An analysis of cancer medicines: failure to use TRIPS flexibilities means that SA pays far more for cancer medicines than the cost of generics available internationally

Prepared by TAC. October 2012

The table below looks at the cost of a number of cancer medicines in the private and public sectors in South Africa. These medicines are under patent and therefore only branded medicine or 'branded generics' produced by a licensed subsidiary are available in South Africa. Alternatively, generic versions of these medicines are already available in India. India has used a range of flexibilities allowed under to TRIPS to allow for generic production of these medicines. These flexibilities include using the extension period allowed to Middle Income Countries until 2005, refusing new use and new formulation patents and granting a compulsory license. The detailed analysis of each medicine (provided below this table) shows that most of these medicines are excluded from prescribed minimum benefits because of their high costs and, where it says N/A, the medicines are not procured for use in the public sector.

According to Mediscor's annual Medicine Review, cystostatics (cancer medicines) are the second highest cost to South African medical schemes.[1] According to Discovery, oncology treatment in South Africa is 17 times more expensive than any other treatment for non-communicable diseases. Additionally, the cost of oncology in South Africa has grown 11% year on year since 2008 and the increase was mainly because of speciality drugs.[2]

Examples of cancer medicine prices in the South African private and public sectors versus prices available in India

Medicine	South African private sector price	South African public sector price	Indian generic price
Imanitib mesylate	R863 per 400 mg tablet	N/A	R46.20 per 400 mg tablet
Sorafenib	R381 per 200 mg table	N/A	R8.55 per 200 mg tablet
Bortezomib	R11,548.70 per 3.5 mg vial	N/A	R2,980 per 3.5 mg vial
Oxaliplatin	R2,331.79 per 50mg/10ml injection R4,663.53 per 100mg/20ml injection	R702 for 50 mg injection for infusion R1,405.34 for 100 mg injection for infusion	50 mg price not sourced R585 per 100 mg vial for injection
Rituximab	R2,789.50 per 10mg/ml infusion R13,947 per 500 mg injection	R1,589.99 for 100 mg injection R 7,950.01 for 500mg injection	R1,542 per 100 mg vial R6,173 per 500 mg vial
Temozolomide	R958.73 per 100 mg tablet	R903.44 per 100 mg tablet	R273.79 per 100 mg tablet (Note: Cipla has announced it will reduce the price to R74 per tablet)

N/A means the medicines is not procured in the public sector. More detailed information is available in the table below.

[1] According to the Mediscor Review, anti-hypertensive medicines accounted for the top expenditure by medical schemes on a medicine group in 2011.

[2] Coetzee, G. 2012. 'Generic drugs are vital for a healthy Africa'. Mail&Guardian [online] 6 October 2012. Available at http://mg.co.za/article/2012-10-06-generic-drugs-are-vital-for-a-healthy-africa

Annexure: Detailed analysis of availability of 6 cancer medicines in South Africa's private and public sectors with SA versus India cost comparisons

Unless information is explicitly references then:

- All public sector prices are calculated from the current government tender
- All private sector prices were sourced from Medprax on 30 July 2012
- Indian generic prices were supplied by MSF India during September and converted to Rands on 26 September 2012
- Data on prescribed minimum benefit status was sourced from the Council for Medical Schemes (CMS)
- Data on patent status was sourced from the Companies and Intellectual Property Commission's online patent database. However companies are not required to submit applications under the name of the product to which the patent application is subject. Therefore some patents on these medicines may not be included in the table below.
- Data on private sector expenditure was sourced from Mediscor's 2011 Medicine Review

Example 1.

Imanitib mesylate
Brand names: Gleevec/ Glivec

Imanitib mesylate has received approval to treat 10 cancers, including chronic myelogenous leukemia (CML) and gastrointestinal stromal tumors. Numerous studies have demonstrated the efficacy of Gleevec, and improved survival rates for CML patients (from 42 – 65% between 1983 and 2000 to 87% from 2001 onwards) since the introduction of this medicine.[3]

