

# Shortages of Nifedipine products / Discontinuation of Adalat<sup>®</sup> products including all nifedipine 5mg and 10mg immediate release capsules

**Updated: 15<sup>th</sup> July 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.<sup>1</sup>
- The long acting and slow release formulations of Adalat are licensed for the treatment of hypertension and prophylaxis of angina.<sup>2</sup>
- The long acting (XL) formulations of Adipine are licensed for the treatment of hypertension and prophylaxis of chronic stable angina pectoris.<sup>3</sup>
- The modified release (MR) formulations of Tensipine and Nifedipress are licensed for the treatment of hypertension and prophylaxis of chronic stable angina pectoris.<sup>4,5</sup>
- 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 but limited.
- Coracten\* XL 30mg capsules – July 2019 stock available.
- Nifedipress 20mg modified release tablets – July 2019 stock is available.
- Tensipine 10mg modified release tablets – July 2019 stock is available.

All of the above formulations are licensed for:

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

\*The capsule shells of all Coracten formulations are made of gelatin. If this is clinically unacceptable to the patient an alternative calcium-channel blocker should be considered, noting the variance in licensing.

## **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.<sup>1,6</sup> 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 capsules<sup>3</sup>, 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).<sup>7</sup>

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.
- **Coracten XL.** Available as a 30mg modified release capsule.
- **Adipine XL.** Available as a 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.<sup>1</sup> 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 1<sup>st</sup> line CCB) is licensed for both indications.<sup>9</sup>

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

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

### **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.<sup>9</sup> This can cause severe, sudden hypertension which requires immediate treatment with nifedipine capsules administered sublingually (5 or 10 mg).<sup>10,11</sup>

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; it is currently estimated that supplies could be available April to May 2019.

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](mailto: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.<sup>3,4,13</sup> 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 (Coracten XL 30mg capsules). 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](mailto: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. Wigley FM. Initial treatment of the Raynaud phenomenon. UpToDate, topic last updated: Nov 07, 2016
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

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Document updated 15 July 2019 to reflect current stock situation of nifedipine products.

**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 (updated 15/07/2019)**

<b>Manufacturer</b>	<b>Formulation</b>	<b>Availability</b>
Advanz	Adanif XL 30mg tablets	<b>Available.</b>
	Adanif XL 60mg tablets	Expected end of August.
	Fortipine LA 40mg	<b>Available via Alliance HC.</b>
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 - long term issue.
	Adipine MR 20mg tablets	Unavailable – long term issue.
	Adipine XL 30mg tablets	Limited stock being sent to wholesalers weekly.
	Adipine XL 60mg tablets	Limited stock being sent to wholesalers weekly.
Dexcel Pharma	Nifedipress MR 10mg tablets	<b>Available.</b>
	Nifedipress MR 20mg tablets	<b>Available.</b>
Genus	Tensipine MR 10mg tablets	<b>Available.</b>
	Tensipine MR 20mg tablets	Unavailable and expected end of July.
Morningside	Nidef 30mg m/r tablets	Unavailable until September 2019.
	Nidef 60mg m/r tablets	Unavailable until September 2019.
Tillomed	Valni 20 Retard tablets	<b>Available.</b>
UCB Pharma	Coracten SR 10mg capsules	Unavailable – expected 29 <sup>th</sup> July.
	Coracten SR 20mg capsules	<b>Available – Alliance HC.</b>
	Coracten XL 30mg capsules	<b>Available – Alliance HC.</b>
	Coracten XL 60mg capsules	Unavailable – expected 22 <sup>nd</sup> July.
Zentiva	Valni XL 30mg tablets	Unavailable expected 22 <sup>nd</sup> July
	Valni XL 60mg tablets	<b>Available.</b>