health

Department:
Health
REPUBLIC OF SOUTH AFRICA

National Essential Medicines List Committee (NEMLC)

TERTIARY AND QUATERNARY LEVEL ESSENTIAL MEDICINES LIST

Reviewed Items

JANUARY 2020

SUMMARY OF CHANGES TO THE NEMLC TERTIARY AND QUATERNARY LEVEL ESSENTIAL MEDICINES LIST (JANUARY 2020)					
ATC CODE	**MEDICINE**	**INDICATION**	**NEMLC OUTCOMES**	**REVIEW INDICATORS**	**DATE RATIFIED**
L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS					
L01CD02	Docetaxel	Patients with hormone sensitive prostate cancer (HSPC)	**Approved** **For patients with high volume disease:** defined as the presence of visceral metastases or ≥4 bone lesions with ≥1 beyond the vertebral bodies and pelvis.	• New evidence	30 January 2020
L03AB07/ L03AB08	Interferon beta	Relapsing remitting multiple sclerosis	**Approved**	• New evidence of clear benefit of efficacy of newer classes • Price	30 January 2020
N NERVOUS SYSTEM					
N03AX12/ N03AX16	α2δ calcium channel ligands Gabapentin, Pregabalin	Patients with peripheral neuropathy refractory or intolerant to standard of care (e.g. amitriptyline; or carbamazepine)	**Not Approved** Access can be managed on a named-patient basis, managed by Pharmaceutical and Therapeutics Committees.	• New evidence in the refractory setting • Alternative indications	30 January 2020

TERTIARY AND QUATERNARY LEVEL ESSENTIAL MEDICINES RECOMMENDATIONS					
ATC CODE	**MEDICINE**	**INDICATION**	**NEMLC RECOMMENDATION**	**REVIEW INDICATORS**	**DATE RATIFIED**
A ALIMENTARY TRACT AND METABOLISM					
A04AA01/ A04AA02	**Serotonin-3 (5HT3) antagonists** Ondansetron, Granisetron	Highly emetogenic chemotherapy	**Approved**	n/a	20 September 2007
A05AA02	Ursodeoxycholic acid	Primary biliary cirrhosis.	**Not Approved**	• The emergence of new evidence of efficacy with regard to mortality or transplantation.	13 March 2008
A07EC02	Mesalazine	Ulcerative colitis – maintenance of remission.	**Approved, only** as named patient. May be used on a named-patient basis, on recommendation by PTC for patients with sulphonamide hypersensitivity.	• Price (to be evaluated as a therapeutic class with sulphasalazine)	October 2015
A10BG03	Pioglitazone	Type 2 diabetes mellitus.	**Not Approved**	• Robust safety data	February 2012
A10AE05/ A10AE04	**Long acting insulin analogues** Insulin detemir, Insulin glargine	Diabetes mellitus.	**Not Approved**	• Price decrease (similar to Neutral Protamine Hagedorn (NPH) insulin) • Evidence for superior safety of analogues over NPH	30 June 2016
A16AA03	Glutamine	Glutamine as a component of enteral and parenteral nutrition in critically ill patients.	**Not Approved**	• Robust safety data • Evidence of mortality efficacy.	30 June 2016
B BLOOD AND BLOOD FORMING ORGANS					
B01AC04	Clopidogrel	Percutaneous coronary intervention (stenting).	**Approved** Clopidogrel plus aspirin recommended for a minimum of: • 30 days in situations where a bare metal stent is inserted. • 90 days in situations where a sirolimus drug-eluting stent is inserted. • 180 days when a paclitaxel drug-eluting stent is inserted. Thereafter allow aspirin indefinitely. The evidence currently available to the Committee does not provide support for use beyond 6 months although there are recommendations endorsing longer term use in high risk patients.	n/a	20 September 2007

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B01AC04	Clopidogrel	Ischaemic heart disease (non myocardial infarction).	**Approved** for use only in patients intolerant to aspirin, i.e. allergy or bleeding episodes.		20 September 2007
B01AC04	Clopidogrel	Stroke.	**Approved, only** for long-term therapy where patient has confirmed aspirin intolerance.	• Decrease in clopidogrel price. • New safety or efficacy data for either aspirin (at doses recommended by the DoH) or clopidogrel.	24 July 2014
B01AC04	Clopidogrel	Transient ischaemic attack with/without atrial fibrillation.	**Not Approved**	• Decrease in clopidogrel price. • New safety or efficacy data for either aspirin or clopidogrel.	24 July 2014
B01AD02	Alteplase	For acute ischaemic stroke.	**Approved:** with the following provisos: 1. Patients presenting within 3 hours of onset, and 2. where specialised neuro-radiological services are available.	• New efficacy data re: this or an alternate agent / treatment method for use in this setting.	9 February 2012
B02BD03	Recombinant Factor VIIa (rFVIIa)	Intractable bleeding.	**Not Approved**	• Robust efficacy data.	29 June 2017
B02BD03	Haemophilia bypassing agents (rFVIIa/aPCC)	Haemophilia with inhibitors (on demand, when presenting with a significant bleed).	**Approved** One bypassing agent to be available on the EML (most affordable). An alternative bypassing agent can be made available as emergency stock on a named patient basis for patients not responding to EML item.		14 December 2017
C CARDIAC THERAPY					
C02DC01	Minoxidil	Severe hypertension not responding to other drugs.	**Approved**	n/a	20 September 2007
C09CA	**Angiotensin receptor blockers** (ARBs)	Add on therapy in cardiac failure on patients already on standard treatment including ACE-inhibitors, ß-Blockers and spironolactone.	**Not Approved**	• New efficacy data from large RCT indicating larger benefit of adding ARBs to standard therapy • Decrease in price of ARBs so as to be similarly priced to ACE-inhibitors	20 September 2007

