Government Gazette
Staatskoerant

REPUBLIC OF SOUTH AFRICA
REPUBLIEK VAN SUID-AFRIKA

Vol. 518 Pretoria, 29 August / Augustus 2008 No. 31369

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GENERAL NOTICE

NOTICE 1053 OF 2008

DEPARTMENT OF HEALTH

MEDICINES AND RELATED SUBSTANCES ACT, 1965 (Act No. 101 of 1965)

CALL FOR COMMENT ON A METHODOLOGY FOR INTERNATIONAL BENCHMARKING OF ORIGINATOR MEDICINE PRICES

The Minister of Health intends, on the recommendation of the Pricing Committee under section 22 G of the Medicines and Related Substances Act, 1965(Act No. 101 of 1965) to implement the methodology in the Schedule. Interested persons are invited to submit any substantiated comments or representations in writing on the proposed methodology to the Director-General: Health, Private Bag X828, Pretoria, 0001 (for the attention of the Cluster Manager: Financial Planning and Health Economics - Dr A Pillay) within thirty days from date of publication of this notice.

SCHEDULE

METHODOLOGY FOR INTERNATIONAL BENCHMARKING OF ORIGINATOR MEDICINE PRICES

1. METHODOLOGY

The proposed framework for international benchmarking adopts the position that the *lowest price in a selected basket of countries should be used as the ultimate price for the purposes of benchmarking*.

However, to cater for the possibility that some prices may be drastically reduced unfairly, the recommended approach incorporates two protections for pharmaceutical manufacturer:

1. A phased approach, which delays the implementation of the ultimate benchmark by two-years; and
2. An exemption process, which permits pharmaceutical companies to challenge the ultimate benchmark price based on the full disclosure of all aspects of the pricing of a product.

The method to be followed is:

1. A selection ("basket") of appropriate countries has been identified, the prices of which will be benchmarked against prevailing prices in South Africa. Countries selected are:

   Australia, Canada, New Zealand, South Africa and Spain.

2. Two benchmark methodologies will be applied in sequence to existing medicines:

a. In **Phase 1**: The average of the lowest three prices in the basket, if this is lower than the South African ex-manufacturer price, or remain at the existing South African price if this is lower than the *average of the lowest three prices* ("interim benchmark 1").

b. In **Phase 2**: the *lowest price* in the basket will apply if this is lower than the South African ex-manufacturer price or remain at the existing South African price if this is lower than the lowest price in the benchmark ("final benchmark").

3. Price conversions into Rands will be performed in accordance with the methodology outlined in the **Exchange Rate** section (Section 2) below.

4. In exceptional circumstances, an applicant may apply for exemption from the interim benchmark, but will be required to provide complete disclosure on all factors relevant to the matter.

5. The final benchmark will apply automatically two years after the introduction of the interim benchmark. However, applicants will be required to submit full data on the application of the final benchmark methodology to each of their products within nine months of publication of the benchmarking methodology.

6. Both the *interim* and the *final* benchmark price values will be calculated annually by the affected companies and provided to the *Department of Health*. The Committee will review the benchmarked prices on a regular basis.

7. An exemption from the final benchmark will be permissible, on application, only where an affected company can demonstrate to the satisfaction of the Committee and the Minister that the resulting price is distorted and prejudicial to the manufacturer.

8. Applications for exemption from the final benchmark must be submitted on a form and in the manner to be prescribed, to the *Directorate of Pharmaceutical Economic Evaluations* (Department of

Health) one year before the date for implementation of the final benchmark.

9. A review panel will be established for the purpose of assessing exemption applications.

10. Any new medicine entering the South African market after the publication of the international benchmarking methodology must comply immediately with the *final benchmark*, i.e. must set their ex-manufacturer price at the lowest price in the basket of benchmark countries.

11. New medicines coming onto the market after the initiation of the reform (i.e. within 3 months from the gazetting of the regulations) for which an exemption from the benchmarking methodology is sought, must submit its application concurrently with their application to the Medicines Control Council ("MCC") to register a new medicine.

