**South African National Essential Medicines List**

**[Brief or Standard] Technical Review Report**

**Name of STG ERC**

**Component: STG chapter and section**

**Generic name of health technology and relevant indication (e.g. x for treating x)**

**Date**

**Key findings**

|  |
| --- |
|  |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **[Insert] LEVEL EXPERT REVIEW COMMITEE RECOMMENDATION:** | | | | | |
| **Type of recommendation** | We recommend against the option and for the alternative  **(strong)** | We suggest not to use the option  **(conditional)** | We suggest using either the option or the alternative  **(conditional)** | We suggest  using the option **(conditional)** | We recommend  the option  **(strong)** |
|  |  |  |  |  |
| **Recommendation:**  *Rationale:*  **Level of Evidence:**  **Review indicator:** | | | | | |
| **NEMLC RECOMMENDATION:** | | | | | |
| [**Monitoring and evaluation**](#Monitoring) **considerations** | | | | | |
| **Research priorities** | | | | | |

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# List of tables

# List of figures

# Abbreviations

# EXECUTIVE SUMMARY

|  |
| --- |
| **Medicine:**  **Indication:**  **Research question:**  **Patient population:**  **Prevalence of the condition:**  **Level of Care:**  **Prescriber level:**  **Current Standard of Care/ Comparator(s):**  **Outcome:**  **Methods:**  **Evidence base:**  **Findings:**  **Recommendations:**  **Reviewers:**  **PTC affiliation:**  **Disclosures:**  **Funding support:** |

**NAMES OF REVIEWERS**

**AFFILIATION AND CONFLICT OF INTEREST**

Potential conflict of interest statement included here.

Official form should be completed and sent to EDP prior to undertaking the review.

# INTRODUCTION

## Population impact of the disease / condition

* Prevalence and incidence of the disease or condition for the indication to be assessed.
* Number of patients who may be eligible to receive the intervention under review
* Information on subgroups (e.g. age, province) if available.
* Information or assessment of severity of disease, including quality of life implications

## Current clinical care pathway

Information about the condition and current standard of care within the South African public health sector, including details on:

* Alternatives already available in South Africa
* Any relevant policy considerations or related clinical guidelines
* Any relevant international trends

Use South African data if available. International information may be presented if justification can provided for its use.

## Description of technology under review

Complete the following table:

|  |  |  |
| --- | --- | --- |
| Information Requested | Details | Potential data source |
| Name of the technology | SA approved brand name as well as generic name |  |
| Name of manufacturer | If intervention is a branded technology |  |
| Licensing status | Actual or anticipated date for issuance of SAHPRA approval | <https://www.sahpra.org.za/registered-health-products/> |
| Reimbursement status | Currently approved for use on EML? | <https://www.idealhealthfacility.org.za> |
| Drug class | Anatomical Therapeutic Chemical (ATC) | <http://www.whocc.no/atc_ddd_index/>  <https://www.sahpra.org.za/pi-pil-repository/> |
| Mechanism of action |  | <https://www.sahpra.org.za/pi-pil-repository/> |
| Indication relevant to this review, as per SAHPRA registration | Exact wording of the indication(s) approved by SAHPRA | <https://www.sahpra.org.za/pi-pil-repository/> |
| Other indications (not part of this review), as per SAHPRA registration | Exact wording of the indication(s) approved by SAHPRA | <https://www.sahpra.org.za/pi-pil-repository/> |
| Dosage form and strength(s) | All the dosage forms and strengths of the drug relevant to the indication under review. | <https://www.sahpra.org.za/pi-pil-repository/> |
| Route of administration | Only routes relevant to indication under review. E.g., oral, intravenous | <https://www.sahpra.org.za/pi-pil-repository/> |
| Dosage regimen | Dose, frequency and duration of administration relevant to the indication under review | <https://www.sahpra.org.za/pi-pil-repository/> |
| Setting | E.g. Community and/or hospital setting |  |
| Additional tests or investigations required to administer technology | Only for indication under review |  |
| Description of how the medicine will be used in practice, including additional technologies required to use the technology | If relevant for indication under review, briefly describe the co-dependent[[1]](#footnote-1) technology in terms of achievement or enhancement of the intended clinical effect of either health technology. Cite the mechanism of co-dependency. |  |
| Anticipated place in therapy |  | <https://www.idealhealthfacility.org.za> |
| Comparator(s) | Provide a list of the other treatment(s) used for the condition[[2]](#footnote-2) | <https://www.idealhealthfacility.org.za> |

