

Shortages of Nifedipine products / Discontinuation of Adalat[®] products

Updated: 7th February 2020

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

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 10mg modified release tablets – stock available.
- Nifedipress 20mg modified release tablets – stock available.

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.

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

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

Nifedipine 5mg and 10mg capsules are now being manufactured and are available to order via RelonChem. These are licensed for the prophylaxis of chronic stable angina pectoris, hypertension and also 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 immediate-acting preparations. Therefore, it is recommended in Cambridgeshire and Peterborough based upon clinical experience, and the risks recognised above that patients should be switched to a similar dose of a modified release preparation (off-label) rather than prescribed the immediate release preparations.⁷ No other dihydropyridines are licensed for the treatment of Raynaud's phenomenon.

There are no guidance or data on dose conversion between immediate and modified release nifedipine preparations so when switching 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, comorbidities, 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 (MODIFIED RELEASE)	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.

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 (Nifedipress 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

1. Bayer plc. Adalat 5. SPC, date of revision of the text: 31 August 2017: <https://www.medicines.org.uk/emc/product/6278/smpc>
2. SPCs for Adalat preparations accessed via electronic Medicines Compendium, 17 Jul 2018: <https://www.medicines.org.uk/emc/search?q=adalat>
3. SPCs for Adipine XL preparations accessed via electronic Medicines Compendium, 30 May 2018: <https://www.medicines.org.uk/emc/search?q=adipine>
4. SPCs for Tensipine MR preparations accessed via electronic Medicines Compendium, 30 May 2018: <https://www.medicines.org.uk/emc/search?q=tensipine>
5. SPCs for Nifedipress MR 20mg preparation accessed via electronic Medicines Compendium, 27 June 2019: <https://www.medicines.org.uk/emc/product/658/smpc>
6. Bayer plc. Adalat. SPC, date of revision of the text: 31 August 2017: <https://www.medicines.org.uk/emc/product/6280/smpc>
7. Relonchem. Nifedipine 5mg capsules. SPC, date of revision of the text: 23 December 2019: <http://www.mhra.gov.uk/spc-pil/?prodName=NIFEDIPINE%205MG%20CAPSULES&subsName=NIFEDIPINE&pageID=SecondLevel>
8. Pfizer Limited. Istin 5 mg Tablets. SPC, date of revision of the text, 01/2018::: <https://www.medicines.org.uk/emc/product/1069/smpc>
9. AstraZeneca UK Limited. Plendil 2.5mg. SPC, date of revision of the text, 9th November 2016: <https://www.medicines.org.uk/emc/product/879/smpc>
10. Royal College of Physicians, British Society of Rehabilitation Medicine, Multidisciplinary Association of Spinal Cord Injury Professionals, British Association of Spinal Cord Injury Specialists, Spinal Injuries Association. Chronic spinal cord injury: management of patients in acute hospital settings: national guidelines. Concise Guidance to Good Practice series, No 9. London: RCP, 2008: <https://www.rcplondon.ac.uk/guidelines-policy/chronic-spinal-cord-injury>
11. National Spinal Injuries centre, Stoke Mandeville Hospital Autonomic Dysreflexia (July 2013): <https://spinal.co.uk/wp-content/uploads/2017/02/NSIC-Autonomic-Dysreflexia.pdf>
12. Personal communication, Lisa Pazik, Lead Pharmacist National Spinal Injuries Centre, Buckinghamshire Healthcare NHS Trust, 10 Dec 2018.
13. SPCs for nifedipine product accessed via electronic Medicines Compendium; 16 Aug 2018: [https://www.medicines.org.uk/emc/search?q=nifedipine&filters=attributes\[spc\],activeingredients\[23\]&offset=1&limit=50&orderBy=product&refreshFilters=true](https://www.medicines.org.uk/emc/search?q=nifedipine&filters=attributes[spc],activeingredients[23]&offset=1&limit=50&orderBy=product&refreshFilters=true)
14. SPCs for Coracten XL preparations accessed via electronic Medicines Compendium, 17 May 2017: <https://www.medicines.org.uk/emc/search?q=coracten>
15. NICE CKS Hypertension – not diabetic last revised January 2018: <https://cks.nice.org.uk/hypertension-not-diabetic#!prescribingInfoSub:24>
16. Personal communication, Clinical/Regional Medicines Information Pharmacist East Anglia Medicines Information Service, UKMi, 26 June 2019.
17. SPC for Fortipine LA 40mg tablets accessed via electronic Medicines Compendium, 27 June 2019: <https://www.medicines.org.uk/EMC/medicine/23761/SPC/Fortipine+LA+40mg+Modified-Release+Tablets/>

