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

P&T 80

Drugs excluded	New drugs included
♦ Novorapid, Penfill 3ml	♦ Difflam Mouth Gel
♦ Humalog, Penfill 3ml	♦ Alendronate (Fosamax Plus 5600 iu)
♦ Humulin R, Vial 10ml	♦ Norgesic Tablet (Paracetamol+ Orphanedrine)
♦ Mixtard HM30/70, Vial 10ml	♦ Benzydamine HCL Mouthwash
♦ Insulatard HM, Vial 10ml	
♦ Monotard HM, Vial 10ml	
♦ Humulin N, Vial 10ml	
♦ Benzydamine HCL + Chlor-hexedine Mouthwash	

P&T 81

Drugs excluded

-Nil-

New drugs included

IV Albumin 5%

P&T 82

Drugs excluded	New drugs included
Halothane Liquid	Sterofundin
Cholestyramine Powder	Oseltamivir, 75mg capsules
Inj Vecuronium	Insulin Lispro Mix 50, Penfill 3ml

P&T 83

Drugs excluded

-Nil-

New drugs included

Sitagliptin + Metformin (Janumet)

Vildagliptin + Metformin (Galvusmet)

Linagliptin + Metformin (Trajenta Duo)

Saxagliptin + Metformin (Kombiglyze)

Oxycodone + Naloxone (Targin)

IV Anidulafungin

What's interesting?

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HIGHLIGHTS

New Restricted Indication and Contraindication for the use of Protaxos® (Strontium Ranelate)

Strontium ranelate is used to treat severe osteoporosis in post menopausal women who are at high risk of fracture and men who are at increased risk of fracture.

In Hospital USM, strontium ranelate is a category I* item available in sachets of 2g powder. Its criteria of use should be in accordance with the algorithm for the management of postmenopausal osteoporosis.

However, data from randomized placebo-controlled studies of 7500 postmenopausal osteoporotic patients, a significant increase of myocardial infarction was observed in patients treated with strontium ranelate as compared to placebo. The observed signal is an isolated increase in the frequency of non-fatal myocardial infarction in clinical trials with no increase in cardiovascular mortality nor in total mortality. The available data do not show evidence of an increase cardiovascular risk in patients without established, current or past history of ischaemic heart disease, peripheral arterial disease or cerebrovascular disease or those without uncontrolled hypertension. On the flip side, the efficacy of strontium ranelate remains the same. Strontium ranelate can reduce the relative risk of new vertebral fracture by 41%, and hip fractures by 36% over 3 years.

Hence, from the result of the study, Committee for Medicinal Products for Human Use (CHMP) has decided to maintain Strontium Ranelate on the market but should only be used, if all alternative treatments are considered unsuitable. Moreover, Malaysian Adverse Drug Reaction Comitee (MADRAC) has decided that each product information on strontium ranelate to include a new black box warning, restricted indication, additional contraindication and special warning and precaution related to the cardiovascular risks.

As a **risk minimization measures**, prescribers are advised to:

- Assess patient's risk of developing cardiovascular disease before starting treatment
- Monitoring patients' cardiovascular risk on regular basis generally every **6 to 12 months**.
- **Stop treatment** if the patient develops ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or if hypertension is uncontrolled.
- Strontium ranelate should be **used with caution** in patient with significant risk factors for cardiovascular events such as hypertension, hyperlipidemia, diabetes mellitus or smoking.
- Patient at risk of VTE. When treating patients over 80 years who are at **risk of VTE**, the need for continued strontium ranelate should be re-evaluated.

References:

1. Direct Healthcare Professional Communication, New Restricted indication and contraindicatios for the use of Protaxos (Strontium Ranelate).by Servier Malaysia Sdn.Bhd
2. Memo dari Biro Pengawalan Farmaseutikal Kebangsaan, Kementerian Kesihatan Malaysia. Makluman sususlan status keselamatan Terkini bagi Produk yang Mengandungi Strontium Ranelate

The **indications** have been revised to the following:

- Treatment of severe/established osteoporosis in post menopausal women at high risk of fracture to reduce the risk of vertebral and hips fractures.
- Treatment of severe/established osteoporosis in men at increased risk of fracture.

Black Box Warning

Protaxos® should only be used for whom treatment with other medicinal products approved for the treatment of osteoporosis is not possible due to for example, contraindications or intolerance.

Protaxos® is contraindicated in patients with:

- Established, current or past history or ischaemic heart disease; peripheral arterial disease and/or cerebrovascular disease;
- Uncontrolled hypertension;
- Current or previous venous thromboembolic events (VTE);
- Temporary or permanent immobalisation.

HIGHLIGHTS

Warning labels due to serious adverse skin reaction

Due to serious adverse skin reactions National Pharmaceutical Control Bureau(NPCB) has released circular that enforce the need of additional warning labels. The labels must be attached to the envelopes or boxes of medications supplied to patients in order to help them identify early signs of adverse skin reactions and seeking for medical attention.

In accordance with this circular, the Pharmacy Department of Hospital USM has recently initiated the use of these labels for the indicated drugs particularly at its Outpatient Pharmacy Unit.

The medications involved are differentiated by 2 different warning labels as listed below:

1. **Allopurinol, Co-trimoxazole, Diclofenac, Mefenamic acid:** To stop immediately.

> **WARNING**
>
> If you have side effects such as a rash, fever, sore throat, or eye irritation, **SEEK medical advice from your doctor/pharmacist IMMEDIATELY.**

2. **Phenytoin, Carbamazepine**: Should not suddenly stopped.