12. A medicine that has been registered by the MCC without any exemption application having been submitted, will not be permitted an exemption.

13. The decisions of the review panel will be made public and will include a non-confidential set of reasons. However, the information submitted to motivate for the exemption, and the full decision, will be kept confidential.

14. The review panel will be permitted to require full disclosure of all information relevant to reach a final determination. Any failure to provide this information will prejudice an application.

2. EXCHANGE RATE[1]

1. **Three-year linear regression**: A 3-year linear regression, using monthly exchange rate averages, will be used to produce a projection

[1] All exchange rate and inflation data was sourced from the South African Reserve Bank.

of the monthly nominal exchange rates in the benchmark year. The average of the monthly rates is used as the conversion rate for benchmarking. This approach essentially applies the formula produced by the regression analysis to project forward the nominal exchange rate monthly averages for the benchmark year (2008 in this instance). (See **Table 2.1** for the equations used and **Figure 2.1**).

Table 2.1: Equations

Australian Dollar ("AUD"):	**Y** = 0.0457***X*** + 4.4415
European Euro ("Euro"):	**Y** = 0.0733***X*** + 7.3358
New Zealand Dollar ("NZD"):	**Y** = 0.0302***X*** + 4.1366
Canadian Dollar ("CAN"):	**Y** = 0.0605***X*** + 4.8233

Figure 2.1: Actual Trends, Linear Regression Lines, Regression Equations for 36 months starting from 1 January 2005 and ending 31 December 2007[2]

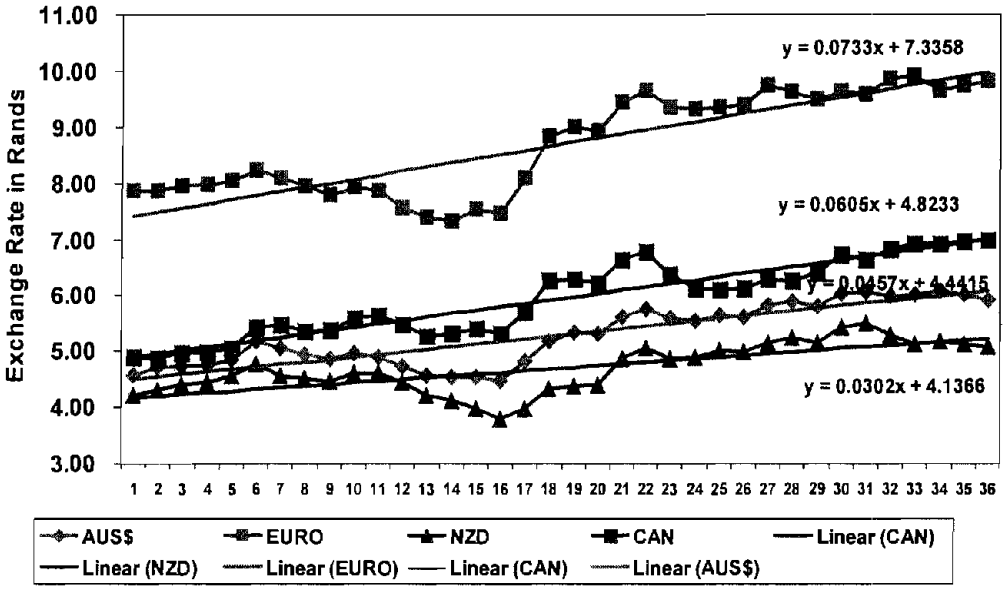

Table 2.2: Comparison of Exchange Rate Options to Convert Pharmaceutical Prices from Foreign to Domestic Prices

Date	AUD	EURO	NZD	CAN
ACTUAL				
2005	4.85	7.91	4.49	5.26
2006	5.10	8.52	4.41	5.97
2007	5.90	9.64	5.18	6.60
RESULTS OF REGRESSION ANALYSIS				
2006	5.29	8.69	4.70	5.94
2007	5.84	9.57	5.06	6.67
2008	*6.38*	*10.45*	*5.42*	*7.39*

[2] The general "upward" trend in the rates indicates that the nominal value of the Rand is depreciating steadily over time. This trend will primarily be a consequence of relative inflation rates. Any country with a sustained higher inflation rate will depreciate in nominal terms against the Rand.

