Cancer Alliance motivation for provision of trastuzumab in South Africa's public sector to women with HER2 positive breast cancer

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1. The Cancer Alliance is a collective group of 20 cancer control non-profit organisations and cancer advocates brought together under a common mandate, to provide a platform of collaboration for cancer civil society to speak with one voice and be a powerful tool to affect change for all South African adults and children affected by cancer. Member organisations of the Cancer Alliance work closely with people affected by cancer, often in underserved communities, providing a range of support services. Many of the individuals working or volunteering with member organisations of the Cancer Alliance are cancer survivors themselves. Under the umbrella of the Cancer Alliance, member groups jointly undertake advocacy on issues related to cancer prevention, detection and treatment. During 2015 and 2016, the Cancer Alliance has led advocacy efforts by the Fix the Patent Laws coalition for affordable and equitable access to trastuzumab in South Africa. The Fix the Patent Laws coalition is a coalition of 31 patients groups and health-focused organisations in South Africa seeking reform of the country's patent laws to improve medicine access.

Rates of HER2 positive breast cancer in South Africa and globally

2. Breast cancer is the second most common cancer globally, and the most common cancer faced by women.[1] Breast cancer is the leading cause of cancer death faced by women in developing countries and the 5th leading cause of cancer death globally.[2] In South Africa, breast cancer is the second leading cause of cancer death after cervical cancer.[3] Approximately 1 in 29 women in South Africa will experience breast cancer in their lifetime.[4] While

[1] Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D. M., Forman, D. and Bray, F. (2015), Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int. J. Cancer, 136: E359–E386. doi:10.1002/ijc.29210
[2] Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D. M., Forman, D. and Bray, F. (2015), Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int. J. Cancer, 136: E359–E386. doi:10.1002/ijc.29210
[3] http://www.who.int/cancer/country-profiles/zaf_en.pdf?ua=1
[4] http://www.cansa.org.za/womens-health/

Africa generally experiences lower rates of breast cancer than other regions, incidence rates are increasing in the region[5] and in South Africa[6].

3. Approximately 1 in 5 women diagnosed with breast cancer are HER2 positive – meaning that the human epidermal growth factor receptor (HER2) is over expressed in the breast cancer tumor.[7] HER2 overexpression is associated with more aggressive disease, higher rates of recurrence and higher mortality rates than HER2 negative tumors.[8] International evidence has demonstrated that HER2 overexpression is generally more common among younger women with breast cancer than older women.[9],[10] Evidence from South Africa indicates that young black women may be more at risk for developing breast cancer at a younger age and HER2-enriched breast cancer than other racial groups:

    a. A study of black women diagnosed with breast cancer at Chris Hani Baragwanath between October 2006 to July 2012, showed that 26% (of the 942 for whom data was available on molecular subtype was available) were HER2 positive.[11]

    b. A study comparing breast cancer receptor status with race in Namibia and South Africa considered diagnostic results of 10,047 women (with known receptor statuses) diagnosed between 2009–2011 in South Africa's public sector or between 2011-2013 in Namibia. The study found that overall 25.2% of tumours were HER2 positive. The study also demonstrated that black women are more likely to be diagnosed with HER2 enriched breast cancer[12] - a subtype of HER2 breast cancer that is more responsive to trastuzumab.[13]

    c. A study at the Mammogram Clinic of the Universitas Hospital, Bloemfontein compared the demographic status of women who consented to participate in the study, with their breast cancer profiles. While the study found that breast cancer was most common amongst women between 50 and 60, breast cancer under the age of 40 occurred more frequently in black women than other racial groups. The

