

Shortages of Nifedipine products / Discontinuation of Adalat[®] products including all nifedipine 5mg and 10mg immediate release capsules

Updated: 5th September 2019

Description of products affected

- Nifedipine capsule 5mg is licensed for the prophylaxis of chronic stable angina pectoris, the treatment of Raynaud's phenomenon and essential hypertension. The recommended starting dose is 5 mg every eight hours with subsequent titration of dose according to response, permitting an increase to a maximum of 20 mg every eight hours.¹
- The long acting and slow release formulations of Adalat are licensed for the treatment of hypertension and prophylaxis of angina.²
- The long acting (XL) formulations of Adipine are licensed for the treatment of hypertension and prophylaxis of chronic stable angina pectoris.³
- The modified release (MR) formulations of Tensipine and Nifedipress are licensed for the treatment of hypertension and prophylaxis of chronic stable angina pectoris.^{4,5}
- Coracten formulations are licensed for:
 - Treatment of hypertension.
 - Prophylaxis of chronic stable angina pectoris.
 - Treatment of Prinzmetal (variant) angina when diagnosed by a cardiologist.

Background

UKMi nationally have informed C&P CCG:

Although there have been intermittent supply issues with some nifedipine MR products, particular Coracten products, these supply issues are now resolving and all products should be available and stock situation back to normal within next 2 weeks, though there may be problems at local wholesalers.

Please see Appendix 1 for current availability of all nifedipine products in Cambridgeshire and Peterborough.

Current formulary choices

Therefore, due to stock availability issues of the current nifedipine prolonged release formulary choices, where patients in primary care are unable to obtain their normal brand of nifedipine we recommend prescribing:

- Adipine XL 60mg prolonged release tablets – stock available.
- Adipine XL 30mg prolonged release tablets – stock available.
- Nifedipress 20mg modified release tablets – stock available but limited.
- Tensipine 10mg modified release tablets – stock available but limited.

All of the above formulations are licensed for:

- Treatment of hypertension.
- Prophylaxis of chronic stable angina pectoris.

Alternative agents and management options

Immediate release capsules (5mg and 10mg)

Nifedipine is a dihydropyridine calcium-channel blocker (CCB). In practice, the immediate release capsules should only have been used for treating patients with essential hypertension or chronic stable angina pectoris if no other treatment is appropriate because of a risk of a dose dependent increase in the risk of cardiovascular complications (e.g. myocardial infarction) and mortality which may occur with use of fast release nifedipine capsules.^{1,6} In addition, use of the immediate release capsules can be associated with precipitate and uncontrolled reduction in blood pressure. It would therefore not be the initial treatment of choice for patients with hypertension and angina.

Nifedipine is also formulated as slow release tablets and capsules³, but they are not licensed for the treatment of Raynaud's phenomenon, which is an indication for the immediate-release formulation. No other dihydropyridines are licensed for the treatment of Raynaud's phenomenon. There is clinical experience suggesting that long-acting nifedipine is effective for the treatment of Raynaud's and has fewer adverse reactions than rapid-acting preparations, therefore patients could be switched to a similar dose of a modified release preparation (off-label).⁷

Within primary care nifedipine modified release / prolonged release which are currently available and should be considered are:

- **Tensipine MR.** Available as a 10mg modified release tablet.
- **Nifedipress MR.** Available as a 20mg modified release tablet.
- **Adipine XL.** Available as a 30mg or 60mg prolonged release tablet.

There are no guidance or data on dose conversion between immediate and modified release nifedipine preparations so if a patient needs to be switched, the nearest equivalent daily dose should be prescribed and patient's blood pressure and / or frequency of angina attacks (if applicable) monitored in the initial stages of the switch, in addition to monitoring for adverse effects such as headaches, dizziness and oedema.

Immediate-release nifedipine capsules are administered three times a day.¹ Modified release nifedipine preparations are dosed once or twice daily depending on brand selected. Patients will need to be counselled on the change in frequency of dosing to avoid potential errors. Likewise, they should be advised to report any adverse effects.

Alternatively, for the treatment of angina and hypertension, amlodipine (formulary 1st line CCB) is licensed for both indications.⁹

Switching to another formulary choice calcium channel blocker, Amlodipine or Felodipine, may be appropriate but there is no direct dose equivalent. See Table 1 for NICE CKS prescribing information for calcium channel blockers. When switching between medicines with no direct dose equivalence, we would recommend erring on the side of caution. As such, you may want to consider switching patients to the usual starting doses and then titrating up as necessary. Choice of therapy may also be dependent on other individual patient factors (e.g. past medication history, co-morbidities, concurrent medication etc.). Patients will need to be counselled on the change in frequency of dosing to avoid potential errors. Likewise, they should be advised to report any adverse effects and deterioration in their condition for angina.

