?

Adobe Acrobat Document

Recommendation: After the first iteration of this review, the Primary Healthcare expert review committee (ERC) recommendation was as follows:

> *Based on the appraisal of the evidence presented in this technical review, the Primary Healthcare ERC recommends that dolutegravir be introduced into the first-line antiretroviral regimen (in combination with 2 N(t)RTIs) for HIV-infected adult patients commencing ART.*
>
> *However, in response to the neural tube defect signal, DTG is not recommended for use in early pregnancy and DTG should be avoided in women of child-bearing potential who are not on reliable contraception.*
>
> *Patients requiring concomitant rifampicin-containing TB therapy would require DTG dose adjustment.*
>
> *Alternatively switching to efavirenz-based ART for the duration of the TB therapy could be considered.*

Rationale: Evidence of superior efficacy and potenitally superior barrier to resistance of dolutegravir compared with efavirenz; though there is limited evidence for use in pregnancy. Pharmacokinetic data indicate dose adjustment is necessary with concomitant rifampicin (rifampicin is a strong inducer of UGTIA3 and CYP3A4, and reduces DTG concentrations).

Level of Evidence: I Systematic review, RCT

Pharmacoeconomics - Progressive evolution

International price comparisons

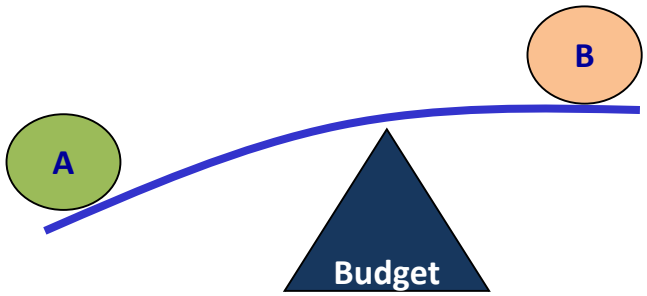
Progress of pharmacoeconomics in decision-making

COST COMPARISON → **COST MINIMISATION** → **CEA, CUA, BIA** (modelling)

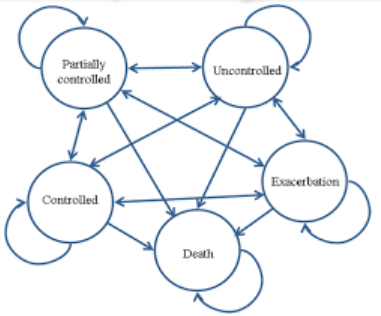
Budget = R20.00

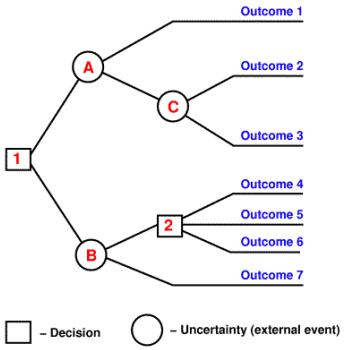
Option 1 = R19.95

Option 2 = R55.95



Option A comparable to option B in terms of efficacy (& safety)





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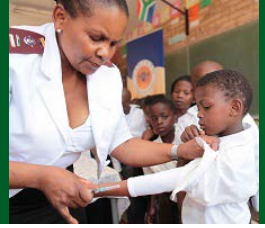
Example

Adobe Acrobat Document

Cost effectiveness analysis - *Adult Hospital Level EML*

Medicine	Evidence	Results	Limitations
• Rivaroxaban vs warfarin-enoxaparin (with INR monitoring) protocol • *Indication:* Treatment of venous thromboembolism (VTE) and pulmonary embolism (PE) and prevention of recurrent VTE.	• EINSTEIN studies show rivaroxaban is comparable to standard of care; • Lower risk of first major bleed and reduction in length of hospital stay. *[LoE: I RCTs]*	• Incremental cost of 12 months treatment vs enoxaparin – warfarin per patient was ± R8240 (Base case using SEP). • Reduce price by 80% results in 3 and 6 month treatment periods to be cost-saving.	• Local prevalence data not available ***– baseline data not available? scope creep for use in other indications?*** • Initial budget outlay would be considerable & trade off would be required – ***affordable?*** • Will the projected cost savings (reduced hospital stay, bleeds, recurrent VTEs) materialise ***– M&E is important.***

Accessing the STGs and EML



MOBILE APPLICATION

for the Standard Treatment Guidelines (STGs)
and Essential Medicines List (EML)
for Primary Health Care (PHC) Level

HOW TO DOWNLOAD ON ANDROID?

1 2 3

STEP 1: Go to Google Play Store

STEP 2: Open search function

STEP 3: Type in "PHC Clinical Guide" and click INSTALL

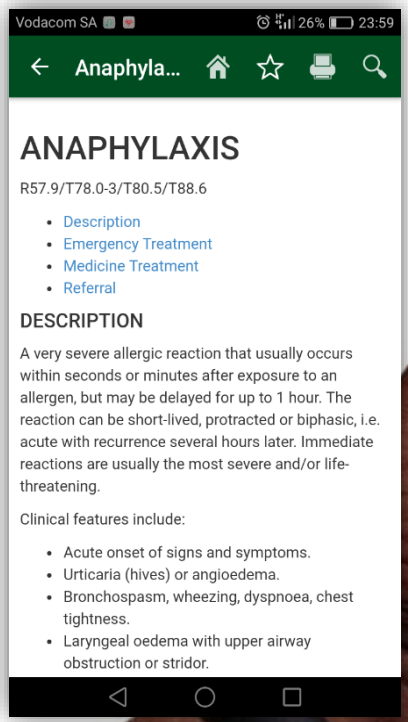
HOW TO DOWNLOAD ON IOS?

1 2 3

STEP 1: Go to App Store

STEP 2: Open search function

STEP 3: Type in "PHC Clinical Guide" and click INSTALL



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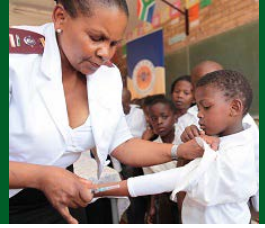
Strengths and Challenges



Strengths

- **Robust evidence-based review and strong governance processes**
- **Improved access, transparency and stakeholder engagement:**
  - Level of evidence listed in STGs, with evidence citations
  - Dynamic process, continuous updating – short time period between review cycles
  - Peer review through external stakeholder commenting process
  - Implementation of new decisions through technology – mobile application
  - Medical scheme experts on the Technical Expert review Committees and representation from Council of Medical Schemes

Opportunities to strengthen the process

- Stronger collaborative efforts required to ensure alignment between STGs and EML with other clinical guidelines
- Lack of skilled experts in evidence-based medicine and pharmacoeconomics
- No current mechanism to deal with Industry Submissions
- To achieve patient centred universal healthcare, patient/community education and involvement in decision-making processes is needed
- Guideline implementation needs to be strengthened
- Assessment of clinical outcomes would provide an effective measure of the impact of the STGs and EML

Thank You!

EDP Team:

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NDoH website: http://www.health.gov.za/index.php/affordable-medicines/category/195-essential-drugs-programme-edp