[5] http://www.who.int/cancer/country-profiles/zaf_en.pdf?ua=1
[6] http://www.gov.za/international-breast-cancer-month-2015
[7] Mitri Z, Constantine T, O'Regan R. The HER2 Receptor in Breast Cancer: Pathophysiology, Clinical Use, and New Advances in Therapy. *Chemotherapy Research and Practice*. 2012;2012:743193. doi:10.1155/2012/743193.
[8] Mitri Z, Constantine T, O'Regan R. The HER2 Receptor in Breast Cancer: Pathophysiology, Clinical Use, and New Advances in Therapy. *Chemotherapy Research and Practice*. 2012;2012:743193. doi:10.1155/2012/743193.
[9] Cronin K, Harlan L, Dodd K, Abrams J, and Ballard-Barbash R. Population-based Estimate of the Prevalence of HER-2 Positive Breast Cancer Tumors for Early Stage Patients in the US. Cancer Investigation Vol. 28 , Iss. 9,2010
[10] Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast Cancer Before Age 40 Years. *Seminars in oncology*. 2009;36(3):237-249. doi:10.1053/j.seminoncol.2009.03.001.
[11] Cubash H et al. Breast cancer characteristics and HIV among 1,092 women in Soweto, South Africa. Breast Cancer Res Treat. 2013 Jul; 140(1): 177–186.
[12] Dickens C et al. Racial Comparison of Receptor-Defined Breast Cancer in Southern African Women: Subtype Prevalence and Age–Incidence Analysis of Nationwide Cancer Registry Data. Cancer Epidemiol Biomarkers Prev November 1 2014 (23) (11) 2311-2321; DOI: 10.1158/1055-9965.EPI-14-0603
[13] Montemurro et al. Potential biomarkers of long-term benefit from single-agent trastuzumab or lapatinib in HER2-positive metastatic breast cancer. Volume 8, Issue 1, February 2014, Pages 20–26

authors concluded that "[t]his may suggest that pregnancy and parity were risk factors in this racial group."[14]

Evidence and recommendations for the use of trastuzumab to treat HER2 positive breast cancer

4. Trastuzumab is a biologic therapy known as a humanized monoclonal antibody. Trastuzumab binds to the human epidermal growth factor receptor that are overexpressed in women with HER2 positive cancer – inhibiting the proliferation of tumor cells.[15]

5. Multiple studies have evaluated the safety and efficacy of trastuzumab for treating HER2 positive breast cancer. The results of which have been compared in two systematic Cochrane reviews:

    a. Moja et al (2012) reviewed evidence from 8 clinical trials involving 11,991 patients with early or locally advanced HER2 positive breast cancer that did, or did not receive, trastuzumab in addition to standard chemotherapy alone or with hormone blocking medications. Moja et al reported that trastuzumab improved overall survival by 33% (HR 0.66; 95% CI 0.57 to 0.77, P < 0.00001) and disease free survival by 40% (HR 0.60; 95% CI 0.50 to 0.71, P < 0.00001) – while patients receiving trastuzumab had a five times higher risk of congestive heart failure (RR 5.11; 90% CI 3.00 to 8.72, P < 0.00001) than patients in the control group.[16]

    b. Balduzzi et al. (2014) reviewed evidence from 7 clinical trials involving 1,497 patients, in which trastuzumab was co-administered with chemotherapy, hormonal therapy or targeted therapy. The duration of trastuzumab varied between 8.7 and 30 months with average follow-up at 2 years. Balduzzi et al reported that administration of trastuzumab improved overall survival by 18% (HR 0.82, 95% CI 0.71 to 0.94, P = 0.004) and progression free survival by 39% (HR 0.61, 95% CI 0.54 to 0.70, P < 0.00001) at a median of two years follow up - while patients receiving trastuzumab had a 3.49 higher risk of congestive heart failure **(**RR 3.49, 90% CI 1.88 to 6.47, P = 0.0009) than patients in the control group.[17]

6. Taking account of efficacy and safety evidence, the World Health Organisation added trastuzumab to its complementary Essential Medicines Lists for the treatment of early and metastatic HER2 positive breast cancer in 2015. "The [WHO's] complementary list presents essential medicines for priority

[14] Matatiele PR & Van den Heever WMJ. Breast cancer profiles of women presenting with newly diagnosed breast cancer at Universitas Hospital (Bloemfontein, South Africa). SA Fam Pract 2008, Volume 50 No 6

[15] http://www.herceptin.com/breast/metastatic

[16] Moja L, Tagliabue L, Balduzzi S, et al. Trastuzumab containing regimens for early breast cancer. Cochrane Database Syst Rev 2012, Issue 4. Art. No.: CD006243. DOI:10.1002/14651858.CD006243