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C09CA	**Angiotensin receptor blockers** (ARBs)	As add on therapy in proteinuric nephropathies in patients already using an ACE-inhibitor.	**Not Approved** Insufficient evidence to support its use.	• New evidence indicating benefit in the form of a RCT of sufficient size with maximal doses of ACE-inhibitor used. • New safety concerns. • Decrease in price so as to be similarly priced to ACE-inhibitors.	20 September 2007
D ANTIPRURITICS, INCLUDING ANTIHISTAMINES, ANAESTHETICS, ETC.					
D07AD	**Very potent topical corticosteroid – Group IV** e.g. Clobetasol 0.05% Examples: Cream/ointment: • Clobetasol propionate 0.05%.		**Approved** Lowest price high potency corticosteroid to be used.	n/a	20 September 2007
D10BA01	Isotretinoin	Cystic nodular acne.	**Not Approved**	• Improved quality of life evidence. • Price. • Safety.	09 February 2012
G GENITO URINARY SYSTEM AND SEX HORMONES					
G03AC03	Levonorgestrel Intrauterine system	Abnormal Uterine Bleeding (3rd line therapy)	**Approved** • Third line therapy where there has been treatment failure. • Prescribed and inserted by a gynaecologist.	n/a	27 September 2018
G03CA	Estrogen	Gender Dysphoria – Feminising regimen	**Approved**	New evidence	5 December 2019
G03BA03	Testosterone	Gender Dysphoria – Masculinising regimen	**Approved**	New evidence	5 December 2019
G03DA02/ G03HA01	Medroxyprogesterone acetate OR Cyproterone acetate	Patients with hypersexual behaviour including paraphilia's	**Approved** • Most affordable agent should be procured. If price parity: cyproterone is preferred due to decreased frequency of dosing.	• Evidence of harm Price reductions	11 April 2019

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G03HB01	Cyproterone, Ethinyl Oestradiol	Hirsutism.	**Approved**	n/a	20 September 2007
G04BD10	**Urinary antispasmodics** Darifenacin	Over active bladder (OAB) with symptoms of urinary urgency, frequency and/or urge incontinence.	**Not Approved**	• Price. • New safety/efficacy data.	13 March 2008
G04CB01	Finasteride	Benign prostatic hyperplasia.	**Not Approved**	• Price.	13 March 2008
H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS					
H01AA01	Adrenocorticotrophic hormone (ACTH)	Infantile spasms.	**Not Approved**	• Well controlled studies of proven efficacy of ACTH.	September 2010
H01AC01	Somatropin (Growth Hormone)	Turner's syndrome.	**Not Approved**	• Improved cost-effectiveness.	20 September 2007
H01AC01	Somatropin (Growth Hormone)	Prader Willi syndrome.	**Not Approved**	• Price.	20 September 2007
H01AC01	Somatropin (Growth Hormone)	Intrauterine growth failure.	**Not Approved**	• Price.	20 September 2007
H01AC01	Somatropin (Growth Hormone)	Idiopathic short stature.	**Not Approved**	• Improved cost-effectiveness.	20 September 2007
H01AC01	Somatropin (Growth Hormone)	Chronic renal insufficiency.	**Not Approved**	• Evidence of benefit.	20 September 2007
H01AC01	Somatropin (Growth Hormone)	Growth hormone deficiency.	**Approved** Approved for confirmed growth hormone deficiency for use by endocrinologists only. Rationale: • The condition is a well-defined deficiency state that can be managed and monitored. • Number of patients requiring treatment is small.	• New evidence on quality of life assessment in local and specific populations.	24 July 2008
H01BA05	Ornipressin	Bleeding associated with bronchoscopy and renal biopsy.	**Not Approved**	• New high quality evidence of superior efficacy to adrenalin.	29 October 2012

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ATC CODE	**MEDICINE**	**INDICATION**	**NEMLC RECOMMENDATION**	**REVIEW INDICATORS**	**DATE RATIFIED**
H01CB02	Octreotide (Short-acting)	Persistent neonatal hyperinsulinism and hypoglycaemia.	**Approved** The condition is rare; usage is for short term; alternative agents are limited and the consequences of not having treatment available are serious.		
H01CB	Somatostatin analogs Octreotide, Lanreotide	Neuro-endocrine tumours.	**Not Approved**	• Long term survival and quality of life data.	26 March 2015
J ANTI-INFECTIVES FOR SYSTEMIC USE					
J01XC01	Fusidic acid	Treatment of staphylococcal infections, mainly involving bone and joints: • Methicillin-sensitive organisms, as alternative to cloxacillin or flucloxacillin. • Methicillin-sensitive organisms, in combination with cloxacillin or flucloxacillin. • Methicillin-resistant organisms, as an alternative to e.g. glycopeptides or oxazolidinones (linezolid), especially in cases where prolonged treatment is required.	**Not Approved**	• New evidence of clinical comparative efficacy against alternatives, especially regarding long term treatment of. MRSA where the oral preparation may be of benefit in comparison to parenteral glycopeptides and infections with glycopeptide resistant organisms where the potential toxicity of oxazolidinones (linezolid) when used for prolonged periods of time, may be problematic.	13 March 2008
J01XX08	Linezolid	Resistant gram positive infections where vancomycin is contra-indicated.	**Not Approved** It may be available on named patient basis: • only with a microbiology report confirming vancomycin resistance in a relative organism or confirmation of severe adverse effect to vancomycin, (i.e. vancomycin induced neutropenia or anaphylaxis, but not the “red man syndrome”). • confirmed contra-indication to the use of vancomycin.	• Clinically significant increase in vancomycin resistance in the public sector. • Significant decrease in cost of linezolid.	27 November 2008