Table 1 – NICE CKS prescribing information for calcium channel blockers

CALCIUM-CHANNEL BLOCKER	USUAL STARTING DOSES	USUAL MAINTENANCE DOSE	MAXIMUM DOSE
AMLODIPINE	5 mg once a day	5-10 mg once a day	10 mg once a day
FELODIPINE	5 mg once a day*	5-10 mg once a day	20 mg once a day
NIFEDIPINE	20-30 mg once a day	30-90 mg once a day	90 mg once a day
* A LOWER STARTING DOSE OF 2.5 MG IS REQUIRED FOR ELDERLY PEOPLE.			

Autonomic dysreflexia

Individuals with spinal cord injury (SCI) at or above T6 level are at risk of autonomic dysreflexia (AD), an acute and potentially life threatening condition resulting from an excessive autonomic response to stimuli below the level of the SCI.⁹ This can cause severe, sudden hypertension which requires immediate treatment with nifedipine capsules administered sublingually (5 or 10 mg).^{10,11}

Use of nifedipine for this indication is 'Hospital Only'. Prescribing in primary care is not recommended.

Imports of 5mg immediate release capsules

The Department of Health have been working with potential alternative manufacturers and are working to get another licensed supply to the UK market.

Whilst imports of unlicensed product are available, use of an unlicensed product in primary care is not recommended where an alternative product, prescribed off-label, is clinically suitable for the patient. Please consult the Medicines Optimisation Team (CAPCCG.prescribingpartnership@nhs.net) before prescribing imports of unlicensed products or specials.

Long acting/ slow release formulations

The long acting preparations are administered once daily and the slow release preparations twice daily. There are generic versions of all Adalat modified release preparations apart from Adalat LA 20mg.^{3,4,13} When switching between brands, closer monitoring of BP may be required in the initial stages and patients reassured that they are receiving the same drug and dose but to report any adverse effects.

For patients on Adalat LA 20mg, an option is to switch to slow release preparation of 10mg strength which is administered twice a day (Tensipine 10mg MR tablets) and titrate accordingly or depending on current BP, trial next strength up (30mg) of a once daily preparation (Adipine XL 30mg prolonged-release tablets). Other long acting CCBs are available and licensed indications should be checked as they may not all share the same ones as the Adalat range.

Administration via enteral feeding tubes or for patients unable to swallow modified release or prolonged release nifedipine tablets

Clinicians in primary care who require information on administration of nifedipine via enteral feeding tubes or for patients unable to swallow modified release / prolonged release formulations should contact the Medicines Optimisation Team via CAPCCG.prescribingpartnership@nhs.net for further advice.

References

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Disclaimer: The content of this memo may not reflect national guidance. Some of this memo is based on **clinical opinion** from practitioners. Users should bear this in mind. Any decision to prescribe off-label must take into account the relevant GMC guidance and governance procedures for unlicensed medicines. Prescribers are advised to pay particular attention to the risks associated with using unlicensed medicines or using a licensed medicine off-label. As with all prescribing, the prescriber is medically and legally responsible for the prescriptions they sign and for their decisions and actions when they supply and administer medicines or authorise or instruct others to do so.

Appendix 1 – Availability of Nifedipine Products in Cambridgeshire and Peterborough

Manufacturer	Formulation	Availability
Advanz Pharma	Adanif XL 30mg tablets	Unavailable – Stock expected September 2019.
	Adanif XL 60mg tablets	Available.
	Fortipine LA 40mg	Available.
Bayer	Adalat 5mg immediate release capsules	Discontinued from February 2019.
	Adalat 10mg immediate release capsules	Discontinued from March 2019.
	Adalat Retard 10mg m/r tablets	Discontinued after November 2018.
	Adalat Retard 20mg m/r tablets	Discontinued after August 2018.
	Adalat LA 20mg capsules	Unavailable.
	Adalat LA 30mg capsules	Unavailable.
	Adalat LA 60mg capsules.	Unavailable.
Chiesi	Adipine MR 10mg tablets	Unavailable.
	Adipine MR 20mg tablets	Unavailable.
	Adipine XL 30mg tablets	Available - Stock management on a weekly basis.
	Adipine XL 60mg tablets	Available - Stock management on a weekly basis.
Dexcel Pharma	Nifedipress MR 10mg tablets	Available – limited stock.
	Nifedipress MR 20mg tablets	Available – limited stock.
Genus	Tensipine MR 10mg tablets	Available – limited stock.
	Tensipine MR 20mg tablets	Unavailable – Stock expected 9 th September.
Morningside	Nidef 30mg m/r tablets	Unavailable – Stock expected September 2019.
	Nidef 60mg m/r tablets	Unavailable – Stock expected September 2019.
Tillomed	Valni 20 Retard tablets	Unavailable.
UCB Pharma	Coracten SR 10mg capsules	Available.
	Coracten SR 20mg capsules	Available.
	Coracten XL 30mg capsules	Unavailable – Stock expected end of September.
	Coracten XL 60mg capsules	Available.
Zentiva	Valni XL 30mg tablets	Available.
	Valni XL 60mg tablets	Available.