

# PHARMACY BULLETIN

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## ENOXAPARIN (CLEXANE®) AND FONDAPARINUX (ARIXTRA®): IS THERE A NEED FOR DOSE ADJUSTMENT IN OBESE PATIENTS?

Enoxaparin (Clexane®) and Fondaparinux (Arixtra®) are frequently prescribed for the treatment and prophylaxis of deep vein thrombosis (DVT) in UKM Medical Centre. Enoxaparin is a low molecular weight heparin (LMWH) which exert their anticoagulant effect primarily through the inactivation of factor Xa (anti-Xa activity). Fondaparinux on the other hand is a synthetic, highly sulfated pentasaccharide selective Factor Xa inhibitor. In contrast to heparin, fondaparinux does not inhibit thrombin.

There were studies published recently on dose adjustments of enoxaparin and fondaparinux in obese patients (BMI >30 kg/m<sup>2</sup>). This is due to the fact that obesity alters the disposition of drugs in the body or pharmacokinetics of the drug. Failure to adjust doses in obesity may result either in therapeutic failure or increased toxicity. In obese patients, weight-based dosing of low-molecular-weight heparins (LMWH) is recommended on the basis of data showing reduced anti-Xa levels with an increase in weight. However, the optimal weight-based dose remains to be established. Suggested enoxaparin regimens for the prophylaxis of venous thromboembolism (VTE) that are based on small studies in morbidly obese patients include 30% increases in usual LMWH dose, 40 mg SC every 12 hours, and 0.5 mg/kg SC once daily.

Meanwhile for fondaparinux, because it is a newer antithrombotic agent, limited data is available for dosing in obese patients. Current dosing recommendations are based on pharmacokinetic results from Phase II clinical trials. Fondaparinux dosing for treatment of deep venous thrombo-embolism (DVT) or pulmonary embolism (PE) in patients weighing >100 kg, is adjusted to 10 mg subcutaneously daily. However, the limitation of this dosing recommendation is that clinical trials only use subjects with the maximum weight of 160kg. [Grade 2C : ACCP CPG on antithrombotic therapy and prevention of thrombosis]

Table below described the dose recommendation for enoxaparin and fondaparinux in obese patients. It is important to remember dosage adjustments may not be as simple as doubling the dose because a patient is morbidly obese. In a nutshell, individualizing drug dosing is imperative in the obese, postoperative patient to ensure they simultaneously have therapeutic serum concentrations without drug toxicity.

Table 2

### Dosing Recommendations for Select Medications in Obesity

Drug	Nonobese	Obese
Enoxaparin <sup>22,23</sup>	<b>Prophylaxis:</b> 30 mg SC every 12 hours, or 40 mg SC every 24 hours based on CrCr  <b>Therapeutic:</b> 1 mg/kg SC every 12 hours or 1.5 mg/kg SC every 24 hours	<b>Prophylaxis:</b> 30 mg SC every 12 hours in obesity 40 mg SC every 12 hours in morbid obesity (BMI >40 kg/m <sup>2</sup> ), based on CrCr  <b>Therapeutic:</b> Not recommended for ABW>150 kg
Heparin <sup>33-37</sup>	<b>Prophylaxis:</b> 5000 units SC every 12 hours or every 8 hours  <b>Therapeutic:</b> 60–80 units/kg IV bolus Followed by 15–18 units/kg/hr based on actual body weight	<b>Prophylaxis:</b> 5000 units SC every 8 hours, 7500 units SC every 8 hours in morbid obesity (BMI >50 kg/m <sup>2</sup> )  <b>Therapeutic:</b> 60–80 units/kg IV bolus Followed by 15–18 units/kg/hr Based on adjusted body weight [(ABW–IBW) ×0.25+IBW]
Fondaparinux <sup>25,26</sup>	<b>Prophylaxis:</b> 2.5 mg SC daily, based on CrCr  <b>Therapeutic:</b> 5 mg SC daily (Wt <50 kg) 7.5mg SC daily (Wt 50–100 kg) 10 mg SC daily (Wt >100 kg), and based on CrCr	<b>Prophylaxis:</b> 2.5 mg SC daily, based on CrCr  <b>Therapeutic:</b> 5 mg SC daily (Wt <50 kg) 7.5mg SC daily (Wt 50–100 kg) 10mg SC daily (Wt >100 kg), and based on CrCr

