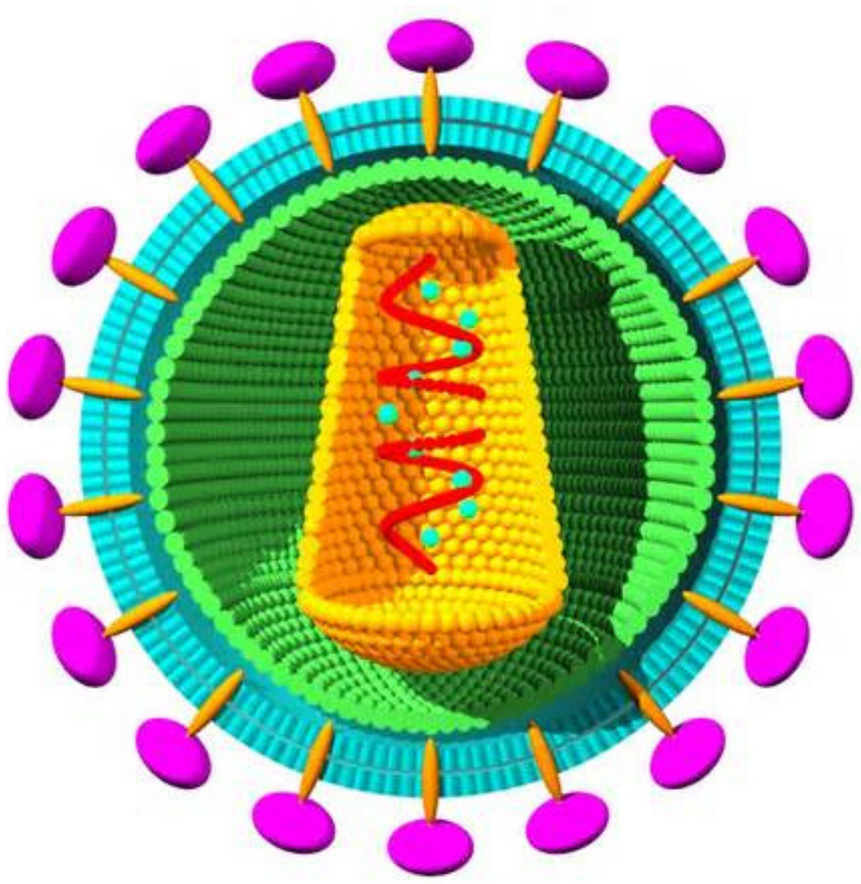
EDITION SEPTEMBER - DECEMBER 2018

PHARMACY BULLETIN

SPECIAL TOPIC :

Retroviral Disease (RVD)

General Information and Management to Prevent Vertical Transmission



WHAT'S INSIDE?

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NUR HIDAYAH BT AHMAD TERMIZI
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welcoming

NEW TEAM MEMBERS

NEWLY APPOINTED

- PN MELATI BINTI MOHD TUMIRAN
- PEGAWAI FARMASI (KONTRAK) UF 41
- DATE REPORTED DUTY: 15 OCTOBER 2018
- COMPLETED PRP TRAINING IN HOSPITAL KOTA TINGGI, JOHOR
- FARMASI KLINIK PAKAR

- PN SYARIFAH NASYIRAH BT SYED ROSITE
- PEGAWAI FARMASI (KONTRAK) UF 41
- DATE REPORTED DUTY: 15 OKTOBER 2018
- COMPLETED PRP TRAINING IN HOSPITAL JENGKA, PAHANG
- UNIT FARMASI LOGISTIK

- CHEW KOK YIP
- PEGAWAI FARMASI (KONTRAK) UF 41
- DATE REPORTED DUTY: 15 DECEMBER 2018
- COMPLETED PRP TRAINING IN HOSPITAL TENGKU AMPUAN AFZAN, PAHANG
- FARMASI BEKALAN WAD

TRANSFERRED OUT

PN SITI NUR SHAFINA BT ABDULLAH
PENOLONG PEGAWAI FARMASI U29
DATE TRANSFERRED OUT: 12 NOVEMBER 2018
TRANSFERRED TO: HOSPITAL SULTAN ABDUL HALIM, KEDAH

RETIREMENT

GANESAN A/L VAIRAPERUMAL
PENOLONG PEGAWAI FARMASI UF 38
DATE OF RETIREMENT : OKTOBER 2018

thank you

PRESCRIBING MEDICATION IN ELDERLY

It is commonly agreed that older people are at greater risk of adverse effects from their medicines due to age related changes in their major organs which in turn alter pharmacokinetics and pharmacodynamics. They also often have multiple comorbidities leading to drug-drug interactions or cautions and contraindications to preferred treatments.