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J02AB02	Ketoconazole	Cushing's syndrome.	**Approved**	• Availability of alternate medication for this indication with superior efficacy or safety profile. New safety concerns.	10 July 2008
J02AC02	Itraconazole	Histoplasmosis.	**Not Approved**	• New evidence of clinical comparative efficacy against alternatives, especially weekly Amphotericin B. • Significant increase in incidence of the condition. • Significant change in pricing.	13 March 2008
J02AX04/J02AX05/ J02AX06	**Echinocandins** (caspofungin/ micafungin/ anidulafungin)	Invasive candidiasis (resistant to fluconazole/amphotericin B and/or where renal dysfunction is present and amphotericin B cannot be used).	**Approved** • Echinocandins approved as a class, with the most affordable agent to be procured. • The use of echinocandins should be managed through motivation/ appropriate restrictions at facilities, as part of Antimicrobial Stewardship activities. (See addendum – clinical criteria for use)	• Availability of amphotericin B • Changing resistance patterns • New evidence	12 April 2018
J02AC03	Voriconazole (VCZ)	Treatment of invasive Aspergillosis.	**Not Approved**	• High quality randomised controlled trial with amphotericin B as the comparator.	13 March 2008
J05AB04	Ribavirin	Viral haemorrhagic fever (VHF).	**Approved** To be supplied on motivation from a central supply point.	n/a	
J06BA02	Intravenous Immunoglobulin (IVIG)	Acute Immune thrombocytopenic Purpura (ITP)	**Approved** • Life-threatening bleed with platelets <50 x 109/l. • Urgent surgery (any surgery urgently required within 24 hours) where rapid rise in platelets is required. • Pregnant patient prior to delivery as above. • Rapid rise in platelets required when a patient has platelet count of < 20 x 109/L, with	• Evidence of harm	5 July 2018

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			additional risk factors for bleeding (such as severe hypertension, ongoing sepsis).		
J06BA02	Intravenous Immunoglobulin (IVIG)	Primary antibody immune deficiency with recurrent infections	**Approved**	• New data on dosing • Availability of more affordable subcutaneous formulations	11 April 2019
J06BA02	Intravenous Immunoglobulin (IVIG)	Guillain-Barré syndrome (GBS) presenting within the first 2 weeks of onset of moderate to severe weakness.	**Approved** The recommended regimen is 0.4 g/kg daily for 5 days.	• New evidence	5 December 2019
J06BB16	Palivizumab	Respiratory syncytial virus (RSV) infection in high-risk premature infants.	**Not Approved**	• Price reduction.	25 April 2013
L ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS					
L01	**Chemotherapy** Platinum coordination compounds, Taxanes, Doxorubicin, Cyclophosphamide	Uterine Cancer/ Endometrial Cancer (Advanced stage and recurrent).	**Not Approved**	• Better quality data	22 January 2015
L01AA01	Cyclophosphamide	Adjuvant breast cancer.	**Approved** (Cyclophosphamide plus Doxorubicin (AC)).	n/a	27 November 2008
L01AA01	Cyclophosphamide	Adjuvant breast cancer.	**Approved** (Cyclophosphamide plus methotrexate plus fluoro-uracil (CMF)).	n/a	27 November 2008
L01AA01	Cyclophosphamide	Adjuvant breast cancer.	**Approved** (Fluoro-uracil plus Doxorubicin plus cyclophosphamide (FAC)).	n/a	27 November 2008
L01AA02	Chlorambucil	Chronic lymphocytic leukemia, low grade non-Hodgkin's lymphoma	**Approved**	n/a	11July 2019
L01AA03	Melphalan	Multiple myeloma (oral-remission induction combined with steroids in older) (IV –pre-autologous	**Approved**	n/a	11July 2019

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		stem cell transplant in multiple myeloma and lymphomas)			
L01AA06	Ifosfomide	Germ cell tumours, soft tissue sarcomas, salvage therapy in lymphomas pre-autologous stem cell transplant.	**Approved**	n/a	11July 2019
L01AB01	Busulfan	Pre allogeneic and autologous stem cell transplant conditioning	**Approved**	n/a	11July 2019
L01AX03	Temozolomide	Glioblastoma multiforme.	**Not Approved**	• Prospective RCTs demonstrating a significant increase in effect size. Significant price reduction.	25 July 2013
L03AX03	Bacille Calmette-Guerin (BCG)	Bladder Cancer (non-muscle invasive)	**Approved**	None	25 February 2016
L01AX04	Dacarbazine	Hodgkin's lymphoma	**Approved**	n/a	11July 2019
L01BA01	Methotrexate	Adjuvant breast cancer.	**Approved** (Cyclophosphamide plus methotrexate plus fluoro-uracil (CMF)).	n/a	27 November 2008
L01BA04	Pemetrexed	Lung mesothelioma.	**Not Approved**	Price changes or access programmes.	27 November 2008
L01BA04	Pemetrexed	Non-small cell lung cancer.	**Not Approved**	• Evidence of superior efficacy versus cisplatin/gemcitabine. Price reduction.	29 September 2011
L01BB02	Mercaptopurine	acute leukaemia	**Approved**	n/a	11July 2019
L01BB03	Thioguanine	Acute leukemia	**Approved**	n/a	11July 2019
L01BB05	Fludarabine	Chronic lymphocytic leukaemia, non-Hodgkin's lymphomas, pre-conditioning regimen for	**Approved**	n/a	11July 2019