[17] Balduzzi S, Mantarro S, Guarneri V, Tagliabue L, Pistotti V, Moja L, D'Amico R. Trastuzumab-containing regimens for metastatic breast cancer. Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD006242. DOI: 10.1002/14651858.CD006242.pub2.

diseases, for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed".[18]

7. One year of trastuzumab, in addition to chemotherapy, is already recommended as standard care in a number of countries for women with early and metastatic HER2 positive breast cancer.[19] However the high price charged by Roche for trastuzumab remains a barrier to access and completion of trastuzumab in countries where its cost is not fully covered by governments or insurers.[20] [21]

Access to trastuzumab in South Africa

8. South Africa has a dual and highly inequitable health care system. The vast majority of people living in South Africa, for whom private medical insurance is unaffordable and inaccessible, are dependent on the government-funded public sector for healthcare services. Only 16.2% of people living in South Africa have private insurance enabling them to access private sector care[2], which they purchase personally or receive via their employer or family members. Private sector expenditure on medical scheme members is approximately 5,25 times greater than per capita spending on individuals that are dependent on the public sector.[22] Demographic data demonstrates racial disparity in access to private sector care, with black South Africans being the least likely to have private insurance coverage of all racial groups.[23]

9. Trastuzumab is not included on South Africa's essential drugs list and is unavailable to the vast majority of women seeking care in the public health care sector – except in rare cases where motivated oncologists have successfully advocated for facility level budgets to be allocated for trastuzumab.[24]

10. In the private sector, not all medical schemes will pay for the cost of trastuzumab treatment even though cancer is a prescribed minimum benefit. The amount of coverage provided for trastuzumab varies across different insurance plans.[25]

[18]http://www.who.int/medicines/publications/essentialmedicines/EML_2015_FINAL_amended_NOV2015.pdf?ua=1

[19] KEI, UC, UAEM, TWN, TP-CDN. Proposal for the inclusion of trastuzumab in WHO EML for treatment of HER2-Positive Breast Cancer. 2013. Available at: http://keionline.org/node/2070

[20] Freedman, Rachel A et al. "Use of Adjuvant Trastuzumab in Women with Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast Cancer by Race/Ethnicity and Education within the National Comprehensive Cancer Network." *Cancer* 119.4 (2013): 839–846. *PMC*. Web. 28 Oct. 2016.

[21] Lammers, Philip et al. "Barriers to the Use of Trastuzumab for HER2+ Breast Cancer and the Potential Impact of Biosimilars: A Physician Survey in the United States and Emerging Markets." *Pharmaceuticals* 7.9 (2014): 943–953.*PMC*. Web. 28 Oct. 2016.

[22] Ataguba J & Akazili H. Health care financing in South Africa: Moving towards universal coverage. *Continuing Medical Education* 2010;28(2):74.

[23] StatsSA. Use of health facilities and levels of selected health conditions in South Africa: Findings from the General Household Survey, 2011. Available at: Use of health facilities and levels of selected health conditions in South Africa: Findings from the General Household Survey, 2011

[24] Conversation with public sector oncologist October 2016

[25] Conversations with medical aid members seeking trastuzumab for HER2 positive breast cancer

11. Members have challenged their medical schemes to cover the cost of trastuzumab. In 2006, Samantha Galliet successfully challenged her medical aid Discovery's refusal to cover the full cost of trastuzumab in the Johannesburg High Court.[26] In 2014, HER2 positive breast cancer patient Veroney Judd-Stevens challenged her medical scheme (Bonitas) for refusing to cover the cost of a full one year course of trastuzumab at the Council for Medical Schemes. While the Council for Medical Schemes initially ruled that Bonitas must cover 12 months of trastuzumab for Judd-Stevens, this ruling was overturned on appeal.[27] [28] The CMS ruled that Bonitas need not pay for trastuzumab due to its high cost.

12. Given the high cost of trastuzumab, and the limited access in the public and private sector, a small number of women that can afford its high cost are able to access trastuzumab out-of-pocket. Despite limited access in the country, Roche is able to reap significant income from the sale of trastuzumab in South Africa. During 2013, Herceptin was one of the three top-selling anticancer drugs in South Africa[29], and earned Roche more than ZAR 100 million (US$ 7.07 million) in annual revenue.[30] Between 2013 and 2014, Herceptin moved from the fifth to the second highest driver of expenditure on medicines in the private sector – where it remained in 2015.[31] [32] Roche has been able to recoup huge profits by charging extremely high prices for trastuzumab - despite the large amounts of public sector funding that contributed to the medicine's development[33] and extremely limited access.