SA PRIVATE SECTOR PRICE	SA PUBLIC SECTOR PRICE	GENERICS AVAILABLE IN INDIA
R863 per 400 mg tablet (Novartis) In 2011, the SEP for Gleevec was R360 000 per patient per annum	Not procured for use in the public sector.	R46.20 per 400 mg tablet (Cipla) R53.18 per 400 mg tablet (Natco) India rejected the patent application on Imanitib mesylate because it is a new formulation of an existing molecule.
SA PRIVATE SECTOR USAGE AND PMB STATUS	**SA PUBLIC SECTOR USAGE/ NEED**	
In 2010 and 2011 the private sector spent more on Gleevec than any other cancer medicine. CML is a prescribed minimum benefit. According to the CMS, 233 medical scheme users suffered from CML in 2011. However, according to the CMS, 'Although Gleevec is effective [in treating CML], it is not considered PMB level of care due to [un]affordability.'	The incidence of CML is cited at 2/100 000/year; however local South African incidence and prevalence data are lacking.[4] According to the CMS, 233 medical scheme users suffered from CML in 2011. However, only roughly 16% of the population is covered by medical schemes. The rest of the population receives care from the public sector. The public sector does not procure Gleevec but receives some free through Novartis's free assistance programme. Novartis has provided Gleevec to 553 patients in the public sector (it is not clear whether this figure is for current patients or total patients over the last decade).[5]	

Patent status:
Imanitib mesylate is under patent in South Africa and therefore can only be purchased from the patent holder, Novartis. In South Africa there are a total of seven patents containing the word 'imatinib' of which three are accepted and four granted. The expiration dates rank from 2025 to 2029.

[3] H Kantarjian et a. Imrpover survival in chronic myeloid leukemia since the introduction of imanitb therapy: a single-institution historical experience. Blood: Journal of the American Society of Haemotology. January 2012 0.1182/blood-2011-08-358135

[4] V J Louw et al., Recommendations for the management of adult chronic myeloid leukaemia in South Africa. November 2011, Vol. 101, No. 11 SAMJ

[5] This figure was accessed through email communication with Novartis on 8 October. Novartis has failed to respond to follow up queries as to whether this is the total number of patients that have received Gleevec since GiPAP began in 2002, or if this is current patients.

Example 2.

Sorafenib
Brand name: Nexavar

Sorafenib is used to treat kidney and liver cancers, mainly hepatocellular carcinoma and renal cell carcinoma. Clinical trials have shown that sorafenib extend survival by three months in patients with advanced heptocellular carcinoma.[6] When used in renal cell carcinoma, a planned analysis of overall survival at this time demonstrated a 28% reduction in the risk of death among patients receiving sorafenib, as compared with those receiving placebo.[7] Following demonstration of progression free survival with Sorafenib, patients receiving placebo were switched to sorafenib. The final analysis did not demonstrate an improvement of overall survival between the two groups, but the authors suggested that this may have been confounded by the cross-over of patients from placebo to sorafenib.[8]

SA PRIVATE SECTOR PRICE	SA PUBLIC SECTOR PRICE	GENERICS AVAILABLE IN INDIA
R381.00 per 200 mg tablet (Bayer) A cycle costs R240 000, total treatment costs exceed R1 million	Not procured for use in the public sector.	R8.55 per 200 mg tablet[9] (Cipla) R11.00 per 200 mg tablet (Natco) India granted a compulsory licence on sorafenib in 2012, allowing generic production and sale of the medicine.
PMB STATUS		
Renal cell carcinoma is a PMB. However sorafenib is not considered a PMB for the condition because according to CMS, 'it is costly and may not be cost effective' given limited benefit the patient.		

Patent status:
Three patent applications on the 'antitumor combination including AVE0862 and sorafenib', 'the process for the preparation of sorafenib tosylate' and 'sorafenib dimethyl sulphoxide solvate' are currently pending.

[6] J M Llovet et al. Sorafenib in Advanced Hepatocellular Carcinoma. N Engl J Med 2008; 359:378-390
[7] B Escudie et al. Sorafenib in Advanced Clear-Cell Renal-Cell Carcinoma. N Engl J Med 2007; 356:125-134
[8] B Escudier et al. Sorafenib for Treatment of Renal Cell Carcinoma: Final Efficacy and Safety Results of the Phase III Treatment Approaches in Renal Cancer Global Evaluation Trial. *JCO July 10, 2009 vol. 27 no. 20 3312-3318*
[9] Price converted from Rs on 25 July

Example 3.