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		allogeneic stem cell transplant, AML salvage therapy.			
L01BC01	Cytarabine	acute myeloid leukaemia (AML) and acute lymphoid leukaemia (ALL)	**Approved**	n/a	11July 2019
L01BC06	Capecitabine	Relapsed metastatic breast cancer failing an anthracycline and a taxane.	**Not Approved**	• Price	15 September 2016
L01BC06	Capecitabine	Metastatic colorectal – first-line.	**Approved** (as part of the XELOX regimen).	• Availability of data for alternative oral fluoropyrimidines. • Price increases not commensurate with approved SEP increases.	27 November 2008
L01BC06	Capecitabine	First-line therapy for advanced stomach/gastro-oesophageal junction cancer.	**Approved**	None	27 July 2014
L01BC06/ L01BC05	Capecitabine plus Gemcitabine	Adjuvant chemotherapy of fully resected potentially curable pancreatic adenocarcinoma).	**Approved** • Only for fully resected patients.	• New adjuvant chemotherapy data in patients with R0 or R1 resected adenocarcinoma of the pancreas.	6 December 2018
L01BC52	Fluoro-uracil	Adjuvant breast cancer.	**Approved** (Cyclophosphamide plus methotrexate plus fluoro-uracil (CMF)).	n/a	27 November 2008
L01BC52	Fluoro-uracil	Adjuvant colorectal cancer.	**Approved** (Fluoro-uracil plus Doxorubicin plus cyclophosphamide (FAC)).	n/a	27 November 2008
L01CA01	Vinblastine	Relapsed metastatic breast cancer (mBC) failing an anthracycline and a taxane.	**Approved**	n/a	15 September 2016
L01CA02	Vincristine	General haematology and oncology	**Approved**	n/a	27 September 2018
L01CA04	Vinorelbine	Adjuvant non-small cell lung cancer (NSCLC) – completely resected.	**Approved** To be used with cisplatin for adjuvant therapy for stage IIIA NSCLC but not stage IB or stage II.	New evidence of efficacy of adjuvant therapy in NSCLC.	03 December 2009

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L01CA04	Vinorelbine (IV)	Relapsed metastatic breast cancer (mBC) failing an anthracycline and a taxane.	**Approved**	n/a	15 September 2016
L01CA04	Vinorelbine (oral)	Relapsed metastatic breast cancer (mBC) failing an anthracycline and a taxane.	**Not Approved**	• Price similar to oral • Evidence of clinical superiority	15 September 2016
L01CD	**Taxanes** Docetaxel, Paclitaxel	Adjuvant breast cancer.	**Approved** Approved for patients with high grade, node positive ER negative disease.	n/a	23 August 2012
L01CD01	Paclitaxel	Neoadjuvant/recurrent/ metastatic head and neck cancer.	**Not Approved**	n/a	27 July 2014
L01CD01	Paclitaxel	First-line chemotherapy in advanced non-small cell lung cancer (NSCLC).	**Approved**	None	22 January 2015
L01CD01	Paclitaxel	Metastatic cervical carcinoma	**Approved**	n/a	11July 2019
L01CD	**Taxanes**	Metastatic breast cancer – first- and second-line.	**Approved**	Change in the price of taxanes, specifically docetaxel.	16 September 2010
L01CD02	Docetaxel	Squamous cell carcinoma of head and neck.	**Approved** Approved for patients with good performance status and adequate follow-up used in combination with cisplatin plus 5-fluoro-uracil.	None	25 July 2013
L01CD02	Docetaxel	Second-line therapy for advanced non-small cell lung cancer (NSCLC) in selected patients with good performance status (ECOG 0;1).	**Approved**	None	22 January 2015
L01CD02	Docetaxel	Castrate resistant prostate cancer	**Approved** Allow the use of combination chemotherapy with paclitaxel for patients who are:	Reduction in cost and availability of 3rd generation ARBs eg.	11July 2019

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			1. Newly diagnosed with metastatic diasease 2. Patients who are > 12 months from pri Note - Patients with GFR <30ml/min are not suitable for any platinum-based chemotherapy • Performance status <0, • No previous cisplatin.	enzalutamide and CYP17 inhibitors e.g. abiraterone	
L01CD02	Docetaxel	Patients with hormone sensitive prostate cancer (HSPC)	**Approved** **For patients with high volume disease:** defined as the presence of visceral metastases or ≥4 bone lesions with ≥1 beyond the vertebral bodies and pelvis	New evidence	30 January 2020
L01DB01	Doxorubicin	Adjuvant breast cancer.	**Approved** (Doxorubicin plus cyclophosphamide (AC)).	None	27 November 2008
L01DB01	Doxorubicin	Adjuvant breast cancer.	**Approved** (Fluoro-uracil plus Doxorubicin plus cyclophosphamide (FAC)).	None	27 November 2008
L01DB02	Daunorubicin	acute myeloid leukaemia (AML) and acute lymphoid leukaemia (ALL)	**Approved**	n/a	11July 2019
L01DB06	Idarubicin	Acute Myeloid Leukemia.	**Approved**	n/a	10 December 2015
L01DB07	Mitoxantrone	General oncology.	**Approved** Indications for consideration: Advanced stage carcinomas, paediatric relapsed acute lymphoblastic leukaemia (ALL), paediatric acute myeloid leukaemia (AML).	None	30 June 2016
L01DB03	Epirubicin	Advanced stage or metastatic oesophageal junction and gastric carcinoma.	**Approved**	None	10 December 2015
L01DC01	Bleomycin	Hodgkin's, Kaposi, Germ cell tumours, Pleuradhesis	**Approved**	None	27 September 2018
L01DC03	Mitomycin C	Bladder Cancer	**Not Approved**	None	25 February 2016