Abbreviations: ABW=actual body weight, BMI=body mass index, IBW=ideal body weight, and SC=subcutaneous.

#### References:

1. Lee, J.B., Winstead, P.S. and Cook, A.M.(2006). Pharmacokinetic Alterations in Obesity. ORTHOPEDICS November 2006;29(11):984.
2. Lehman, L.S. (2011). How should enoxaparin be dosed for VTE prevention?. Retrieved from <http://www.medscape.com/viewarticle/737253>

# For Your Drug Information

## Can Aciclovir Cream be used for herpes simplex induced ulcers in the mouth or buccal area?

Zovirax (originator company) does not recommend its use for mucous membrane area because no data has been established yet for this usage.

### Warnings and Precautions from the Product Leaflet

Acyclovir Cream is **not recommended** for application to **mucous membranes, such as in the mouth, eye or vagina**, as it may be **irritant**. Particular care should be taken to avoid accidental introduction into the eye. For eyes, please use Acyclovir Ophthalmic Ointment.

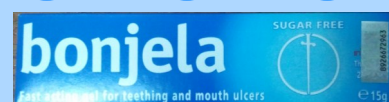
In severely immune-compromised patients (eg AIDS patients or bone marrow transplant recipients) oral acyclovir dosing should be considered.

**For symptomatic relief of ulcers, PPUKM has these two medications available:**

- 1) **Triamcinolone Acetonide 0.1% Dental Paste (KENALOG generic)**
- 2) **Choline Salicylate 8.7% + Cetalkonium Chloride 0.01% (BONJELA) Gel**



Triamcinolone: Apply a small dab 3-4 times daily preferably AFTER meals.



Bonjela is a pain relieving gel, reduces inflammation in ulcers, denture sore spots and cold sores. Safe for children from 4 months onwards. Massage approximately one half cm (for children) and one cm (for adults) of Bonjela onto sore area. Repeat after 3 hours. No more than 6 doses in 24 hrs.

## Cerumol Ear Wax in Children

Cerumol is used to treat earwax problem, or to prepare ears before syringing prior to otologic therapy or audiometry. It should not be used in children less than 6 years old or children with ear drum problems or damaged ear drum. Currently in PPUKM, we have the generic Cerumol ie Soliwax-E by NuLife Pharmaceuticals. It acts as a ceruminolytic agent that emulsifies and disperses the excess earwax, and helps to loosen the impacted earwax easily and effectively without painful instrumentation.

### Instructions on how to use SOLIWAX-E:

1. Lay patient on your side with the affected ear up.
2. Instill 5-10 drops of Soliwax-E drops into the ear canal.
3. Insert a cotton plug into the meatus and allow Soliwax-E Ear Drops to remain in the ear canal for about 15-30min.
4. Soliwax-E will promptly begin to emulsify and disperse the excess of the impacted cerumen, exerting mild antibacterial and antifungal action.
5. Clean the ear canal of the softened cerumen using a cotton swab.
6. Flush ear canal gently with lukewarm or saline water, using a soft rubber syringe, avoiding any excess pressure.
7. Instill Soliwax-E Ear Drops once again into the ear canal and insert a cotton plug.



## ANNOUNCEMENT

Due to unforeseen circumstances, the 2nd JKTU meeting which was scheduled to be on 15th June 2012 has been postponed to Friday, **29th June 2012**. The meeting will be discussing new drug applications as well as submissions for add-ons.

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