Polypharmacy and inappropriate prescribing (IP) are well-known risk factors for adverse drug reactions, which commonly cause adverse clinical outcomes in older people. The screening tool of older people's prescription (STOPP) and screening tool to alert doctors to right treatment (START) criteria for potential IP in older people both recognizes the dual nature of IP by including a list of potentially inappropriate medication (STOPP criteria) and potential prescribing omissions (START criteria).

AGING AND BODY CHANGES:

Gastrointestinal, respiratory and musculoskeletal systems

The aging process generally affects the oropharyngeal and upper esophageal motility, colonic function, gastrointestinal (GI) immunity, and GI drug metabolism. As people age, the strength of esophageal contractions and the tension in the upper esophageal sphincter generally decrease. Not to mention, the decreasing stomach lining's capacity to resist damage substantially increase the risk of peptic ulcer disease, especially in people who use aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs). Other than GI, respiratory system also undergoes various anatomical, physiological and immunological changes with age. This includes chest wall and thoracic spine deformities which impairs the lung ability to stretch and expand. The lung parenchyma loses its supporting structure causing dilation of air spaces called as "senile emphysema". Respiratory muscle strength decreases with age and can impair effective coughing, which is important for airway clearance.

> *"Older people are at greater risk of adverse effects from medicines due to age related changes in the major organs which in turn alter pharmacokinetics and pharmacodynamics"*

As people age, their joints are affected by changes in cartilage and connective tissue. The cartilage inside the joint becomes thinner and the altered proteoglycans made the joint less resilient and more susceptible to damage. Additionally, the joints become stiffer as the connective tissue within ligaments and tendons becomes more rigid and brittle. This change also limits the range of motion of joints. Osteoporosis is a common problem, especially for older women. Muscle weakness substantially contributes to fatigue, weakness, and reduced activity tolerance.

STOPP CRITERIA

	STOPP medication	Circumstances	Reason to review
GASTROINTESTINAL SYSTEM	Diphenoxylate, loperamide, codeine phosphate	Diarrhea of unknown cause	● Risk of delayed diagnosis which may exacerbate constipation with overflow diarrhea ● May precipitate toxic megacolon in inflammatory bowel disease ● May delay recovery of unknown gastroenteritis
	Diphenoxylate, loperamide, codeine phosphate	Severe infective gastroenteritis	Risk of exacerbation or protraction of infection
	Prochlorperazine or metoclopramide	Parkinsonism	Risk of Parkinsonism exacerbation
	Proton-pump inhibitor	Peptic ulcer disease for full therapeutic dosage for >8 weeks	Earlier discontinuation or dose reduction for maintenance/ prophylactic treatment of peptic ulcer disease, esophagitis or GORD indicated
	Anticholinergic antispasmodic drugs	Chronic constipation	Risk of exacerbation of constipation
RESPIRATORY SYSTEM	Theophylline	As monotherapy for chronic obstructive pulmonary disease (COPD)	Risk of adverse effects due to narrow therapeutic index
	Systemic corticosteroid instead of inhaled corticosteroid	Maintenance therapy in moderate-severe COPD	Unnecessary exposure to long term side effects of systemic steroids
	Nebulised ipratropium	Patient with underlying glaucoma	May exacerbate glaucoma
MUSCULOSKELETAL SYSTEM	Non-steroidal anti-inflammatory drug (NSAIDs)	History of peptic ulcer or gastro-intestinal bleeding (unless with concurrent histamine H2 receptor antagonist, PPI or misoprostol	Risk of peptic ulcer relapsed
	NSAIDs	● Moderate hypertension ● Heart failure ● Chronic renal failure ● Long term use (> 3months) in osteoarthritis joint pain ● With warfarin	● Risk of exacerbation of hypertension ● Risk of exacerbation of heart failure ● Risk of deterioration in renal function ● Simple analgesic preferable ● Risk of gastrointestinal bleeding
	Corticosteroids	> 3 months as monotherapy for rheumatoid arthritis or osteoarthritis	Risk of major systemic corticosteroid side effects
	NSAIDs/colchicine	For chronic treatment of gout where no contraindication to Allopurinol	Allopurinol is the first choice prophylaxis drug in gout

