UNIT KAJIAN DAN MAKLUMAT DRUG | JABATAN FARMASI | HOSPITAL USM

DRUG Newsletter

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Formulary Update

New drugs included and excluded in HUSM Formulary after P & T Meeting

Notes : ST indicates 'Standard Terkawal' need to fill up LP form

P & T 84

New drugs included

- Cap. Oseltamivir 75mg
- Tab. Ticagrelor 90 mg (ST)

P & T 85

New drugs included

- Tab. Ezetimibe + Simvastatin (10/10mg, 10/20mg, 10/40mg)
- IV Glamin 13.4%
- Neutral Buffered Formalin

P & T 86

New drugs included

- Tab. Leflunomide 20mg (ST)
- Tab. Raltegravir 400mg (ST)
- Eltrombopag Olamine 25mg (ST)
- Tab. Deferiperone 500mg (ST)

P & T 87

Drugs excluded

- Tab. Aluminium Hydroxide Gel 600mg
- Cap. Chloramphenicol 250mg
- Cap. Piroxicam 10mg
- Inj. Fusidic Acid 500mg
- IV Potassium Acetate 2mEq/ml (20ml)
- IV Tirofiban HCl 0.25mg/ml
- Cream Tioconazole 1%
- IV Drotrecogin Alfa 5mg/ml
- IV Netilmycin 150mg
- Ointment Fibrinolysin Loomis + Desoxyribonuclease (Elase®)
- Monobasic Sodium Phosphate + Dibasic Sodium Phosphate Solution(48% + 18%) (Colclean®-90ml)
- Solution for irrigation Amino Acetic 1.5%
- Solution Isoflurane 100ml & 250ml

P & T 88

New drugs included

- Stavudine 30 mg
- Lamivudine 150mg/Zidovudine 300 mg
- Stavudine 30mg/ Lamivudine 150mg/Nevirapine 200mg
- Tenofovir Fumarate 300 mg
- Efavirenz 600 mg
- Nevirapine 200 mg
- Tenofovir 300 mg /Emtricitabine 200mg
- Lopinavir 200 mg/Ritonavir 50 mg
- Ritonavir 100 mg
- Abacavir 300 mg
- Indinavir 400 mg
- Didanosine 250 mg
- Abacavir 600 mg/Lamivudine 300 mg
- Darunavir 300 mg

P & T 89

New drug included

- IV Paracetamol 1g dan 500mg (ST)

P & T 90

New drugs included

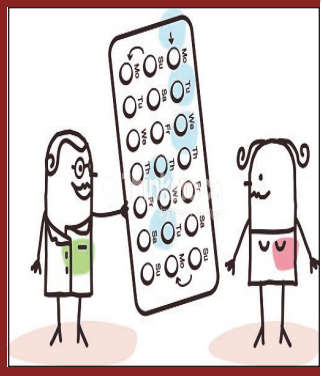
- IV Moxifloxacin 400 mg (ST) & Tablet Moxifloxacin 400 mg (ST)

P & T 91

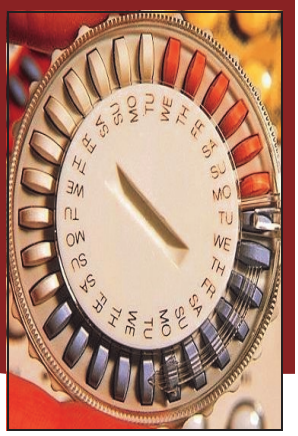
New drugs included

- Caffein Powder
- Tab. Misoprostol 200mcg
- Oral Phosphate
- IV Sodium Glycerophosphate 20

Hormonal Therapy



Approximately 80% of menopausal women experience symptoms. While a quarter have severe symptoms, only a small proportion of menopausal women currently take hormone replacement therapy (HRT)[2].



Hormone Replacement Therapy, or HRT, is widely used for treatment of menopausal symptoms, and is considered by many to be the most effective[1]. Approximately 80% of menopausal women experience symptoms. While a quarter have severe symptoms, only a small proportion of menopausal women currently take hormone replacement therapy (HRT)[2].