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L01DC03	Mitomycin C	Relapsed metastatic breast cancer (mBC) failing an anthracycline and a taxane.	**Not Approved**	None	15 September 2016
L01XA01	Cisplatin	Adjuvant small cell lung cancer.	**Approved**	None	27 November 2008
L01XA01	Cisplatin	Adjuvant lung cancer.	**Approved**	None	27 November 2008
L01XA01	Cisplatin	Relapsed metastatic breast cancer (mBC) failing an anthracycline and a taxane.	**Approved** To be used with gemcitabine	None	15 September 2016
L01XA01	Cisplatin	Radio-sensitizer in cervical cancer	**Approved**	None	6 December 2018
L01XA01	Cisplatin	Advanced/Metastatic: Various Cancers	**Approved**	n/a	11July 2019
L01XA01	Cisplatin	Adjuvant/Neoadjuvant: various cancers.	**Approved**	n/a	11July 2019
L01XA02	Carboplatin	Adjuvant lung cancer.	**Approved**	None	27 November 2008
L01XA02	Etoposide	Adjuvant small cell lung cancer.	**Approved**	None	27 November 2008
L01XA03	Oxaliplatin	Adjuvant colorectal.	**Not Approved**	Mature published data.	27 November 2008
L01XA03	Oxaliplatin	First or second-line metastatic colorectal cancer.	**Approved**	None	10 December 2015
L01XC07	Bevacizumab	Sub-retinal neovascular membranes and non-resolving macular odema.	**Approved** (off label indication).	None	10 December 2015
L01XE01	Imatinib	Chronic phase of chronic myeloid leukemia.	**Approved**	None	27 March 2014
L01XE01	Imatinib	Gastrointestinal Stromal Tumours (GIST) - adjuvant therapy.	**Approved**	None	25 June 2015
L01XE01	Imatinib	Gastrointestinal Stromal Tumours (GIST) - metastatic therapy.	**Approved**	None	25 June 2015
L01XE08	Nilotinib	Chronic Myeloid Leukemia in patients resistant or intolerant to imatinib.	**Approved**	• Longer term follow-up of nilotinib versus imatinib showing clinical benefits in the first line.	22 January 2015

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				• Reduction in cost or availability of nilotinib generics.	
L01XC02	Rituximab	CD20 positive B-cell non-Hodgkin's lymphoma: first-line.	**Approved** for treatment in diffuse large B-cell non-Hodgkin's lymphoma (DLBCL) patients except those with International Prognostic Index (IPI) of 0.	• New anti-CD20 monoclonal antibodies, more data and international consensus statements in FL patients, rituximab price changes	23 August 2012
L01XC02	Rituximab	Rheumatoid Arthritis patients refractory to synthetic DMARDs	**Approved** • For patients with refractory RA, who have failed ≥ 3 DMARDs taken for ≥ 6 months. (in accordance with algorithm)	• Evidence of harm	5 July 2018
L01XC02	Rituximab	Refractory lupus nephritis	**Approved** Name patient only • Used as per NEMLC approved treatment algorithm. Use must be monitored and managed by PTCs through a registry. Clinical outcomes to be shared with the National registry database for biological therapy.	• Changes in evidence of efficacy/safety Changes in cost	11 April 2019
L01XC03	Trastuzumab	Adjuvant treatment for early stage HER-2 positive breast cancer, 6 month regimen	**Approved** Regimen: administered 3 weekly for a period of **6 months.**	New evidence	5 December 2019 *(previously reviewed: 29 June 2017)*
L01XC03	Trastuzumab	Adjuvant treatment for early stage HER-2 positive breast cancer, 12 month regimen	**Not Approved** Decision re-evaluated – see above – 6 month regimen recommended.	n/a	Previous recommendation: 29 June 2017
L01XX02	Asparaginase	Acute lymphoblastic leukemia (ALL)	**Approved**	n/a	11July 2019
L01XX14	All-trans retinoic acid (tretinoin)	Acute promyelocytic leukaemia	**Approved**	None	27 September 2018
L01XX19	Irinotecan	Adjuvant colorectal.	**Not Approved**	Evidence to show benefit.	27 November 2008
L01XX19	Irinotecan	First- or second-line metastatic colorectal cancer.	**Approved**	None	10 December 2015