START CRITERIA

Gastrointestinal	Respiratory	Musculoskeletal
Proton pump inhibitor with severe gastro-oesophageal acid reflux disease or peptic stricture requiring dilatation	Regular inhaled β2-agonist or anticholinergic agent for mild to moderate asthma or COPD	Disease-modifying anti rheumatic drug (DMARD) with active moderate-severe rheumatoid disease lasting >12 weeks
Fibre supplement for chronic, symptomatic diverticular disease with constipation	Regular inhaled corticosteroid for moderate-severe asthma or COPD (predicted FEV1<50%)	Bisphosphonates in patients taking maintenance oral corticosteroid therapy
	Home continuous oxygen with documented chronic type 1 respiratory failure (po_2<8.0kPa,pCO_2<6.5kPa) or type 2 respiratory failure (po_2<8.0kPa,pCO_2>6.5kPa)	Calcium and vitamin D supplement in patients with known osteoporosis (radiological evidence or previous fragility fracture or acquired dorsal kyphosis)

1. O'Connor D., Gallaher P., Ryan C., Byrne S., Hamilton H., Barry P., O'Connor M. & Kennedy J. 2010. STOPP & START criteria: a new approach to detecting potential inappropriate prescribing in old age. European Geriatric Medicine 1: 45-51.
2. O'Connor M., O'Sullivan D., Byrne S., O'Connor M. N., Ryan C. & Gallagher P. 2014. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. Age and Ageing 44(2): 213-218.
3. Ryan C. 2011. The basics of the STOPP/START criteria. PCNE Medication Review Working Symposium 9-17.
4. Aging changes in the bones - muscles - joints: MedlinePlus Medical Encyclopedia. (n.d.). Retrieved from https://medlineplus.gov/ency/article/004015.htm

RETROVIRAL DISEASE

By Nur Aqilah bt Bakhtiar

Introduction

Human Immunodeficiency Virus (HIV) is a retrovirus that destroys white blood cells which fight diseases and infection in the human body. There are two types of HIV viruses which are HIV-1 and HIV-2. HIV-1 is known to cause greater viral load compared to HIV-2, and thus is associated with more rapid progression to Acquired Immune Deficiency Syndrome (AIDS) whereas HIV-2 has lower risk of transmission and tends to progress more slowly to AIDS.

Mechanism of HIV

HIV enters into the human body (host) and seeks out the CD4+ receptors on T-helper lymphocytes and other cells with CD4+ molecule

↓

The virus then fuses with host cell, releases its RNA and Reverse Transcriptase enzyme, resulting in production of HIV DNA. The HIV DNA then integrates with host DNA.

↓

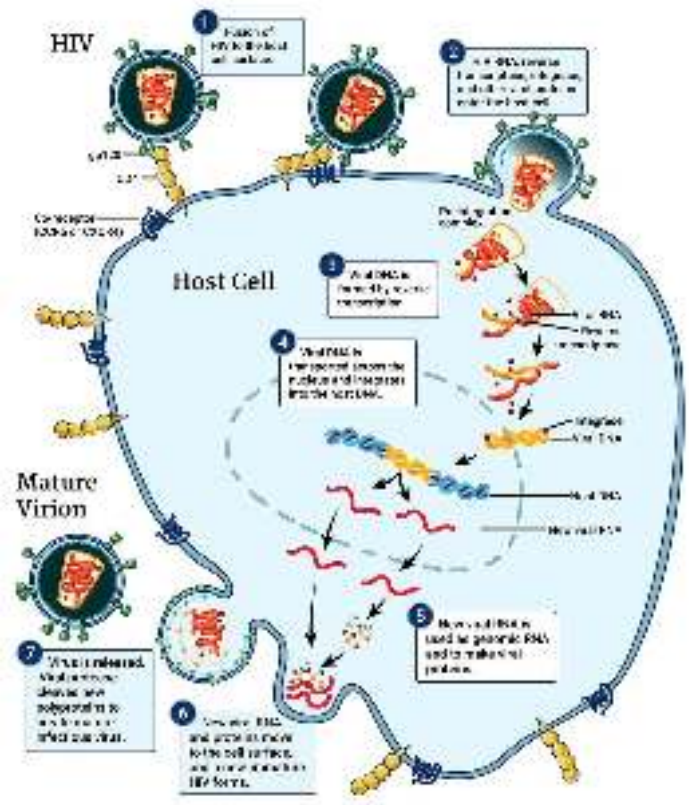
The integration will later result in budding of new mature viruses from the host cells. New viruses are produced each time HIV infected cells divide. However, host cells eventually go through programmed cell death (apoptosis).

