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HOSPITAL CANSELOR TUANKU MUHRIZ, PPUKM

UPDATES IN FELODIPINE EXTENDED RELEASE TABLETS

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Felodipine (Plendil) is a dihydropyridine antihypertensive calcium channel blocker that lowers blood pressure (BP) with a pronounced selective action on vascular smooth muscle over myocardial tissue. It lacks the negative inotropic effects of nifedipine and amlodipine at doses producing equivalent vasodilation.

Although the half-life of the elimination phase of felodipine is about 20-25 hours, the plain tablet is not optimal for a once-daily dosage regimen. This is due to the reduction in BP related to the felodipine plasma concentration. The concentration vs time curve after a 10mg plain tablet is characterized by an early and high peak and comparatively low felodipine levels in the 12-24 hours interval because of rapid distribution and elimination of felodipine in the early phase. The BP response mirrors this profile i.e. there is a pronounced effect at the time of peak level and less effect after 12 hours. A higher dose will prolong effect of felodipine on BP to 24 hours, but it would also increase the risk of adverse effects such as hypotension, flushing, and excessive tachycardia.

In order to provide a more even effect on BP over 24 hours, an extended-release (ER) formulation of felodipine has been developed. This ER formulation produces a prolonged absorption phase and more even plasma felodipine concentration versus time curve, without the pronounced peak seen with conventional formulations and, therefore, allows once daily administration.

Once-daily administered felodipine ER has been well studied in clinical trials in patients with essential hypertension, congestive heart failure or angina pectoris. As monotherapy in patients with mild to moderate essential hypertension, the antihypertensive efficacy of felodipine ER appears at least comparable to that of other calcium antagonists, β -blockers, diuretics, and ACE inhibitors, and results of some studies favoured felodipine ER at a statistically significant level. The drug has also been effectively combined with controlled release metoprolol or enalapril in patients with mild to moderate essential hypertension.

Based on recommendations from various drug references, the initial dose of felodipine ER in the treatment of hypertension and angina is 5mg once daily (2.5mg for elderly patients), and it can be increased if necessary by 5mg at 2-week intervals up to a maximum of 20mg once daily. However, most patients do not require daily doses of 20mg or more for effective control of BP. These recommendations are summarised in Table 1.

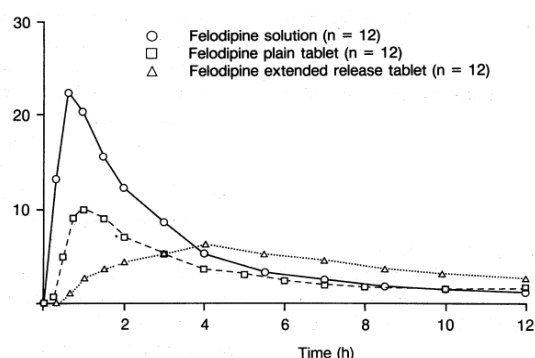


Fig 1: Mean plasma felodipine concentrations in healthy volunteers after oral administration of a single 10mg dose (Edgar et al. 1987)

Announcement from JKTU Committee

Dear Profs, Specialists & doctors,

Due to the recent hospital financial review where drug budget were slashed, the JKTU Meeting 2/2016 scheduled on 3rd June 2016 will be **postponed** until further notice. The existing drug budget allocation will be utilized for the purchase of existing drugs only.

For applications that have been submitted, it will be put on hold and will be considered when the financial situation allows.

For further information regarding drug submission into PPUKM Formulary, please call Drug Information at ext 5401/5401. Thank you.

References	Pharmacokinetic/ Pharmacodynamic	Dosing
BNF 70 (September 2015- March 2016)	Nil	Hypertension: Initially 5mg (elderly 2.5mg) daily in the morning; usual maintenance 5-10mg once daily; doses above 20mg daily rarely needed. Angina: initially 5mg (elderly 2.5mg) daily in the morning, increased if necessary to 10mg once daily.
MIMS online	Oral bioavailability is approximately 15%.	Hypertension: initiate at 5mg once daily, increased as required. Maintenance 5-10mg once daily. Elderly initially 2.5mg daily. Angina: initiate at 5mg once daily, maybe increased to 10mg once daily.
DRUG INFORMATION HANDBOOK (LEXICOMP) 22 nd Edition	Onset of action: Antihypertensive: 2-5hours Duration of antihypertensive effect: 24 hours	Children (unlabelled use): Initial 2.5mg once daily; maximum: 10mg/day Adults: 2.5- 10mg once daily; usual initial dose:5mg; increase by 5mg at 2 week intervals, as needed, to a maximum of 20mg/day Usual dose range (JNC 7) for hypertension: 2.5mg-20mg once daily. Elderly: consider lower initial doses (eg, 2.5mg once daily) and titrate to response.
FORMULARI UBAT KKM 2014	Nil	Initiate at 5mg once daily. Usual dose, 5-10mg once daily in the morning.
MARTINDALE 37 th edition Volume A	The terminal elimination half-life is reported to be about 11 to 16 hours after oral dosage with an immediate release preparation, but longer with a modified-release formulation.	Felodipine is given orally, generally in a modified-release formulation for use once daily in the morning. Hypertension: Initial dose is 5mg daily, adjusted as required; the usual maintenance dose is 2.5mg to 10mg daily and doses above 20mg daily are not usually needed. Angina: Initial dose is 5mg daily increased if necessary to 10mg daily
MICROMEDEX (www.micromedex.com)	Absorption: Tmax, oral: 2-6 hours Bioavailability: 13-20% Elimination Half Life: Extended-release, 26.7-33.2 hours Immediate-release, 11-16 hours	Hypertension: Initial, 5 mg orally once daily; adjust dose at intervals of not less than 2 weeks as needed to a maintenance dose of 2.5 to 10 mg orally once daily Angina: 2.5 to 5 mg orally twice daily or 10mg to 20 mg orally once daily
ASTRAZENECA Teoh Yiew Wen (Patient Safety and Medical Information Executive)	Nil	A number of studies have evaluated the use of felodipine ER at doses higher than the maximum recommended dose of 10 mg once daily . The majority of these studies evaluated the efficacy and safety of felodipine ER at doses up to 20 mg once daily. In general, these studies found that felodipine ER 5 to 20 mg once daily produced statistically significant reductions in systolic and diastolic blood pressure compared with placebo. Although the antihypertensive effects of felodipine ER are dose related over this range, doses of 5 to 10 mg once daily were effective in most patients, and the 20 mg dose was not usually required .
Medscape.com	Onset : 2-5 hours Duration: 24 hours Half life : 10-16 hours	Hypertension: Initial 2.5-5mg orally once daily. Maintenance 2.5-10mg orally once daily; some recommend up to 20mg/day

Table 1: Usual recommended dosages of felodipine according to other references

References :

1. <http://www.mims.com/malaysia/drug/info/plendil/plendil?type=full>
2. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1380059/>
3. <http://www.ncbi.nlm.nih.gov/pubmed/3327676>
4. <http://reference.medscape.com/drug/cabren-cardioplen-xl-felodipine-342375>
5. https://www.researchgate.net/publication/21461509_Felodipine_extended-release_tablets_once_daily_are_equivalent_to_plain_tablets_twice_daily_in_treating_hypertension_Dutch_Hospital_Multicentre_Group
6. <http://www.micromedexsolutions.com/micromedex2/>

We are on the web!
<http://www.ppukm.ukm.my/farmasi/>

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