Considering cost-effectiveness and equity

13. A recent article published in the South African Medical Journal considered the cost-effectiveness of providing trastuzumab in the public sector. Using figures from Moja et al.'s systematic review (a baseline survival rate of 90% at 15 years and a hazard ratio of 0.69), Abbratt calculated that the number needed to treat to prevent 1 death is 33.[34] (A number of other studies have calculated to NNT to prevent 1 death related to HER2 positive breast cancer ranging between 13 and 35.[35] [36] [37][38]) Using an NNT of 33 and Roche's private sector price for trastuzumab, Abbratt questioned the cost-effectiveness of providing

[26] http://mg.co.za/article/2006-10-09-you-can-make-a-difference
[27] http://m.timeslive.co.za/thetimes/?articleId=15283787
[28] http://www.timeslive.co.za/thetimes/2015/10/08/Medical-aid-allowed-to-cap-cancer-drug-benefit
[29] Mediscor Medicines Review 2013
[30] Data on pharmaceutical companies' earnings on medicines during 2013 was sourced from IMS Health. Available via request from http://www.imshealth.com/portal/site/ imshealth
[31] Mediscor Medicines Review 2014
[32] Mediscor Medicines Review 2015
[33] http://keionline.org/node/1031
[34] Abratt, R P. Cost considerations in determining the affordability of adjuvant trastuzumab in breast cancer. South African Medical Journal, [S.l.], v. 106, n. 10, p. 981-982, sep. 2016. ISSN 2078-5135. Available at: http://www.samj.org.za/index.php/samj/article/view/11141
[35] Curigliano G, Viale G, Bagnardi V et al. Clinical relevance of HER2 overexpression/amplification in patients with small tumor size and node-negative breast cancer. J Clin Oncol 2009; 27: 5693–5699.
[36] Gonzalez-Angulo AM, Litton JK, Broglio KR et al. High risk of recurrence for patients with breast cancer who have human epidermal growth factor receptor 2-positive, node-negative tumors 1 cm or smaller. J Clin Oncol 2009; 27: 5700–5706.
[37] Mt-Isa S. Weighing benefit–risk of medicines: concepts and approaches. Innovative Methods in Drug Regulatory Sciences. Volume 8, Issue 1, Spring 2011, Pages e29–e35
[38] Untch et al. Adjuvant Treatment with Trastuzumab in Patients with Breast Cancer. Dtsch Arztebl 2006; 103(50):A 3406–10.

trastuzumab in the public sector for patients with low-risk disease (baseline survival rate > 90%).

14. While the NNT for trastuzumab does not justify denial of the WHO recommended essential treatment to public sector patients, it is important to note that the expansion of molecular diagnostics would allow for better detection of patients that could benefit from trastuzumab.[39]

15. Importantly, while cost-effectiveness is a useful measure to inform policy decisions related to treatment protocols – it must be considered in addition to other factors, including equity considerations, governments' legal obligations to protect health, available resources and available mechanisms to secure more affordable prices. As noted by Kishore et al. "[a]lthough the notion of 'cost-effectiveness' is a useful concept in public health, it can end up punishing the poor. Indeed, the dangers of letting cost-effectiveness dictate treatment harkens back to arguments previously used to justify keeping HIV/AIDS medications out of the developing world." With regards to trastuzumab, Robertson et al. noted that "[i]n including trastuzumab on its 2015 Model List of Essential Medicines, WHO has made a strong statement about the medicine's utility and – as happened with therapy for human immunodeficiency virus – this may promote efforts to reduce the medicine's costs and so increase its affordability and availability"[40]

16. When prices inhibit medicine access, rather than concluding that their use in not cost-effective, governments must explore all available means to improve affordability and expand access.