<table>
<tr><td colspan="3">Bortezomib
Brand name: Velcade</td></tr>
<tr><td colspan="3">Bortezomib is used to treat multiple myeloma and in second line treatment for patients with mantle cell lymphoma. A study published in 2010 showed that the addition of Bortezomib, with other medicines used to treat multiple myeloma, reduced the risk of death by 35%.[10]</td></tr>
<tr><td>SA PRIVATE SECTOR PRICE</td><td>SA PUBLIC SECTOR PRICE</td><td>GENERICS AVAILABLE IN INDIA</td></tr>
<tr><td>R11,548.70 per 3.5 mg vial
(Janssen Pharmaceuticals)</td><td rowspan="2">Not procured for use in the public sector.</td><td rowspan="2">R2,980 per 3.5 mg vial
(Intas Biopharmaceuticals)

R2,849 per 3.5 mg vial
(Natco)

The molecule was developed before 1995 and therefore the medicine was not patented. Additionally, unlike SA, India does not grant new use or new formulation patents.</td></tr>
<tr><td>SA PRIVATE SECTOR USAGE AND PMB STATUS
Bortezomib ranked 5th according to overall expenditure on cystostatics in the private sector.

According to the CMS this medicine is not a PMB because it is unaffordable.</td></tr>
<tr><td colspan="3">Patent status:
In South Africa patent on the ‘lipsomal formulation of bortezomib’ was granted in 2007 and a process patent application is currently pending.</td></tr>
</table>

[10] Mateos M-V et al. Bortezomib Plus Melphalan and Prednisone Compared With Melphalan and Prednisone in Previously Untreated Multiple Myeloma: Updated Follow-Up and Impact of Subsequent Therapy in the Phase III VISTA Trial. Journal of Clinical Oncology. Volume 28, Number 13, May 2010. Available at http://jco.ascopubs.org/content/28/13/2259.full.pdf

Example 4.

<table>
<tr><td colspan="3">Oxaliplatin
Brand name: Eloxatin</td></tr>
<tr><td colspan="3">Oxaliplatin is used in advanced colorectal cancer and stage III colon cancer. A trial demonstrated that the addition of oxaliplatin to a regimen of 5FU and leucovorin improved the probability of disease-free survival at three years from 72.9 to 78.2% (P=0.002).[11]</td></tr>
<tr><td>SA PRIVATE SECTOR PRICE</td><td>SA PUBLIC SECTOR PRICE</td><td>GENERICS AVAILABLE IN INDIA</td></tr>
<tr><td>R2,331.79 per 50mg/10ml injection
(Sanofi-Aventis)

R4,663.53 per 100mg/20ml injection
(Sanofi-Aventis)</td><td>R702 for 50 mg injection for infusion
(Winthrope Pharmaceuticals – a member of the Sanofi-Aventis group)

R1,405.34 for 100 mg injection for infusion
(Winthrope Pharmaceuticals – a member of the Sanofi-Aventis group)</td><td rowspan="2">R585 per 100 mg vial
(Cipla)

R705.24 per 100 mg vial
(Glenmark Pharmaceuticals)

R1,518.29 per 100 mg vial
(Dr Reddy)

The molecule was developed before 1995 and therefore the medicine was not patented. Additionally, unlike SA, India does not grant new use or new formulation patents.</td></tr>
<tr><td>SA PRIVATE SECTOR USAGE AND PMB STATUS</td><td>SA PUBLIC SECTOR USAGE</td></tr>
<tr><td>Oxaliplatin ranks 6th in terms of overall expenditure on cancer medicines in the private sector.

The medicine is included as a PMB for patients with colon cancer.</td><td>2,100 50 mg injections and 4,4000 100 mg injections were purchased in the 2012/14 tender.</td><td></td></tr>
<tr><td colspan="3">Patent status:
A patent on ‘oxaliplatin solution formulations and the method of use thereof’ was granted in 1999. A patent on ‘pharmaceutically stable oxaliplatin preparation for parental administration’ was granted in 2002. And a patent for ‘treatment with oxaliplatin and an egfe-inhibitor’ was granted in 2006.</td></tr>
</table>

[11] Andre. T, Boni. C, Mounedji-Boudiaf. L et al. Oxaliplatin, Fluorouracil, Leucovorin as adjuvant treatment for colon cancer. NEJM 2004;350:2343-51

Example 5.