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L02AE03	**Gonadotrophin-releasing hormone (GnRH) analogue** Goserelin, Buserelin	Endometriosis.	**Approved** for use in the following situations: • For endometriosis-associated infertility prior to in vitro fertilisation (IVF). For medical management in situations in which a trial of adequate analgesia or the use of combined oral contraceptives is unsuccessful.	• New evidence based on Goserelin vs. Placebo. • Large comparative trials with COCs for both "trial of hormone therapy" and for relief of pain. • Comparisons with new agents such as aromatase inhibitors.	13 March 2008
L02AE03	**Gonadotrophin-releasing hormone (GnRH) analogue**	Precocious puberty.	**Approved** Choice of GnRH analogue will depend on best tender price.	• Change in price or registration of new agents which are cheaper or more efficacious, or both. New safety concerns.	13 March 2008
L02AE03	**Gonadotrophin-releasing hormone (GnRH) analogue**	As bridging therapy until orchiectomy.	**Approved** Only Approved as bridging therapy - not long-term management.	Price.	25 February 2016
L02AE03	Goserelin	Hormone receptor positive breast cancer in premenopausal women.	**Not Approved**	None	10 December 2015
L02BA01	Tamoxifen	Adjuvant breast cancer.	**Approved**	None	27 November 2008
L02BA01	Tamoxifen	Metastatic breast cancer.	**Approved**	None	27 November 2008
L02BB01/ L02BB03	**Anti-androgens** Flutamide, Bicalutamide	Advanced prostate cancer.	**Not Approved** Orchiectomy preferred.	None	29 October 2012
L01BC05	Gemcitabine	Pancreatic cancer.	**Not Approved**	• Reduction in cost of gemcitabine.	29 October 2012
L01BC05	Gemcitabine	First-line chemotherapy in advanced non-small cell lung cancer (NSCLC) in patients intolerant to paclitaxel.	**Approved** Approved in patients intolerant to paclitaxel.	n/a	22 January 2015
L01BC05	Gemcitabine	Relapsed metastatic breast cancer (mBC) failing an anthracycline and a taxane.	**Approved**	n/a	15 September 2016

TERTIARY AND QUATERNARY LEVEL ESSENTIAL MEDICINES RECOMMENDATIONS					
ATC CODE	**MEDICINE**	**INDICATION**	**NEMLC RECOMMENDATION**	**REVIEW INDICATORS**	**DATE RATIFIED**
L02BG	**Aromatase inhibitors** Anastrozole, Letrozole, Exemestane	Adjuvant breast cancer.	**Approved** for use in women with confirmed intolerance to tamoxifen, i.e. thrombo-embolic disease or endometrial hyperplasia (proven on ultrasound). Choice of aromatase inhibitor will depend on best tender price.	• Publication of the ongoing Secondary Adjuvant Long term Study with Arimidex (SALSA) study and ATAC. • Long term data BIG 1-98 • TEAM data late in 2008. • Price parity with tamoxifen.	27 November 2008
L02BG	**Aromatase inhibitors**	Metastatic breast cancer.	**Approved** for use as second-line therapy after tamoxifen in advanced breast cancer in postmenopausal women who do not have visceral metastases. Choice of aromatase inhibitor will depend on best tender price.	• Further developments regarding tamoxifen pharmacogenetics.	September 2010
L03AA02	Filgrastim	Febrile neutropaenia.	**Approved** under the following conditions: • Patients must have had 3 days of appropriate antimicrobial therapy without resolution of infection. • Filgrastim can be used up to a maximum of 5 days with a daily review of white cell count (WCC). Failure to respond must prompt further investigation of neutropenia.	None	27 November 2008
L03AA02	Filgrastim	ARV-induced neutropenia.	**Not Approved** This does not preclude the use of filgrastim in the management of febrile neutropenia (see above) in HIV infected patients.	• RCTs, with improved clinically relevant outcomes, especially mortality	27 November 2008
L03AA02	Filgrastim	Prophylactic use in children with high-risk acute lymphoblastic leukaemia (HR-ALL).	**Not Approved**	• The emergence of evidence that routine use of GCSF improves outcomes in HR-ALL. • A significant reduction in the price of GCSF.	3 December 2009
L03AA02	Filgrastim	Peripheral blood stem cell harvesting in autologous stem cell harvesting in haematological malignancies.	**Approved**	n/a	24 July 2014
L03AA02	Filgrastim	Chemotherapy-induced febrile neutropenia.	**Approved** for secondary prophylaxis in curable cancers requiring full dosing on-schedule, i.e. Hodgkins and germ cell tumours.	n/a	9 February 2012

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L03AA02	Filgrastim	Chemotherapy-induced febrile neutropenia.	**Not Approved** for primary prophylaxis as no overall survival benefit and limited mortality benefit has been shown.	n/a	9 February 2012
L04AA04	ATG	Induction therapy in high risk renal transplantation recipients.	**Approved**	None	29 June 2017
L04AA10	Sirolimus	Renal transplant.	**Approved** for use only patients with biopsy-confirmed calcineurin inhibitor toxicity because of deteriorating kidney function (i.e. in patients at ongoing risk of acute rejection with no overt proteinuria and preserved GFR > 40mL/min) where mycophenolate mofetil is contra-indicated.	• Reduction in cost or new efficacy data.	16 September 2010
L04AA06	Mycophenolate mofetil (MMF)	Lupus Nephritis.	**Approved** for both the induction and maintenance phases of treatment of lupus nephritis.	None	18 September 2014
L04AA06	Mycophenolate mofetil (MMF)	Prevention of acute rejection post-renal transplantation.	**Approved** for prevention of acute rejection post-renal transplantation.	• Reduction in cost or new efficacy data.	16 September 2010
L04AA13	Leflunomide	As add-on therapy in Rheumatoid Arthritis.	**Not Approved** May be used on a named-patient basis, on recommendation by PTC for intolerance to standard therapy.	• New efficacy data or reduction in cost.	31 March 2016
L04AA13	Leflunomide	Rheumatoid Arthritis where patients are intolerant or have contraindications to methotrexate and sulphasalazine.	**Approved** Only for use in patients with intolerance to standard DMARD therapy (methotrexate or sulphasalazine)	• New evidence. • Safety concerns. • Price change.	12 April 2018
L04AA04	Antithymocyte immunoglobulin (ATG)	Aplastic Anaemia.	**Approved** (in combination with ciclosporin and corticosteroids)	None	10 December 2015
L04AB02	Infliximab	Fistulising Crohn's Disease.	**Not Approved**	• A considerable change in the price of the drug.	20 September 2007
L04AB02	Infliximab	Rheumatoid Arthritis.	**Not Approved**	• Demonstration in randomized trials of reduction in clinically significant endpoints, e.g. hospitalizations, joint replacements, etc. • Evidence of sustained, clinically relevant improvement upon withdrawal of infliximab	13 March 2008