Mechanisms to secure more affordable prices for trastuzumb

17. Currently Roche is the only provider of trastuzumab in South Africa – sold under the brand names Herceptin and Herclon. In the private sector a 440 mg vial of Herceptin costs ZAR 25,835 – or approximately ZAR 516,700 per 12-month course[41]. Roche offers a lower price for its Herclon product in the public sector, which may be procured from facility budgets. A 400 mg vial of Herclon costs ZAR 10,596 -or approximately ZAR 211,920 per 12-month course.[42]

18. In negotiating a price with Roche, the Department of Health must ensure that patent barriers do not block competitor products from entering the market to reduce price. Additionally, South Africa should require greater transparency of research, development and production costs to make more informed judgements about the division of resources.

a. Ensuring competitor products are not blocked from the market

19. Patent monopolies held by Roche and Genentech (which provides exclusive marketing rights to Roche) in South Africa could block the use of biosimilar

[39] Hagemann IS. Molecular Testing in Breast Cancer: A Guide to Current Practices. Arch Pathol Lab Med. 2016 Aug;140(8):815-24. doi: 10.5858/arpa.2016-0051-RA.
[40] http://www.who.int/bulletin/volumes/94/10/15-163998/en/
[41] Price accessed at the Medicines Price Registry during November 2016: http://www.mpr.gov.za/
[42] Price accessed from conversation with Roche, November 2016

products in the country until 2033.[43] Patent monopolies on trastuzumab have been overcome in a number of countries, such as India and the UK, where the patent has expired or been withdrawn by the patent holder, or through successful opposition procedures - opening the door to more cost-effective biosimilar products.

20. In India, a biosimilar product has been registered and is available at ZAR 7,307 per 440 mg vial – or approximately ZAR 146,140 per 12-month course.[44] This biosimilar product is under review for registration at the European Medicines Agency[45] in Europe. Additionally, a number of other biosimilar trastuzumab products are in various stages of testing.[46] As competitors' products enter the market in countries where trastuzumab patents are no longer in force, prices should fall as a result of increased competition. Yet South Africa may miss out on these price reductions given ongoing patent monopolies on trastuzumab.

21. To facilitate the use of competitor products, Roche should publicly commit that it will not assert any ongoing patents in South Africa. In the case that Roche fails to do so, the Department of Health can utilise compulsory licensing or other tools to access biosimilar products.

22. Finally, the Medicines Control Council must act with urgency in reviewing registration applications for biosimilar products, given the excessive prices often charged for biologic products and the urgent need for more affordable products to improve equitable access.

b. Expanding transparency of development and production costs

23. In the long term, the Department of Health must require greater transparency of medicine's development and production costs – as recently recommended by the United Nations High Level Panel on Access to Medicines[47] – and should consider adopting legislation in this vein. Legislated transparency requirements will allow governments to assess cost-effectiveness on the basis of actual costs of drug production – rather than arbitrary prices set by private companies seeking to maximise profits. Hill et al. explain "[a]t current published prices, many treatments may currently not be cost-effective for use in low or middle income countries. However this situation could change significantly if the true cost of production were used, with an appropriate royalty to the originator company if the drug is still on patent."[48]

24. Hill and his research team have undertaken analyses of the production costs of a number of medicines used to treat drug-resistant tuberculosis[49], hepatitis

[43] http://www.fixthepatentlaws.org/wp-content/uploads/2016/09/MSF-FTPL-report-FINAL-VERSION.pdf
[44] http://www.fixthepatentlaws.org/wp-content/uploads/2016/09/MSF-FTPL-report-FINAL-VERSION.pdf
[45] http://www.fiercepharma.com/pharma-asia/biocon-and-mylan-claim-lead-as-ema-starts-review-herceptin-biosimilar
[46] http://www.gabionline.net/Biosimilars/General/Biosimilars-of-trastuzumab
[47] United Nations. Report of the United Nation's Secretary General's High Level Panel on Access to Medicines. Available at http://www.unsgaccessmeds.org/final-report
[48] http://www.unsgaccessmeds.org/inbox/2016/2/25/andrew-hill-dr-anton-pozniak-and-dr-james-freeman?rq=hill
[49] Hill A. Target Generic Prices for Novel Treatments for Drug-resistant Tuberculosis. EACS Online Library. Hill A. Oct 22, 2015; 114914