<table>
<tr><td colspan="3">Rituximab
Brand names: Rituxan and MabThera</td></tr>
<tr><td colspan="3">Rituximab is used to treat non-Hodgkin lymphoma and chronic lymphocytic leukemia. A number of studies have found that Rituximab, in addition to chemotherapy, improves overall survival in comparison to patients receiving chemo alone statistical significant better overall survival in the R-chemo group compared with the chemotherapy-alone group (RR, 1.09, 95% CI: 1.06–1.12, p <0.0000).[12] Additionally, trials have shown that the addition of Rituximab to chemotherapy with fludarabine and cyclophosphamide, improved outcomes. In two trials complete response (the disappearance of all signs of cancer) was almost doubled in patients receiving rituximab.[13]</td></tr>
<tr><td>SA PRIVATE SECTOR PRICE</td><td>SA PUBLIC SECTOR PRICE</td><td>GENERICS AVAILABLE IN INDIA</td></tr>
<tr><td>R2,789.50 per 10mg/ml infusion
(Roche)

R13,947 per 500 mg injection
(Roche)</td><td>R1,589.99 for 100 mg injection, 10 ml vial for infusion
(Roche)

R 7,950.01 for 500mg injection, 50ml vial for infusion
(Roche)</td><td rowspan="3">R1,542 per 100 mg vial
(Dr Reddy)

R6,173 per 500 mg vial
(Dr Reddy)

The molecule was developed before 1995 and therefore the medicine was not patented. Additionally, unlike SA, India does not grant new use or new formulation patents</td></tr>
<tr><td>SA PRIVATE SECTOR USAGE</td><td>SA PUBLIC SECTOR USAGE</td></tr>
<tr><td>Rituximab ranks 3rd, in terms of total expenditure on cancer medicines by medical schemes.</td><td>2,700 100 mg injections and 2,100 500 mg injections were purchased in the 2012/14 tender.</td></tr>
<tr><td colspan="3">Patent status:
In South Africa, a patent was granted for the ‘intrathecal administration of rituximab for the treatment of central nervous system lymphomas”, which will expire in 2022 and for ‘antineoplastic combinations of CCI-779 and Rituximab’ which will expire in 2026.</td></tr>
</table>

[12] G Gao. A systematic review and meta-analysis of immunochemotherapy with rituximab for B-cell non-Hodgkin's lymphoma. Informa Healthcare. January 2010, Vol. 49, No. 1 ,

[13] National Cancer Institute. Rituximab Improves Outcomes for Patients With Chronic Lymphocytic Leukemia. Posted**:** 01/14/2009

Example 6.

<table>
<tr><td colspan="3">Temozolomide
Brand names: Temodar/ Temodal/Temcad</td></tr>
<tr><td colspan="3">Temozolomide is used to treat, melanoma (a form of skin cancer), as well as, aggressive brain tumors. A study found that temozolomide reduced the size of brain tumors in 53% of the study's participants.[14]</td></tr>
<tr><td>SA PRIVATE SECTOR PRICE</td><td>SA PUBLIC SECTOR PRICE</td><td rowspan="3">GENERICS AVAILABLE IN INDIA

R273.79 per 100 mg tablet
(Cipla)

R305.53 per 100 mg tablet
(Dr Reddy)

Cipla has announced that it will market the medicine at even lower prices:[15]
R154 per 250 mg tablet
R74 per 100 mg tablet
R14.80 per 20 mg tablet

The molecule was developed before 1995 and therefore the medicine was not patented. Additionally, unlike SA, India does not grant new use or new formulation patents</td></tr>
<tr><td>R2,397.50 per 250 mg capsule
R958.73 per 100 mg capsule
R191 per 20 mg capsule
R48 per 5 mg capsule
(MSD)</td><td>R903.44 per 100 mg tablet
(MSD)</td></tr>
<tr><td>SA PRIVATE SECTOR USAGE</td><td>SA PUBLIC SECTOR USAGE</td></tr>
<tr><td>The medicines is not a PMB for the treatment of brain glioma, because according the the CMS it is not cost effective and it does not provide better results than Carmustine.</td><td>5,500 capsules were ordered in the 2012/14 tender</td><td></td></tr>
<tr><td colspan="3">Patent status:
In South Africa, 10 patents containing the word 'Temozolomide' were granted between 1994 and 2009.</td></tr>
</table>

[14] American Academy of Neurology. Chemotherapy drug shrinks brain tumors. MAY 21, 2007. Available at http://www.aan.com/press/index.cfm?fuseaction=release.view&release=509

[15] http://www.thehindubusinessline.com/companies/article3379501.ece?homepage=true . (Prices converted to Rands on 27 September)