# TECHNOLOGY ASSESSMENT SCOPE

## Why is it important to do this review?

Rationale for why topic has been selected

## Review question

Amend the following statement:

To assess the [effectiveness/ safety/ cost/ cost-effectiveness/ other] of the use of [technology x] compared to [technology b] for [patient population and disease/condition] in [health care setting]

## Scope of the technical review

|  |  |
| --- | --- |
| Criteria | Details |
| Population | * Patient population eligible to receive the health technology. Include specifics on condition/disease, age, sex, comorbidities, and subgroups |
| Intervention | * Technology being assessed and its place in the current care pathway * Replace current treatment or be an add-on therapy? * Include specifics of dose, duration, delivery mode, co-intervention/s, setting (e.g. inpatient/ outpatient) |
| Comparison | * Current standard of care and currently available for use in South African public health sector * Should be the treatment most clinicians will replace with the technology being assessed, or the treatment most prescribed currently for the management of the disease/condition. * Can be active treatment or placebo * Include specifics of dose, duration, mode of delivery |
| Outcomes | * Identify principal measures for clinical effectiveness for population of interest and with consideration of place in care pathway/stage of disease. * Include both clinical and safety outcomes * Specify primary and secondary outcomes (including survival, disease progression and health-related quality of life) * Define time horizon – time it takes to demonstrate the identified outcomes (may vary for clinical and economic outcomes). * If applicable, identify feasibility, acceptability, and cost-effectiveness outcome data |
| Likely study designs or data sources to be included | * Systematic reviews * Clinical practice guidelines and health technology assessments * Primary studies (order of preference: randomised controlled trials, observational studies, case series) |

List any secondary objectives of the review e.g. subgroups, equity concerns.

# CLINICAL EVIDENCE

## PART 1: Summary of methods used to find and select clinical evidence

See the HTA Methods Guide for guidance on methods for Brief and Standard Technical reports

Results of literature search to be presented graphically in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (PRISMA, 2009)

### Database literature search

Brief outline of the database search strategy (e.g. date of search, search terms, databases searched, limits applied), number of records found (search output), methods used for selection of studies (e.g. single/double screening), with detail provided in Appendix 1.

Provide details of all included studies in Appendix 2, and all studies excluded at the full-text screening stage in Appendix 3.

### Grey literature search

Brief outline of the database search strategy (e.g. date of search, search terms, websites/registries searched, limits applied), methods used for selection of evidence, with detail provided in Appendix 1.

Provide details of all included CPGs in Appendix 2.

*A grey literature search is not required for a Brief Technical Report.*

## PART 2: Summary of methods used to appraise clinical evidence

Systematic reviews and clinical practice guidelines must be critically appraised. If clinical inputs from randomised controlled trials are required for economic evaluations (Stage 2 analysis), those studies should be appraised at in Stage 2, using the appropriate measures (see HTA Methods guide).

Systematic reviews should be appraised using the A MeaSurement Tool to Assess systematic Reviews (AMSTAR) checklist (10), which can be found at <https://amstar.ca/Amstar_Checklist.php> .

Clinical practice guidelines should be appraised using the Appraisal of Guidelines and Research and Evaluation (AGREE) II tool (11), which can be found at <https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf> .

Summary of the quality of the systematic reviews and clinical practice guidelines must be provided here, with appraisal details/assessments provided in Appendix 4.

## PART 3: Clinical evidence syntheses

### Systematic reviews

Results presented as a narrative synthesis. Outcomes measured and the measures of effect (with p-values and confidence intervals) should be compared across studies and presented in a table.

If large number of studies available, select the most relevant (highest quality, most recent) studies and provide justification for its selection.

Include data on clinical effectiveness and safety.

Safety data from included studies should reflect the frequent events, irrespective of severity, and then progress onto the rare yet severe events.