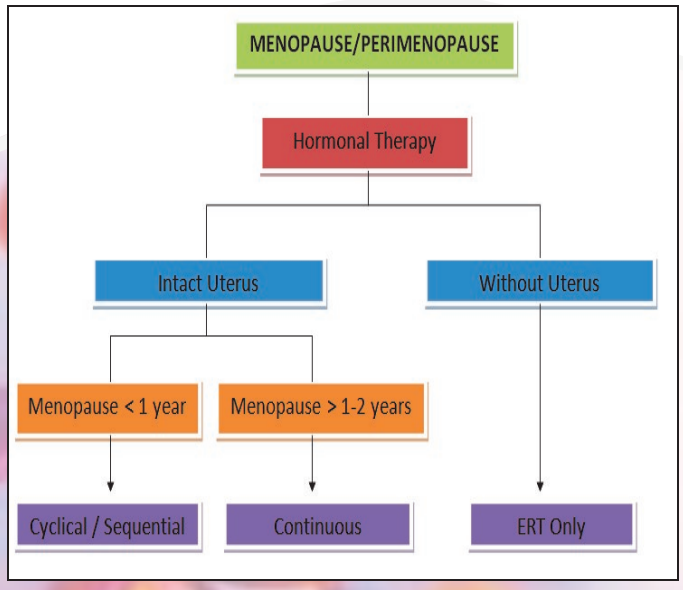
In fact, the common symptoms of the menopause are associated with a decrease of the body's production of oestrogen, including night sweats, vaginal dryness, headaches, low mood, reduced sex drive, and the infamous hot flushes. Thus, HRT is an effective treatment for the typical menopause-related symptoms.

Besides, there are also other long-term health problems associated with the menopause include the risk of osteoporosis, cardiovascular disease and stroke all increase after the menopause. HRT can also have a positive influence on these health problems[2].

It is important that an individualised approach is undertaken at all stages of diagnosis, investigation and management of menopause. The dose, regimen and duration of HRT need to be individualised. There is no maximum duration of time for women to take HRT; for the women who continue to have symptoms, their benefits from HRT usually outweigh any risks.

Different treatment courses of HRT are also available, depending on whether you're still in the early stages of the menopause or have had menopausal symptoms for some time.

There are two types of HRT which are CYCLICAL/ SEQUENTIAL COMBINED HRT and CONTINUOUS COMBINED HRT[3]. Women should be prescribed **CYCLICAL COMBINED HRT** if their last menstrual period was less than one year previously.



1) **Monthly HRT** – you take oestrogen every day, and take progestogen alongside it for the last 14 days of your menstrual cycle
2) **Three-monthly HRT** – you take oestrogen every day, and take progestogen alongside it for around 14 days every three months

Monthly HRT is usually recommended for women having regular periods. Three-monthly HRT is usually recommended for women experiencing irregular periods. You should have a period every three months. It's useful to maintain regular periods so you know when your period naturally stop and when you're likely to progress to the last stage of the menopause.

While **CONTINUOUS COMBINED HRT** is usually recommended for women who are post-menopausal. A woman is usually said to be post-menopausal if she has not had a period for a year. As the name suggests, continuous HRT involves taking oestrogen and progestogen every day without a break. **OESTROGEN ONLY HRT** is also usually taken continuously.

In summary, the woman needing HRT has a greater number of options available today than ever before. The physician will consider individual patient characteristics and desires, side effect profiles, and long-term acceptability to the patient when prescribing HRT.

LIST OF HORMONAL THERAPY FOR MENOPAUSE

Medications	How to take female sex hormones pills?	
	Indications	Cycles
Estradiol + Dydrogestrone	**Relief of symptoms occurring after menopause**	CYCLICAL COMBINED: Femoston®[4] ♦ Day 1 to 14 of the cycle, 1 tablet daily containing 1 or 2 mg oestradiol. ♦ Day 15 to 28 of the cycle, 1 tablet daily containing 1 or 2 mg oestradiol and 10 mg dydrogesterone. Immediately after the 28-day cycle, continue the next treatment.
	Prevention of osteoporosis	CONTINUOUS COMBINED: Estradiol 1mg + Dydrogesterone 5mg (Femoston Conti®) ♦ 1 tablet per day continuosly[5].
Estradiol Valerate [6] (1mg or 2mg)	**Estrogen only replacement therapy**	♦ Either as a continuous daily regimen or as a 21-day regimen with 1 wk of tab-free interval.
Oestrogen Conjugated (Premarin) [7] - 0.625mg or 0.3 mg per tab - 0.625 mg/g cream	**Menopausal symptom**	♦ 0.3-1.25 mg daily from 5th day of cycle for 3 weeks. Then repeat after 1 week in subsequent cycles
	Vaginal cream	♦ 1/2-1 applicatorful (2-4 g) daily intravaginally

References:
1. Hormone Replacement Therapy (HRT), Women's Health Concern, British Menopause Society BMS, (December, 2015). Retreived from https://www.womens-health-concern.org/help-and-advice/factsheets/hrt/
2. Louise N., (February, 2016) Hormone Replacement Therapy including Benefit and Risks. Retrieved from http://patient.info/doctor/hormone-replacement-therapy-including-benefits-and-risks
3. Types of Hormone Replacement Therapy (July, 2016). http://www.nhs.uk/Conditions/Hormone-replacement-therapy/Pages/How-it works.aspx
4. Package Leaflet: Estradiol + Dyrogestrone (Femoston) (2016).
5. Package Leaflet: Estradiol + Dydrogestrone (Femoston Conti) (2016).
6. Package Leaflet: Estradiol Valerate (2015).
7. Package Leaflet: Oestrogen Conjugated (Premarin) (2016).