↓

This results in reduction of CD4+ count, compromising body's defence mechanism & allowing opportunistic organisms to cause life-threatening infections & also developing typical tumours

↓

Leads to failing of immune system



Transmission of HIV

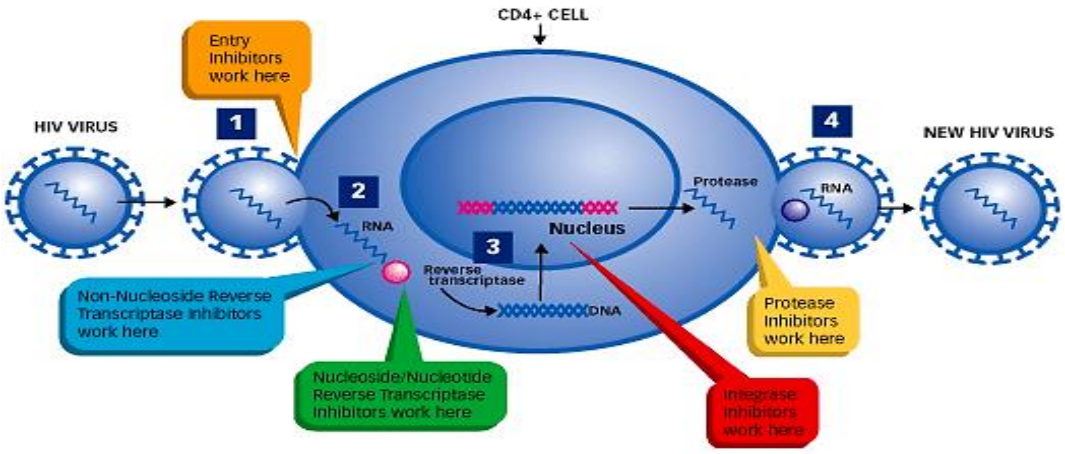
HIV can be transmitted through exchange of a variety of body fluids from an infected individual such as blood, breast milk, semen and vaginal secretions. However, it cannot be transmitted through ordinary day-to-day contact like kissing, hugging, shaking hands or sharing personal objects, food and water.

Sexual	Parenteral	Perinatal
Unprotected sexual intercourse between an infected person and his/her sexual partner	Via transfusion of blood and blood-related products, sharing of contaminated needles and syringes, contaminated sharps/ needle prick injuries, or recipients of body organs/semen/other body tissues from an HIV infected donor.	Transmission from mother to child which may occur during pregnancy, at delivery and breastfeeding.

Management of HIV Infection (Antiretroviral Therapy)

Antiretroviral therapies helps manage the HIV infection by causing decrease in viral replication, increase in CD4+ T-cell count, decrease in the frequency of opportunistic infections, improving quality of life and prolonging life expectancy of HIV infected person.

Groups	Mechanism of Action	Antiretroviral Agents
CCR5 Antagonists	Prevent HIV-1 from entering and infecting immune cells by blocking CCR5 cell-surface receptor	Maraviroc
Fusion Inhibitor	Interfere with entry of HIV-1 into cells by inhibiting fusion of viral & cellular membranes	Enfuvirtide
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI)	Nucleoside analogues → tricks the HIV reverse transcriptase using these imitation nucleosides → incorporate into HIV DNA chain → breaks viral DNA chain	Abacavir, Emtricitabine, Lamivudine, Stavudine, Tenofovir, Zidovudine
Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)	Suppress HIV replication via inhibiting reverse transcriptase enzyme	Efavirenz, Etravirine, Nevirapine, Rilpivirine
Integrase Inhibitors	Inhibits catalytic activity of HIV-1 integrase → inhibit integration & prevent propagation of viral infection	Raltegravir, Dolutegravir
Protease Inhibitors (PI)	Binds to protease active site & inhibits activity of the enzyme. Compete for the active cleavage site on the protease enzyme → blocking cleavage of polyproteins & maturation of new viral particles	Atazanavir, Darunavir, Lopinavir/ritonavir, Ritonavir



Monitoring	CD4 Count	HIV Viral Load
	Successful therapy: increment in CD4+ cell count 50-150 cells/mm^3 per year Monitored 4-6 months after initiation of antiretroviral to assess immunologic response to ART & to assess the need to discontinue prophylaxis for opportunistic infections	More accurate & reliable than CD4+ count to monitor treatment response & early detection of treatment failure Every 4-6 months after initiation of ART to assess treatment response & for early detection of treatment failure, every 6-12 months in patients who have achieved virological suppression for ≥1 year, and before changing treatment regimes. Effective therapy: suppression to less than 20 copies/mL by 6 months
	Once HIV viral load is suppressed & CD4+ counts >350cells/mm^3 on 2 occasions 6 months apart, further CD4+ count is not required (unless treatment failure is suspected.	