3. COMBINATION PRODUCTS

3.1 Definitions

3.1.1 Combination Product

For the purposes of international benchmarking, combination products are defined as:

1. A product comprising of two or more components, which are regulated by the schedules in the **Medicines and Related Substances Act 101 of 1965**, which have been combined or mixed and produced as a single entity.
2. Two or more separate medicinal products co-packed together in a single package.

3.1.2 Primary Mode of Action

The primary mode of action of a combination product is the most important registered indication of the combination product.

3.1.3 Anatomical Therapeutic and Chemical (ATC) classification system

For the purposes of classifying therapeutic effects the Committee *has adopted the World Health Organisation's Anatomical Therapeutic and Chemical ("ATC") classification system.* In this classification system, medicines are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties.

Medicines are classified in groups at five different levels. The medicines are divided into fourteen main groups (1st level), with one pharmacological/ therapeutic subgroup (2nd level). The 3rd and 4th levels are chemical/ pharmacological/ therapeutic subgroups and the 5th level is the chemical substance.

The complete classification of metformin provided in **Table 3.1** illustrates the structure of the code.

Table 3.1: Complete Classification of Metformin

	Description	Example	
1st level	Anatomical main group	A	Alimentary tract and metabolism
2nd level	Therapeutic subgroup	A10	Drugs used in diabetes
3rd level	Pharmacological subgroup	A10B	Oral blood glucose lowering drugs
4th level	Chemical subgroup	A10BA	Biguanides
5th level	Chemical substance	A10BA02	Metformin

3.2 Methodology for benchmarking combination products

3.2.1 Comparator exists for a combination product

In cases where a medicine has a comparator in the basket of benchmark countries it is logical to make use of the comparator. *It is therefore recommended that the international benchmarking methodology for originator medicines, outlined in* ***Section 1****, applies.*

3.2.2 No comparator is identified

Where no comparator is identified two scenarios arise:

1. The combination can exist as a single product; or
2. The combination of products can be co-packaged.

With respect to (1) above the following shall apply:

1. *The applicant designates the primary mode of action and therapeutic category according to the definitions above.*
2. *Once the benchmarking of originator products for which there are comparators has been finalised, the average price for that ATC will then be calculated by the Committee.*
3. *For the purposes of this application the 4th level of the ATC will be used.*

4. *The average price within the ATC will then become the single exit price for all combination products that do not have a comparator in the benchmark countries.*

5. *If the applicant has good quality evidence in the form of a randomized controlled clinical trial/s that demonstrates superior efficacy or safety for the combination product against an appropriate set of comparators, then the applicant may submit such a product for pharmacoeconomic review.*

With respect to (2) *the Committee recommends that the SEP for each individual product be summed together and the total decreased by 10%, given that there will be a saving on the packaging costs for co-packaged products as opposed to each product being individually packaged.*

4. TIMELINES

The indicative timeline for implementation is as follows:

a. **Regulation 5(2)(e) (Government Gazette No. 26304 of 30 April 2004**) requires that the SEP be set in compliance with the international benchmarking methodology "*within 3 months of publication of such methodology*".

b. It is anticipated that after review of the comments the Minister would publish the final methodology by the end of **October 2008**. SEPs must comply with the interim benchmark by the beginning of **February 2009**.

c. Applicants must therefore submit full data on the application of the interim benchmark methodology to each of their products within two months of publication of the benchmarking methodology (e.g. by the end of **December 2008** using the above illustrative timeline).