Q&A WORTH SHARING

DOSING OF IRON SUCROSE (VENOFER®) FOR IRON DEFICIENCY ANEMIA (IDA) IN PREGNANCY ?

The total cumulative dose of Venofer, equivalent to the total iron deficit (mg), is determined by the haemoglobin level (Hb) and body weight (BW). Venofer must be individually calculated according to the total iron deficit using the

GANZONI FORMULA[1]:

TOTAL IRON DEFICIT [mg] =

BW [kg] x (target Hb - actual Hb) [g/dl] x 2.4* + STORAGE IRON [mg]

(* 2.4 = iron factor)

Below 35 kg	Target Hb = 13 g/dl and storage iron = 15 mg/kg
35 kg BW and above	Target Hb = 15 g/dl and storage iron = 500 mg

The cumulative dose of Venofer must be given in divided not more than 3 times per week. The normal recommended dosage is 100-200 mg of iron per dose (1-2 ampoule of Venofer), depends on clinical requirement of a patient[2]. Before administration of first therapeutic dose, a test dose should be given[3].

[*Venofer should be confined to second and third trimester as it only licenced for use in the second and third trimester of pregnancy. IDA occurring in the first trimester of pregnancy in many cases be treated with oral iron*[1]]

DILUTION AND ADMINISTRATION OF IRON SUCROSE (VENOFER®)[3]

For Intravenous drip infusion

Venofer® (100mg/5 ml) must be diluted in sterile 0.9% sodium chloride solution. It is single used thus discard any excess.

Venofer dose	Diluent volume	Infusion Time
50 mg	50 ml	8 minutes
100 mg	100 ml	15 minutes
200 mg	200 ml	30 minutes

For Intravenous injection

Venofer® may be administered by slow intravenous injection at a rate of 1 ml undiluted solution per minute and not exceeding 10ml Venofer® (200 mg iron) per injection.

Reference
1. Breymann C. Iron Supplementation during Pregnancy. Fetal and Maternal Medicine Review 2002
2. Lexi-Comp, Inc. (Lexi-Drugs®). Lexi-Comp, Inc.2015.
3. Package Leaflet: Venofer®.

HALL OF FAME *We would like to congratulate....*

Relationship between ABCB1 polymorphisms and serum methadone concentration in patients undergoing methadone maintenance therapy (MMT).

By: **Zalina Zahari**, Chee Siong Lee, Muslih Al , Rusli Ismail

Article *in The American Journal of Drug and Alcohol Abuse 42(5):1-10 · June 2016*

Background:
Methadone is a substrate of the permeability glycoprotein (P-gp) efflux transporter, which is encoded by the ABCB1 (MDR1) gene. Large interindividual variability in serum methadone levels for therapeutic response has been reported. Genetic variations in ABCB1 gene may be responsible for the variability in observed methadone concentrations.

Objective:
This study investigated the associations of ABCB1 polymorphisms and serum methadone concentration over the 24-hour dosing interval in opioid-dependent patients on methadone maintenance therapy (MMT).

Methods:
One hundred and forty-eight male opioid-dependent patients receiving MMT were recruited. Genomic deoxyribonucleic acid (DNA) was extracted from whole blood and genotyped for ABCB1 polymorphisms [i.e. 1236C>T (dbSNP rs1128503), 2677G>T/A (dbSNP rs2032582), and 3435C>T (dbSNP rs1045642)] using the allelic discrimination real-time polymerase chain reaction (PCR). Blood samples were collected at 0, 0.5, 1, 2, 4, 8, 12, and 24 hours after the dose. Serum methadone concentrations were measured using the Methadone ELISA Kit.

Results:
Our results revealed an association of CGC/TTT diplotype (1236C>T, 2677G>T/A, and 3435C>T) with dose-adjusted serum methadone concentration over the 24-hour dosing interval. Patients with CGC/TTT diplotype had 32.9% higher dose-adjusted serum methadone concentration over the 24-hour dosing interval when compared with those without the diplotype [mean (SD) = 8.12 (0.84) and 6.11 (0.41) ng ml(-1) mg(-1), respectively; p = 0.033].

Conclusion:
There was an association between the CGC/TTT diplotype of ABCB1 polymorphisms and serum methadone concentration over the 24-hour dosing interval among patients on MMT. Genotyping of ABCB1 among opioid-dependent patients on MMT may help individualize and optimize methadone substitution treatment.

Suggestion and coments.
Let us know what you think by reaching us at:

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We are on the web at
http://www.h.usm.my/pharmacy/