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2. MEDSCAPE
3. Malaysian Consensus Guidelines on Antiretroviral Therapy 2017, Ministry of Health Malaysia
4. Briz V, Poveda E, Soriano V (April 2006). "HIV entry inhibitors: mechanisms of action and resistance pathways". *The Journal of Antimicrobial Chemotherapy*. 57 (4): 619–27. doi:10.1093/jac/dkl027. PMID 16464888

MANAGEMENT TO PREVENT VERTICAL TRANSMISSION OF RVD

BY AHMAD FUAD BIN AHMAD SHUKRI

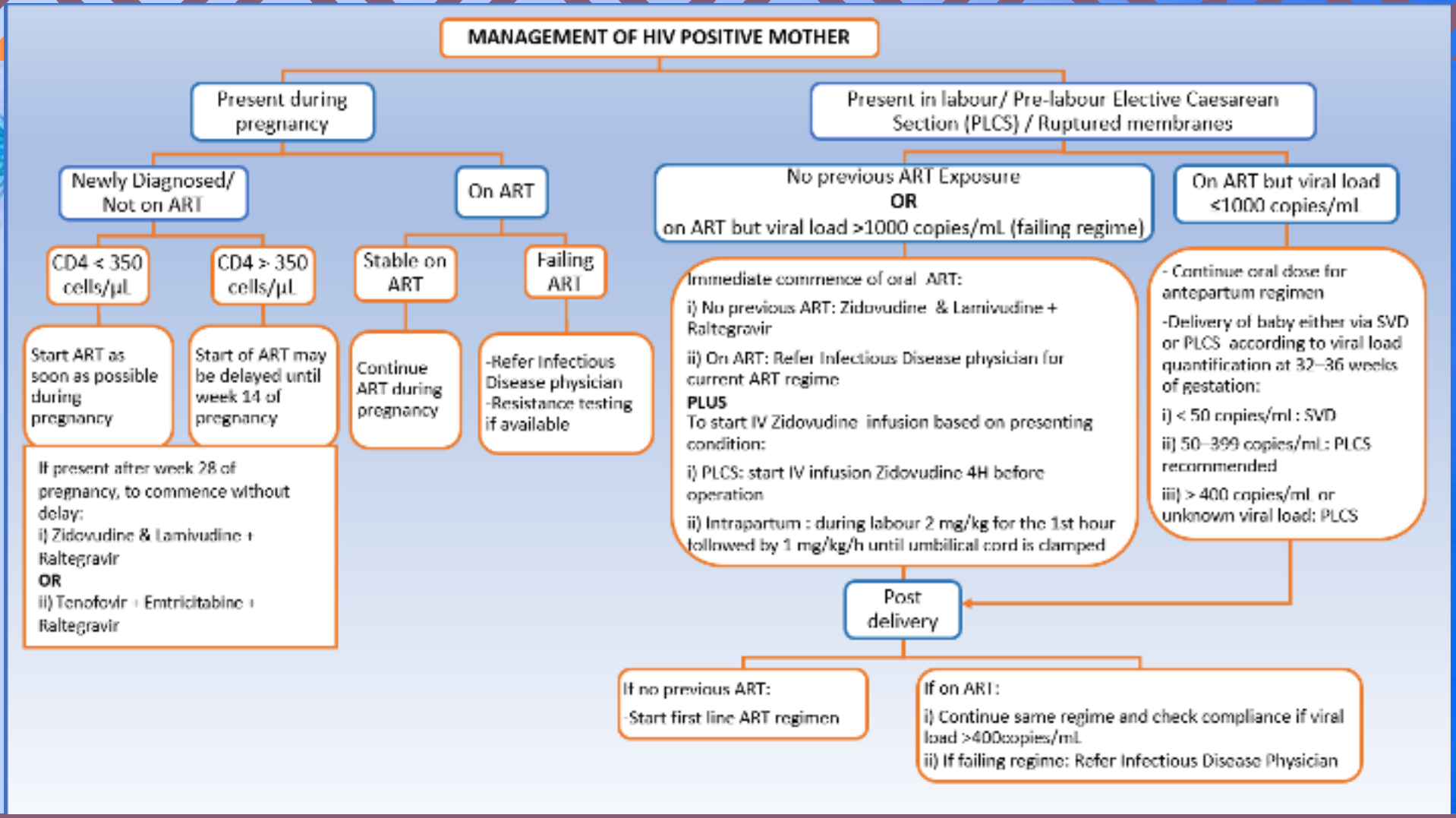
The transmission of human immunodeficiency virus (HIV) from a HIV-positive mother to her child during pregnancy, labour, delivery or breastfeeding is called mother-to-child transmission (MTCT). In the absence of any intervention, transmission rates range from 15% to 45%. This rate can be reduced to below 2% with effective interventions during the periods of pregnancy, labour, delivery and breastfeeding. Today, Malaysia has become the first country in the World Health Organization (WHO) Western Pacific region to be certified as having eliminated MTCT of HIV and syphilis.