B[50], hepatitis C[51] and cancer[52] – revealing that the costs of production are often a small fraction of the high prices charged. Hill et al. have also undertaken a preliminary analysis of the costs of production of trastuzumab active pharmaceutical ingredient (API). Using price data for trastuzumab API imported into, and exported from India, Hill et al. have estimated that biosimilar trastuzumab can be produced for less than $16 per 600 mg vial. This estimated biosimilar price includes a 40% mark-up on the cost of API for formulation and quality assurance and a 50% increase for profit. The researchers note that this is a lower-range estimate, and is drawn from a very small sample of data (3 data points), however appears to be roughly in line with confidential estimates for trastuzumab production from biosimilar producers reported by Balasubramaniam et al. in 2013.[53] [54]

Including trastuzumab on South Africa's essential drugs list

25. To facilitate access to trastuzumab in South Africa to all women that could benefit, the medicine should be added to the country's essential medicines list. However, it is important that its inclusion on the essential medicines lists is not limited to tertiary facilities – given vast geographical disparity in access to this level of care in South Africa. In the Northern Cape Province, where oncologists have successfully motivated for facility resources to provided trastuzumab to public sector patients, trained nurses successfully manage ongoing treatment at designated outreach clinics around the province.[55] This decentralised model of care should be considered for all nine provinces in the country.

Actions to facilitate access to trastuzumab in South Africa

To ensure access to trastuzumab in South Africa for all women that could benefit it, the Cancer Alliance calls for the Department of Health to pursue the following actions in the immediate and medium term.

Immediate:

- Urgently finalise the tender for procurement of trastuzumab for public sector use in South Africa
- Assess required resources for the roll out of trastuzumab and ensure adequate budget is made available
- Notify the Medicines Control Council of the urgency of timeously reviewing registration requests for biosimilar products

[50] Hill A et al. Analysis of minimum target prices for production of entecavir to treat hepatitis B in high- and low-income countries. Journal of Virus Eradication 01/2015; 1:103-110.
[51] Hill A, Simmons B, Gotham D, Fortunak J. Rapid reductions in prices for generic sofosbuvir and daclatasvir to treat hepatitis C. *Journal of Virus Eradication*. 2016;2(1):28-31.
[52] Hill A et al. Target prices for mass production of tyrosine kinase inhibitors for global cancer treatment. *BMJ Open* 2016;6:e009586 doi:10.1136/bmjopen-2015-009586
[53] Personal communication with Dzintars Gotham (4 Nov 2016, Imperial Colelge London, dg1911@ic.ac.uk): preliminary analysis from data on Indian exported and imported goods (shipped between 1 Jul 2010 and 1 Jul 2016) containing 'trastuzumab' in the shipment description, via the InfoDrive India database
[54] KEI, UC, UAEM, TWN, TP-CDN. Proposal for the inclusion of trastuzumab in WHO EML for treatment of HER2-Positive Breast Cancer. 2013. Available at: http://keionline.org/node/2070
[55] Conversation with public sector oncologist October 2016

- Utilise all available TRIPS flexibilities (including compulsory licensing) as necessary to ensure patents do not inhibit access to more affordable biosimilar products

Medium-term:

- Finalise the national policy for detection and treatment of breast cancer in South Africa
- Include trastuzumab on the country's Essential Drugs List at a level that allows for decentralised models of care
- Train specialist nurses to provide decentralised care with guidance and oversight from oncologists
- Expand and ensure proper functioning of breast cancer education and screening services to allow for early stage diagnosis of women with HER2 positive breast cancer that could benefit from trastuzumab
- Resolve interruptions of mammogram services by ensuring access to properly functioning mammogram units[56]
- Provide greater clarity on resources available for cancer, as well as decision making and allocation processes – and allow cancer NGOs the opportunity to provide input on these processes
- Continue to engage in the ongoing process underway for reform of South Africa's patent laws to fully adopt safeguards allowed under international law to protect health
- Assess and implement the recommendations of the UN High Level Panel on Research and Development – including the recommendation for transparency of pharmaceutical research, development and production costs.

[56] See Cancer Alliance letter to Minister Aaron Motsoaledi dated 17 February 2016