**Evidence tables presenting a summary of results:**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Author, date | Study Design | Number of patients | | Effect | | Quality of the study |
| Population | Intervention | Relative (95% CI) | Absolute |
|  |  |  |  |  |  |  | |

\*Include both absolute and relative data with a 95% confidence interval. Dichotomous outcomes should ideally be expressed both as relative risks (or odds ratios) and risk (or rate) differences. For time- to-event analysis, the hazard ratio is an equivalent statistic.

### Randomised controlled trials

Summarised narratively.

See HTA methods guide for approach to meta-analysis (if required).

### CPG recommendations

Relevant recommendations in selected CPGs will be summarised narratively with all the relevant recommendations from the CPGs presented in a table.

**Clinical guideline quality assessments and recommendations**

|  |  |  |  |
| --- | --- | --- | --- |
| Citation of guideline | Relevant recommendations | Strength of evidence | AGREE II overall score\* |
|  |  |  |  |
|  |  |  |  |

\*AGREE II assessments provided in Appendix 3

*Presented in Standard Technical Reports only.*

### Adverse reactions

Summary of adverse drug reactions listed in the medicine’s prescribing information (PI) approved by South African Health Products Regulatory Agency (SAHPRA) (14) should be included if not already presented elsewhere.

## PART 4: Interpretation of clinical evidence

Comment on the similarities and differences between the intervention and comparator groups in terms of both clinical benefit, harms and other listed outcomes.

Provide evidence/insight to whether the statistically significant findings are clinically meaningful.

# ECONOMIC EVIDENCE

## PART 1: Costing data

Present comparison of the pharmaceutical costs of the intervention/s and comparator/s.

Reference acquisition prices listed in the Master Health Product List if possible, otherwise use the latest published single exit price listed in the Medicine Price Registry (<https://medicineprices.org.za>.)

Calculations should be based on the recommended daily dose approved by SAHPRA, or average daily dose sourced from the literature.

Present pharmaceutical cost for a course or cycle of treatment:

* Chronic treatment: costs of treatment for one day and for a year
* Acute/short term treatment: costs of treatment for one course (with indication of number of courses required)

**Acquisition costs of the intervention and comparator technologies**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Intervention | Source | Comparator | Source |
| Pharmaceutical formulation | *e.g. Tablet* | *SAHPRA PI* |  |  |
| Method of administration | *e.g. Oral* | *SAHPRA PI* |  |  |
| Average dose/s and dosing schedule/s | *e.g. 10mg tablet once a day* |  |  |  |
| Average daily dose | *e.g. 10mg* |  |  |  |
| Dose adjustments | *n/a* |  |  |  |
| Acquisition cost for smallest available pack size | *e.g. R25 for 30 x 10mg tablets* | *Master Health Product List\** |  |  |
| Cost of one dosing unit | *e.g. R2530=R0.83* |  |  |  |
| Cost of treatment for one day |  |  |  |  |
| Average length of a course of treatment | *One year (chronic treatment)* |  |  |  |
| Cost of a course of treatment | *R300* |  |  |  |
| (Anticipated) average interval between courses of treatment | *n/a* |  |  |  |
| (Anticipated) number of repeat courses of treatment | *n/a* |  |  |  |

Table adapted from the NICE cost-comparison submission template

\* Source from the latest Master Health Product List with the contract number and item number referenced for each medicine.

## PART 2: Summary of Health Technology Assessment (HTA) Agency decisions

Summarised narratively with an overview of the recommendations presented in a table.

List of websites of reputed HTA agencies listed in HTA Methods Guide.

## PART 3: Interpretation of economic evidence

Consideration of costs and cost-effectiveness of intervention technology compared to comparators.

# EQUITY CONSIDERATIONS

Statement(s) to indicate the potential impact listing the technology on the EML might have on equity in health for marginalised groups in the South African context. Includes equity considerations related to the disease and intervention, characteristics of the intervention population, and other social and financial effects.

See HTA Methods Guide for further guidance and adapt the table below.