Antenatal combination antiretroviral therapy (ART) must be started in all pregnant mothers who are HIV positive regardless of CD4 count. ART used during pregnancy must consist of 2 Nucleoside Reverse Transcriptase Inhibitors (NRTI) plus either a Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI) or a boosted Protease Inhibitor (PI) or an Integrase Strand Transfer Inhibitors. The choice of agents are listed as below:

TABLE: CHOICE OF ART COMBINATIONS:

Preferred	Alternative
Tenofovir + Emtricitabine + Efavirenz[a]	Zidovudine + Lamivudine + Efavirenz[a]
	Zidovudine + Lamivudine + Nevirapine[a]
	Tenofovir + Emtricitabine + Nevirapine[b]
	Tenofovir + Emtricitabine + Lopinavir/Ritonavir
	Tenofovir + Emtricitabine + Raltegravir[c]

a: In the past Efavirenz was considered a Category D drug and contraindicated in the first trimester of pregnancy. However, there is now good level safety evidence to recommend it as the preferred NNRTI even in the first trimester.
b: Nevirapine should be used with caution in women with CD4 > 250 cells/uL because of possible increased risk of hepatotoxicity and rash.
c: Consider Raltegravir-based ART in late presenting women (>28 weeks) with unknown or high viral load (e.g. >100,000 copies/mL) to achieve more rapid viral load suppression and further reduce the risk of perinatal HIV transmission. Raltegravir can be switched to Efavirenz or Nevirapine after delivery.



Note:

*ART: Antiretroviral therapy, PLCS: Pre-labour elective caesarean section, SVD: Spontaneous vaginal delivery

- Post exposure antiretroviral prophylaxis for the infant: HIV exposed infant should receive 6 weeks of oral Zidovudine and 3 doses of Nevirapine at birth, 48 hours later and 96 hours after the second dose.

-Breastfeeding is not recommended as it is associated with risk of transmission up to 14%. For women on ART, compliance must be stressed if they insist on breastfeeding their baby.

References:

i) WHO, Prevention of mother-to-child transmission - Estimates by country. Retrieved from http://apps.who.int/gho/data/node.main.627?lang=en

ii) WHO, Malaysia eliminates mother-to-child transmission of HIV and syphilis. Retrieved from http://www.who.int/westernpacific/news/detail/08-10-2018-malaysia-eliminates-mother-to-child-transmission-of-hiv-and-syphilis

iii) Intrapartum Antiretroviral Therapy/Prophylaxis Intrapartum Care Perinatal. Retrieved from https://aidsinfo.nih.gov/guidelines/html/3/perinatal/180/intrapartum-antiretroviral-therapy-prophylaxis

iv) Mother-to-child transmission of HIV. Retrieved from https://www.who.int/hiv/topics/mtct/about/en/

v) KKM, MALAYSIA CONSENSUS GUIDELINES ON ANTIRETROVIRAL THERAPY 2017. Retrieved from https://www.researchgate.net/publication/319101215_Malaysian_Consensus_Guidelines_on_Antiretroviral_Therapy_2017_MINISTRY_OF_HEALTH_MALAYSIA

vi) KKM, MANAGEMENT OF HIV INFECTION IN PREGNANT WOMEN. Retrieved from http://www.moh.gov.my/penerbitan/CPG2017/3886.pdf