> **WARNING**
>
> If you have side effects such as a rash, fever, sore throat , or eye irritation, **STOP using this medication IMMEDIATELY** and consult your doctor/pharmacist

Q & A WORTH SHARING

Q1:How should isosorbide dinitrate be taken?

Isosorbide dinitrate (immediate- release tablet) is one form of nitrate beside oral glyceryl trinitrate (GTN), isosorbide mononitrate (prolonged-release tablet), transdermal nitroglycerin patch and continuous intravenous infusions of nitroglycerin.

Nitrate is an antianginal drug. The use of nitrate by around the clock method of administration will lead to nitrate tolerance. Nitrate tolerance is the attenuation, or loss, of one or several of the effects of organic nitrates after chronic exposure.

In order to prevent nitrate tolerance, the regimens should be adjusted to provide a 10- to 12-hour nitrate-free interval[1,2]. This means that antianginal prophylaxis can only be provided by nitrate therapy for some portion of each day, and that some patients will develop an increase in angina in the nitrate-free intervals thus require short term therapy with sublingual nitroglycerin or a similar preparation[1].
These are some recommendations of taking oral isosorbide dinitrate[3].

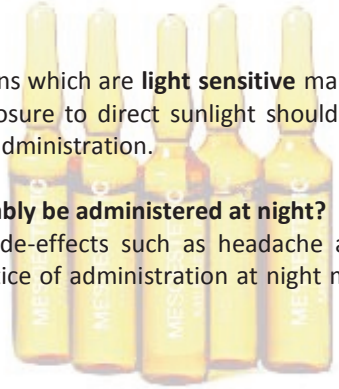
Twice daily regimen : Taken at 7 am and 12 noon
Three times daily regimen: Taken at 7am, 12 noon and 5pm

References:
1. Rutherford JD. Nitrate tolerance in angina therapy. How to avoid it. Drugs. 1995 Feb;49(2):196-9.
2. Cowan JC. Avoiding Nitrate Tolerance. Br. J. Clin. Pharmac. 1992;34 (2):96-101
3. Drug Information Handbook, 17th edition, 2009

Q2: Does Parentrovite need to be protected from light during IV administration?

IV Parentrovite is commonly used to correct vitamin deficiencies in several conditions include surgery, extensive burns, fractures and other trauma, severe infectious diseases, and comatose states.

It contains multivitamins in 2 different ampoules. Prior use, both ampoules should be mixed and diluted in 500 to 1000ml of either normal saline or dextrose 5%. Then, the preparation be infused at rate of 40 to 500ml per hour [1,2]. [Note: 1000 ml is the preferred infusion volume].



IV Parentrovite contains vitamins which are **light sensitive** mainly A, D and riboflavin. Thus, exposure to direct sunlight should be minimized during storage and administration.

Why does Parentrovite preferably be administered at night?
Parentrovite has neurologic side-effects such as headache and dizziness[2]. Therefore, the practice of administration at night may reduce these risks.

References:
1. Rx list :www.rxlist.com
2. Global Rph : www.globalrph.com

Hall Of Fame

Hyperalgesia in opioid dependent patients on methadone maintenance therapy (MMT) in Malaysia

By: Zalina Zahari, Lee Chee Siong, Nurfadhlina Musa, Mohd Azhar Mohd Yasin, Tan Soo Choon, Nasir Mohamad, Rusli Ismail. Published in *Anaesthesia and Intensive Care, Vol. 42, No. 3, May 2014*

Background and Aims: Opioid maintenance therapy may alter sensitivity to pain. Previous studies on pain perception in opioid dependent patients on methadone maintenance therapy (MMT) have yielded contradictory results. This study compared opioid naive subjects and patients on MMT in terms of their pain threshold,pain tolerance, or pain intensity in response to experimental pain stimulus.

Methods: Subjects comprised Malay male opioid naive subjects (n = 152) and patients (n = 148) from MMT clinics in Kelantan,Malaysia between March and October 2013. Pain threshold (time elapsed when the subject starts to perceive pain after immersion of hand), pain tolerance (time required for hand withdrawal), or pain intensity (0 - 100 visual analogue scale (VAS)) in response to cold pressor test (CPT) were measured. Subjects were evaluated at approximately 30 minutes before taking their morning doses of methadone (0 hour), and at 2, 4, 8, 12, and 24 hours after the first CPT. The mean difference of CPT responses between opioid naïve and MMT group were analysed using repeated measure analysis ofvariance (RM-ANOVA).

Results: The opioid dependent patients exhibited shorter pain thresholds (adjusted mean (95% CI) = 25.68 (17.48, 33.89) seconds) than opioid naive group (51.15 (43.13, 59.16) seconds)(RM-ANOVA; F (1) = 19.08, p < 0.001). The adjusted mean pain tolerance to the CPT in the patients was shorter than that of opioid naive subjects (34.27 (24.89, 43.66) seconds versus 61.46 (52.29, 70.62) seconds) (RM-ANOVA; F (1) = 16.64, p < 0.001). The adjusted mean pain intensity scores of the opioid dependent patients was 65.37 (63.00, 67.73) seconds, whereas that of the opioid naive subjects was 64.21 (61.90, 66.52) seconds (RM-ANOVA; F (1) = 0.47, p = 0.492).

Conclusions: This study confirmed hyperalgesia among patients on MMT, as manifested by their quicker detection of pain and quicker hand withdrawal. The results provide further evidence that opioid dependent patients on MMT represent a pain intolerant subset of clinical patients and may has significant clinical implications. The complaints of pain in this population should not be underestimated and the pain should be evaluated seriously and managed aggressively.