**Summary of equity considerations**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Equity criteria | Benefits when proceeding with implementation | Adverse consequences when proceeding | Benefits when refraining from implementation | Adverse consequences when refraining |
| Severity of condition or disease |  |  |  |  |
| Realisation of potential |  |  |  |  |
| Populations with past health loss |  |  |  |  |
| Socioeconomic status |  |  |  |  |
| Geographical disparities |  |  |  |  |
| Age and gender |  |  |  |  |
| Race, ethnicity, religion and sexual orientation |  |  |  |  |
| Economic productivity |  |  |  |  |
| Care for others |  |  |  |  |
| Catastrophic health expenditures |  |  |  |  |

# 

# SOCIAL VALUE CONSIDERATIONS

Consider relative importance and acceptability of the intervention to all or most stakeholders, including how much variability there is amongst stakeholders.

See HTA Methods Guide for further guidance and adapt the table below.

**Social value considerations by stakeholder group**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Stakeholder | Benefits when proceeding with implementation | Adverse consequences when proceeding | Benefits when refraining from implementation | Adverse consequences when refraining |
| Patient |  |  |  |  |
| Family and important others |  |  |  |  |
| Health care providers |  |  |  |  |
| Heads of Pharmaceutical Services (HOPS) |  |  |  |  |
| Pharmaceutical and Therapeutics Committees |  |  |  |  |
| National Programmes |  |  |  |  |
| Society |  |  |  |  |
| Others |  |  |  |  |

# 

# FEASIBITLIY CONSIDERATIONS

Consider organizational and health system impacts that may impact on implementation of the intervention. See HTA Methods Guide for further guidance.

Adapt table below.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Types | Benefits when proceeding with implementation | Adverse consequences when proceeding | Benefits when refraining from implementation | Adverse consequences when refraining |
| Economic considerations |  |  |  |  |
| Operational feasibility |  |  |  |  |
| Legal feasibility |  |  |  |  |

# 

# DISCUSSION

Overview of main findings from the Technical Report

Use Strength of Recommendation Taxonomy [SORT] (15) or Grading of Recommendations Assessment, Development and Evaluation (GRADE) (16) to describe the strength of the evidence used.

# RECOMMENDATION: 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 (comparators) 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: |
| **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 | | |  | | --- | |  | | |  | | --- | |  | | |  | | --- | |  | | |  |

|  |  |  |
| --- | --- | --- |
|  | **JUDGEMENT** | **SUPPORTING EVIDENCE & ADDITIONAL CONSIDERATIONS** |
| **RESOURCE USE** | **How large are the resource requirements?**   |  |  |  | | --- | --- | --- | | More intensive | Less intensive | Uncertain | | |  | | --- | |  | | |  | | --- | |  | | |  | | --- | |  | | | **Cost of medicines / month:**  **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**](#TypeofRecommendation_C) | We recommend against the option or  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**](#TypeofRecommendation_C) |  | | | | |
| **Rationale:** |  | | | | |
| **Level of Evidence** |  | | | | |
| ***Review indicator:*** | |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Evidence of efficacy | | | Evidence of harm | | | Price reduction | | | |  |  |  |  |  |  |  |  |  | | | | | |
| **VEN status:** | |  |  |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | --- | --- | --- | | Vital | | | Essential | | | Necessary | | | |  |  |  |  |  |  |  |  |  | | | | | |
| **[M](#Monitoring" \o "What indicators should be monitored? Is there a need to evaluate the impacts of the option, either in a pilot study or an impact evaluation carried out alongside or before full implementation of the option?)onitoring and Evaluaiton considerations**: |  | | | | |
| **[Research priorities](#Research" \o "Are there any important uncertainties in relation to any of the criteria that are a priority for further research?)**: |  | | | | |

# References

Vancouver style format.

# Appendix 1: Literature search strategy

The table below can be used to report the methods for the database literature search.