INJECTION DENOSUMAB 60MG

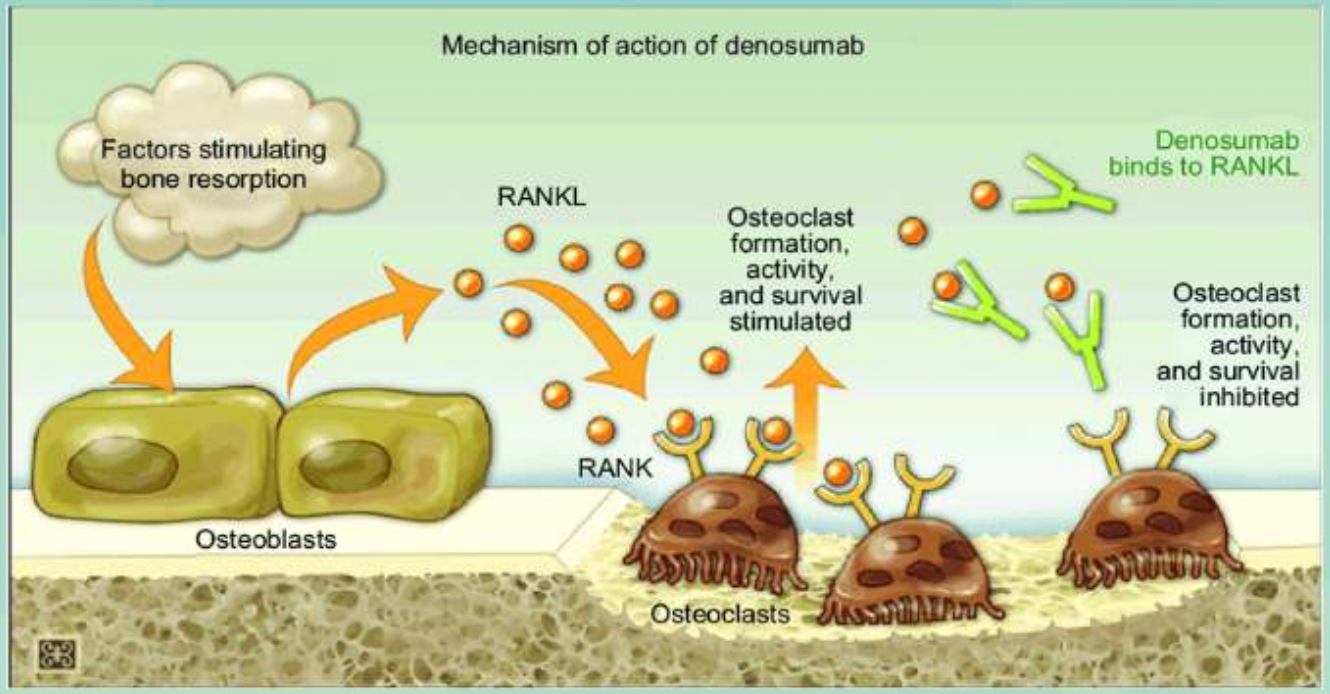
Denosumab is a human IgG2 monoclonal antibody with affinity and specificity for human RANKL (receptor activator of nuclear factor kappa-B ligand). It is indicated for the treatment of post-menopausal women with osteoporosis, to treat men and women who have an increased risk for fractures or who cannot take or did not respond to other medication treatments for osteoporosis, to treat bone loss in men who are being treated for prostate cancer and women treated for breast cancer with certain medications that cause bone loss.

DRUG DOSING

A single subcutaneous injection of 60mg administered every 6 months. Patients should receive calcium and vitamin D supplements whilst undergoing treatment.

MECHANISM OF ACTION

Denosumab is a receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor. Binding to the transmembrane or soluble protein RANKL inhibits the formation, function, and survival of osteoclasts resulting in decreased bone mass resorption and increase bone mass and strength. It also prevents RANKL from activating the RANK receptor on the surface of osteoclast-like giant cells.



Category X. Fetal risk has been demonstrated.

PREGNANCY

Infant risk cannot be ruled out

BREAST-FEEDING

DOSE ADJUSTMENT

Renal impairment: No dose adjustment needed.

Hepatic impairment: No clinical studies have been conducted.

PHARMACOKINETIC

Absorption
Bioavailability: 62%
Tmax: 10 days

Distribution
lack of extravascular distribution
Vd: 29-55ml/kg

Metabolism
Metabolised via Ig clearance pathways, resulting in degradation to small peptides and amino acid

Excretion
Excreted via reticulo-endothelial system
Half-life: 25 to 28 days

ADVERSE EFFECT

#1 Headache

#2 Diarrhea

#3 Vomiting

#4 Athralgia

#5 Dermatitis

DEPARTMENT:
- ENDOCRINE
- HEMATOLOGY
- RHEUMATO-LOGY

PRESCRIBER'S CATEGORY

A*

REFERENCES

Micromedex Drug Information: Denosumab
Ministry of Health Medicine Formulary: Denosumab
MIMS Gateway: Denosumab