TERTIARY AND QUATERNARY LEVEL ESSENTIAL MEDICINES RECOMMENDATIONS					
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				• A significant reduction in the price of the medicine.	
L03AB07/ L03AB08	Interferon beta	Relapsing remitting multiple sclerosis	**Approved**	• New evidence of clear benefit of efficacy of newer classes • Price	30 January 2020
L04AC02	Basiliximab	Induction therapy in low risk patient's renal transplantation recipients.	**Approved**	None	29 June 2017
L04AD01	Ciclosporin	Organ transplantation.	**Approved**	n/a	20 September 2007
L04AD02	Tacrolimus	• Primary therapy in high immunological risk renal allograft recipients. • Renal allograft recipients on ciclosporin who experience steroid resistant acute allograft rejection.	**Approved**	None	29 June 2017
L04AX02	Thalidomide	Multiple myeloma.	**Approved**	• Price	June 2019 (reference price met)
M MUSCULOSKELETAL SYSTEM				•	
M03BX01	Baclofen	Spasticity.	**Not Approved**	• New evidence of clinically relevant efficacy.	25 June 2015
M03AX01	Botulinum toxin	Focal dystonias.	**Approved** for use in carefully selected patients. Only to be administered by suitably experienced practitioners.	• New evidence with clinical relevant/well defined endpoints and well described dosage regimens.	30 June 2016
M03AX01	Botulinum toxin	Spastic cerebral palsy.	**Not Approved**	• New evidence with clinical relevant/well defined endpoints and well described dosage regimens.	Re-review: 30 June 2016
M05BA	**Bisphosphonates** Zoledronate, Ibandronic acid	Malignant bone disease in multiple myeloma.	**Approved**	• New evidence of harm.	25 July 2013

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M05BA03	Pamindronate	Hypercalcaemia of malignancy.	**Approved**	n/a	20 September 2007
M05BA04	Alendronate	Osteogenesis imperfect.	**Not Approved**	• Evidence of efficacy and safety.	25 July 2013
M05BA04	Alendronate	Paget's.	**Not Approved**	• New high quality adequately powered trials providing evidence addressing clinically important parameters. New safety concerns.	September 2007
N NERVOUS SYSTEM					
N03AG04	Vigabatrin	Refractory partial epilepsy.	**Not Approved**	• Good quality evidence to support the efficacy and safety in infantile spasms.	3 December 2009
N03AG04	Vigabatrin	Infantile spasms.	**Not Approved**	• Good quality evidence to support the efficacy and safety in infantile spasms.	3 December 2009
N03AX11	Topiramate	Initial therapy (epilepsy).	**Not Approved**	• New evidence, re: clinical efficacy of Topiramate vs. alternatives as add-on therapy for resistant epilepsy. • New evidence, re: efficacy in comparison with alternatives as initial therapy for epilepsy, where the current evidence supports using the alternative agents.	3 December 2009
N03AX11	Topiramate	Add-on therapy for resistant epilepsy.	**Approved**	• Evidence that the product is accounting for disproportionate amount of anti-epileptic spend.	26 March 2015
N03AX14	Levetiracetam	Epilepsy.	**Not Approved**	• Price.	10 July 2008
N03AX14	Levetiracetam	Add-on therapy for resistant epilepsy.	**Not Approved**	• Price. • Data in HIV patients.	25 June 2015

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N03AX12/ N03AX16	α2δ calcium channel ligands Gabapentin, Pregabalin	Patients with peripheral neuropathy refractory or intolerant to standard of care (e.g. amitriptyline; or carbamazepine)	**Not Approved** Access can be managed on a named patient basis, managed by Pharmaceutical and Therapeutics Committees.	• New evidence in the refractory setting. • Alternative indications.	30 January 2020
N04BC04/ N04BC05 G02CB01	**Dopamine agonist** Ropinarole, Pramipexole, Bromocriptine	Parkinson's disease.	**Approved** for use as add-on therapy to levodopa. The choice of dopamine agonists and selegiline will depend on the lowest tender price.	• Decrease in relative cost. • New safety data.	27 November 2008
N05AH03	Olanzapine, IM	Emergency management of psychotic conditions.	**Not Approved**	• New evidence of superior efficacy to suitable alternatives in patients with severe adverse reactions to FGAs.	03 December 2009
N05AH04	Quetiapine	Third-line Schizophrenia	**Not Approved** Amisulpiride Approved for this indication.	• Price.	15 September 2016
N05AH04	Quetiapine	Bipolar depression	**Not Approved**	• Price.	25 June 2015
N05AX08	Risperidone long acting injection	Schizophrenia.	**Not Approved**	• Price similar to current standard of care.	31 March 2016
N05AL05	Amisulpride	Psychosis.	**Approved** for use as an appropriate alternative to existing agents in patients with negative symptoms failing first and second generation antipsychotics.	• New information suggesting adequate comparative efficacy versus older agents such as sulpiride itself, or new safety information.	03 December 2009
N05AX12	Aripiprazole	Schizophrenia in children.	**Approved** for use as a third-line agent in children with psychotic disorders who are intolerant to typical and atypical antipsychotic agents with: • Obesity, defined as BMI ≥ 30 or age appropriate measures, **or** • Excessive weight gain, if associated with metabolic syndrome in adherent patients on other atypical antipsychotics, not responsive to other interventions (e.g. dietary management and/or physical exercise).	• New evidence of efficacy in children and adolescents.	29 November 2013