Acknowledgements

- Albert Ferro, Professor of Cardiovascular Clinical Pharmacology, Consultant Physician, Guy's and St Thomas' NHS Foundation Trust
- Sotiris Antonious, Consultant Pharmacist, Cardiovascular Medicine, Barts Health NHS Trust
- Helen Williams, Consultant Pharmacist for CVD, South London, Southwark and Lambeth CCGs
- Lisa Pazik, Lead Pharmacist National Spinal Injuries Centre, Buckinghamshire Healthcare NHS Trust

Original document prepared by:

Yuet Wan, London and South East Regional Medicines Information, Guy's and St Thomas' NHS Foundation Trust, 17 August 2018; updated 03 Dec 2018 and 14 Feb 2019; email: medicinesinformation@gstt.nhs.uk

Document modified by and for all correspondence please contact:

Cambridgeshire and Peterborough CCG Medicines Optimisation Team. 19 February 2019 and document updated 7 February 2020 to reflect current stock situation of nifedipine products. Email: CAPCCG.prescribingpartnership@nhs.net

Disclaimer: This memo can be adapted for local use. The content does not reflect national guidance. Some of this memo is based on **clinical opinion** from practitioners. Users should bear this in mind in deciding whether to base their policy on this document. Individual trusts should ensure that procedures for unlicensed medicines are followed where a foreign import drug is required in the interim. Any decision to prescribe off-label must take into account the relevant GMC guidance and NHS Trust 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. Unlicensed medicines: In line with GMC guidance you should usually prescribe licensed medicines in accordance with the terms of their license. However, you may prescribe unlicensed medicines, where, on the basis of assessment of the individual patient, you conclude, for medical reasons, that it is necessary to do so to meet the specific needs of the patient. Prescribing unlicensed medicines may be necessary where there is no suitably licensed medicine that will meet the patient's needs. For example, where a suitably licensed medicine that would meet the patient's need is not available. This may arise where, for example, there is a temporary shortage in supply. 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 – updated 31/01/2020.

<i>Manufacturer</i>	<i>Formulation</i>	<i>Availability</i>
Advanz Pharma	Adanif XL 30mg tablets	Available: AAH, Allied Pharma and Phoenix.
	Adanif XL 60mg tablets	Available: AAH, Allied Pharma and Phoenix.
	Fortipine LA 40mg	Unavailable: No expected date issued.
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: No expected date issued
	Adipine MR 20mg tablets	Unavailable: No expected date issued.
	Adipine XL 30mg tablets	Available: AAH, Alliance Healthcare and Phoenix.
	Adipine XL 60mg tablets	Available: AAH, Alliance Healthcare, and Phoenix.
Dexcel Pharma	Nifedipress MR 10mg tablets	Available but limited, further stock expected this month: AAH, Alliance Healthcare, and Phoenix.
	Nifedipress MR 20mg tablets	Available: AAH, Alliance Healthcare and Phoenix.
Genus	Tensipine MR 10mg tablets	Unavailable: Expected February 2020.
	Tensipine MR 20mg tablets	Unavailable: Expected February 2020.
Morningside	Nidef 30mg m/r tablets	Unavailable: Expected September 2020.
	Nidef 60mg m/r tablets	Unavailable: Expected September 2020.
Tillomed	Valni 20 Retard tablets	Unavailable: No expected date issued.
UCB Pharma	Coracten SR 10mg capsules	Unavailable: No expected date issued.
	Coracten SR 20mg capsules	Available: Alliance Healthcare.
	Coracten XL 30mg capsules	Unavailable: No expected date issued.
	Coracten XL 60mg capsules	Available: Alliance Healthcare.
Zentiva	Valni XL 30mg tablets	Awaiting response from company.
	Valni XL 60mg tablets	Awaiting response from company.