BY: NOR ATIQAH AKMAL

DRUG UPDATE: EMPAGLIFLOZIN 25MG

BY: NUR HIDAYAH AHMAD TARMIZI

Empagliflozin is indicated in the treatment of type 2 diabetes mellitus to improve glyceamic control in adults as: Add-on combination therapy; in combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glyceamic control. Prescribing restriction: Patient must meet all the following criteria:1. HbA1c not more than 8.5% on dual combination anti-diabetic therapy; 2. BMI 30kg/m2 and above; 3. CrCl >60ml/min or eGFR >60ml/min/1.73m2.

MECHANISM OF ACTION

Lowers the renal threshold for glucose and increases urinary glucose excretion by interfering with the reabsorption of renally-filtered glucose across the tubular lumen of the proximal renal tubules.

DOSE ADJUSTMENT

HEPATIC IMPAIRMENT	RENAL IMPAIRMENT
No dose adjustment required	CrCl <60 ml/min – reduce to 10 mg once daily

DOSE

10 mg once daily, may be increased to 25 mg once daily, if necessary.

PRESCRIBER CATEGORY

A*

DEPARTMENT

Endocrino-logy

May be taken with or without food

ABSORPTION

- Achieved Tmax 1.5 hours after oral administration
- AUC decreased by 16%, Cmax decreased by 37% with food

DISTRIBUTION

- Protein binding of empagliflozin ~ 86.2%
- Volume of distribution (Vd) ~ 73.8 L

PHARMACOKINETIC PROFILE

METABOLISM

- Glucoronidation via UGT2B7, UGT1A3, UGT1A8, and UGT1A9

ELIMINATION

- Renal 54.4%
- Fecal 41.2%
- Clearance 10.6 L/hr
- Half-life 12.4 hours

COMMON ADVERSE EFFECTS

- Increased urination
- Urinary tract infections
- Hypoglycemia

PREGNANCY CATEGORY

No data from the use of empagliflozin in pregnant women. It is preferable to avoid usage during any stage of pregnancy

LACTATION CATEGORY

No data in human are available on excretion of Empagliflozin in human milk. Empagliflozin should not be used during breast-feeding

References:
Micromedex Drug Reference: Empagliflozin
Ministry of Health Medicines Formulary (April 2018 Edition)
The electronic Medicines Compendium: Empagliflozin

SuperBowl PHARMCARE

TARIKH: 29 SEPTEMBER 2018 (SABTU)
TEMPAT: PLAYGROUND NO.6 SPORTS CENTRE, SEMAMBU KUANTAN PAHANG
PENGANJUR : PHARMCARE HTAA, KUANTAN

oleh : Maisarah bt Mohd Termizi

Kursus Farmasi Echo Training SIRI 2/2018

TARIKH: 20 OKTOBER 2018 (SABTU)
TEMPAT: BILIK MESYUARAT NILAM 1, BANGUNAN ACC, HTAA
PENGANJUR : JABATAN FARMASI HTAA, KUANTAN

MINGGU FARMASI PERINGKAT HTAA

Oleh: Maisarah binti Mohd Termizi

Tarikh : 1 - 5 Oktober 2018
Tempat: Ruang Legar Pusat Rawatan Harian HTAA
Penganjur: Jabatan Farmasi, HTAA
Perasmi : Pengarah Hospital, Dr. Norazmi bin Abdullah

KUIZ TERBUKA

DEMONSTRASI EKSTEMPORANEOUS

KAUNSELING UBAT-UBATAN

PAMERAN

Majlis perasmian Minggu Farmasi & Pelancaran Locker4U yang dirasmikan oleh Pengarah HTAA.

Annual Grand Meeting & Pharmnight

Disediakan oleh: Muhammad Shazerin Kamarudin

Majlis Perasmian

Tarikh : 17 November 2018

Tempat : Kompleks Dagangan Mahkota, Kuantan

Anjuran : Kelab Kebajikan & Rekreasi Jabatan Farmasi (PharmCare)

Persembahan

World Antibiotic Awareness Week

Disediakan oleh: Muhammad Shazerin Kamarudin

Tarikh : 4-7 Disember 2018

Tempat : Ruang Legar Pusat Rawatan Harian, Hospital Tengku Ampuan Afzan

Anjuran : Unit Kawalan Infeksi, Hospital Tengku Ampuan Afzan

Pameran & Kaunseling