If relevant, additional information should be provided, e.g. justification for search limits applied, inclusion/exclusion criteria used for selection of studies if different from PICOS statement.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| LITERATURE SEARCH METHODS | | | | | |
| Expertise | e.g. The searches will be [informed/verified] by a content expert, conducted by an information specialist [initials], and independently peer reviewed. | | | | |
| Search terms used | Provide list of search terms used | | | | |
| Electronic databases | Database [minimum checked – please specify if other]  MEDLINE  Cochrane CENTRAL  EMBASE  Epistemonikos  Other (please specify, e.g. PsycINFO) | Time limits:  From: | | To: | |
| Other limits (e.g., language): | | | |
| Other searches | Systematic review references  Grey literature (NDoH, CPG and HTA related websites – see table below for list of potential websites)  Other (please specify) | *[provide details]* | | | |
| METHODS FOR SCREENING SEARCH RESULTS | | | | | |
| Screening methods | Dual; second reviewer checks all excluded records  Dual; second reviewer checks *[X%]* of excluded records  Dual; independent screen and cross check  Single; Single screen with no cross check | | *Abstract* | | *Full text* |
| Discrepancy resolution | Consensus and/or third reviewer  Other (please specify) | | | | |
| Excluded studies | All decisions taken during screening will be documented and outlined in the final report with a list of excluded studies | | | | |
| Inclusion of abstracts and conference proceedings | Exclude all  Include if clearly eligible and have usable data  Include if clearly eligible regardless of usable data  Include if eligibility is unclear and add to section in report | | | | |

# Appendix 2: Description of included studies

**Details of all included studies (systematic reviews and/or RCTs)** (adapt as needed)

|  |  |  |
| --- | --- | --- |
|  | Study name | Study name |
| Systematic reviews | | |
| Study design (including methods, location, groups) |  |  |
| Population (note any subgroups) |  |  |
| Intervention (including healthcare setting) |  |  |
| Comparators |  |  |
| Outcomes assessed |  |  |
| Analysis |  |  |
| RCTs | | |
| Study design (including methods, location, sites, groups) |  |  |
| Population (note any subgroups) |  |  |
| Intervention (including healthcare setting) |  |  |
| Comparators |  |  |
| Study end points |  |  |
| Analysis |  |  |

**Details of all included clinical practice guidelines** (adapt as needed)

|  |  |  |
| --- | --- | --- |
|  | Clinical practice guideline name | Clinical practice guideline name |
| Developer |  |  |
| Country |  |  |
| Publication date |  |  |
| Weblink |  |  |
| Overview of content |  |  |

**Details of other relevant clinical evidence found** (not systematic review, RCT or clinical practice guideline)

# Appendix 3: Publications excluded after full text screening

|  |  |  |
| --- | --- | --- |
| Author, date | Type of study | Reason for exclusion |
|  |  |  |
|  |  |  |
|  |  |  |

# Appendix 4: Appraisal of the clinical evidence

Complete one AMSTAR 2 assessment (in duplicate) for each systematic review. See <https://amstar.ca/Amstar_Checklist.php> for guidance.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Systematic review name – x quality review (assessment outcome) | Yes/ Partial Yes/ No | | |
|  | **Criteria** | **Reviewer 1** | **Reviewer 2** | **Consensus** |
| 1 | Did the research questions and inclusion criteria for the review include the components of PICO? |  |  |  |
| 2 | Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol? |  |  |  |
| 3 | Did the review authors explain their selection of the study designs for inclusion in the review? |  |  |  |
| 4 | Did the review authors use a comprehensive literature search strategy? |  |  |  |
| 5 | Did the review authors perform study selection in duplicate? |  |  |  |
| 6 | Did the review authors perform data extraction in duplicate? |  |  |  |
| 7 | Did the review authors provide a list of excluded studies and justify the exclusions? |  |  |  |
| 8 | Did the review authors describe the included studies in adequate detail? |  |  |  |
| 9 | Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?  RCTs |  |  |  |
| 10 | Did the review authors report on the sources of funding for the studies included in the review? |  |  |  |
| 11 | If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results? |  |  |  |
| 12 | If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis? |  |  |  |
| 13 | Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review? |  |  |  |
| 14 | Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? |  |  |  |
| 15 | If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? |  |  |  |
| 16 | Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review? |  |  |  |

Complete one AGREE II assessment (in duplicate) for each CPG. See<https://www.agreetrust.org/wp-content/uploads/2017/12/AGREE-II-Users-Manual-and-23-item-Instrument-2009-Update-2017.pdf>for guidance.

1. Health technologies are co-dependent where the health outcomes related to the use of one health technology (e.g. a medicine) are improved using another health technology (e.g. a pathology test or an imaging technology). The technologies need to be used together to achieve or enhance the intended clinical effect of either technology. [↑](#footnote-ref-1)
2. All comparators must be currently available for use in the South African public health system [↑](#footnote-ref-2)