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			Aripiprazole be initiated, in these cases, in consultation with or, where available, by a subspecialist (i.e. child and adolescent psychiatrist)		
N05BA12	Alprazolam	"As required" adjunctive medication in the treatment of panic disorder.	**Approved** for panic disorder only. To be prescribed by a psychiatrist.	• Any efficacy, safety or cost data.	September 2010
N05CF01/ N05CF02	**Benzodiazepine related drugs** Zopiclone, Zolpidem	Short-term use for insomnia associated with a primary psychiatric condition.	**Not Approved**	• If the price of z-drugs were reduced to within an acceptable distance of the price of oxazepam, consideration would be given to including these on the EML.	03 December 2009
N06AB10	Escitalopram	Depressive and anxiety disorders.	**Not Approved**	• Reduction in cost to equivalent to that of citalopram, or new high quality evidence of superiority to that agent.	03 December 2009
N06AX12	Buproprion	Major depressive disorder.	**Approved** for use as a third-line treatment of major depressive disorder and anxiety associated with depression. To be prescribed by a psychiatrist only. The cheapest of bupropion or venlafaxine to be used.	• n/a	27 January 2011
N06AX16	Venlafaxine	Major depressive disorder.	**Approved** for use as a third-line treatment of major depressive disorder and anxiety associated with depression. To be prescribed by a psychiatrist only. The cheapest of bupropion or venlafaxine to be used.	• New evidence of harm, or a revision in the price of bupropion to make it more economically favourable.	27 January 2011
N06DX01	Memantine	Alzheimer's Disease.	**Not Approved**	• Evidence of true clinical benefit in terms of quality if life for patients and care-givers.	10 July 2008
R RESPIRATORY SYSTEM					

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ATC CODE	**MEDICINE**	**INDICATION**	**NEMLC RECOMMENDATION**	**REVIEW INDICATORS**	**DATE RATIFIED**
R03BB04/ R03BB06	**Long acting muscarinic antagonists (LAMA)** • Tiotropium • Glycopyrronium	Chronic Obstructive Pulmonary Disease (COPD).	**Not Approved**	Price	14 December 2017
R03DC03	Montelukast	Chronic management of severe uncontrolled asthma.	**Approved** for use in: • In adults (>12 years) with difficult to control asthma despite receiving high dose inhaled steroids and long-acting β_2 agonist, a trial of low dose sustained release theophylline should be tried before use of montelukast. If there is no response to low dose theophylline, a 2-week trial of montelukast may be used. • In children between 6 and 12 years of age with severe uncontrolled asthma despite being on high dose corticosteroids and long acting β2 agonist, a 2-week trial of montelukast could be considered. In children less than 6 years with severe uncontrolled asthma on high dose inhaled corticosteroids, a 2-week trial of montelukast could be considered. If no benefit can be demonstrated after this period, montelukast should be discontinued.	• Properly randomized efficacy and safety comparative studies of LTRA, low dose sustained release theophyllines and long acting beta2 agonist at all ages	13 March 2008
S SENSORY ORGANS					
S01LA04	Ranibizumab	Sub-retinal neovascular membranes and non-resolving macular odema.	**Not Approved** Bevacizumab to be agent for this indication	None	10 December 2015
V VARIOUS					
V03AC03	Deferasirox	Treatment of transfusional iron overload	**Approved** Added as an oral alternative to deferoxamine.	n/a	15 September 2016

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V03AF03	Folinic acid, intravenous	Adjuvant colorectal cancer.	**Approved**	n/a	27 November 2008
V03AE	Lanthanum carbonate, Sevelamer	Hyperphosphataemia in patients with chronic renal failure.	**Not Approved** - May be used on a named-patient basis, on recommendation by the PTC.	• Evidence that the use of non-calcium-based phosphate binders significantly reduces all-cause or cardiovascular mortality and/or cardiovascular comorbidities in patients with ESRD. • Reduction in cost of sevelamer through price reduction or the introduction of generic equivalents.	25 June 2015

Abbreviations:
ATC: *Anatomical Therapeutic Chemical Classification*
COCs: *Combined oral contraceptives*
DMARD: *Disease-modifying antirheumatic drugs*
ESRD: *End-stage renal disease*
FGAs*: First generation antipsychotics*
GCSF*: granulocyte colony stimulating factor*
LTRA*: Leukotriene receptor antagonists*
MRSA*: Methicillin-resistant Staphylococcus aureus*
PTC*: Pharmaceutical and Therapeutics Committee*
RCT*: Randomised controlled trials*
SEP*: Single exit price*

NOTE: *General review indicators include, new evidence on efficacy, effectiveness or safety and significant price changes.*

NEMLC ratified Summary and Review documents can be requested as required from: SAEDP@health.gov.za OR jane.riddin@health.gov.za