



**Llywodraeth Cymru**  
**Welsh Government**

## **MEDICINES SHORTAGE ADVISORY GROUP WALES**

### **MEDICINE SHORTAGE**

<b>Distribution:</b>	As Annex 1
<b>From:</b>	Andrew Evans, Chief Pharmaceutical Officer
<b>Date:</b>	12 April 2019
<b>Reference:</b>	CPhO/MedsLet/2019/02
<b>Category:</b>	Level 3 - High impact
<b>Title:</b>	Disruption to supply of Labetalol tablets all strengths.
<b>For Action by:</b>	<ul style="list-style-type: none"><li>• All General Practitioners – please ensure this message is seen by all working in your dispensary and retain a copy in your 'locum information pack'. - Action as below and attached Clinical Memo</li><li>• Dispensing General Practitioners – please ensure this message is seen by all working in your dispensary and retain a copy in your 'locum information pack'. Action as below and attached Clinical Memo</li><li>• Community Pharmacists - Action as below and attached Clinical Memo</li><li>• Hospital Chief Pharmacists - Action as below and attached Clinical Memo</li><li>• Medical Directors of Health Boards - disseminate to relevant clinicians in secondary care setting.</li></ul>
<b>Timeframe:</b>	Action within 24 hrs
<b>For Information:</b>	See Annex 1 – Distribution List
<b>Key Recipients:</b>	Chief Executives of Health Boards

Nurse Directors Health Boards  
Directors of Public Health  
Health Board and NHS Trust Chief Pharmacists  
Health Board Prescribing Advisers  
Chief Executives of NHS Trusts  
Principal Pharmacist Welsh Quality Control  
Principal Pharmacist Continuing Care Services  
Principal Pharmacist Welsh Medicines Information Centre  
CIW  
NHS Direct

**What is this about:**

Medicine shortage effecting supply of Labetalol tablets all strengths:

- Labetalol 50mg tablets;
- Labetalol 100mg tablets;
- Labetalol 200mg tablets;
- Labetalol 400mg tablets.

Labetalol is a non-selective beta-blocker with additional alpha blocking properties. It is licensed for the treatment of mild to severe hypertension, hypertension in pregnancy and angina pectoris with existing hypertension.

Data suggests whilst labetalol is primarily indicated for use in hypertension in pregnancy there may be a significant number of patients prescribed labetalol and who are not pregnant, who could be switched to a number of alternative beta-blockers

Supplies will be very limited from April until early-mid May.

Supply of labetalol IV is not affected.

**Issue & Action to be taken:**

Action

**Prescribers should be aware that no new patients should be commenced on labetalol during this time as there are currently very limited stocks available.**

**Labetalol is indicated for the management of hypertension, particularly in pregnancy. Patients who do not have sufficient supplies to last until early May and who are unable to obtain supplies of labetalol will need to be switched to an appropriate alternative treatment during this time.**

**The clinical management plan for pregnant patients will be different to patients who are not pregnant.**

**Please see attached clinical memo, which advises on management options for patients affected by this supply issue, including the use of alternative anti-hypertensives during pregnancy.**

### Reasons for shortage

There are two suppliers of labetalol tablets in the UK, Mylan and Recipharm:

- Mylan have had a delay in resupply due to an internal delay in serialisation of FMD packs, further stock is expected in early-mid May.
- Recipharm have experienced an issue with the active pharmaceutical ingredient and currently unable to provide a resupply date.

Alternative products include:

- Methyldopa (as per NICE guidance).
- Nifedipine (as per NICE guidance).

Suppliers of the clinical alternatives are aware of the issue. Manufacturers of both nifedipine modified release and methyldopa are confident they are able to support any additional demand on their products during this time.

Different versions of modified-release preparations may not have the same clinical effect. Prescribers should liaise with their community pharmacy to determine which brands of nifedipine modified release tablets are currently available in your area.

Suppliers of alternative beta blockers have been contacted to determine if they can meet any additional demand and currently, the manufacturers of carvedilol and metoprolol have indicated they would be unable to meet demand if patients were switched to this product. Manufacturers of bisoprolol, atenolol and propranolol have indicated they have capacity to support any additional demand on their products.

Some specialist importers have identified unlicensed stock they can bring into the UK from abroad. Lead times for these products vary between 7 and 21 days. Under the medicines legislation, doctors can prescribe unlicensed products for their patients if they think it appropriate, but do so entirely on their own responsibility.

All Hospital Chief Pharmacists, Health Board Prescribing Advisers and Medical Directors of Health Boards to ensure all relevant prescribers and dispensers in secondary care settings receive this medicines shortage letter and attached Clinical Memo.

Full details of the medicine supply disruption are included in the attached PDF file.

Please forward to listed recipients.

This information is also published at:

<https://gov.wales/topics/health/professionals/pharmaceutical/?lang=en>

Yours sincerely



**Andrew Evans**

Chief Pharmaceutical Officer/Prif Swyddog Fferyllol  
Welsh Government/Llywodraeth Cymru

**DISTRIBUTION LIST**

**Send to:**

Chief Executives of Health Boards  
Medical Directors of Health Boards  
Nurse Directors Health Boards  
Directors of Public Health  
Health Board Chief Pharmacists  
Hospital Chief Pharmacists  
Health Board Prescribing Advisers  
PHW Consultants in Pharmaceutical Public Health  
Chief Executives of NHS Trusts  
Principal Pharmacist Welsh Quality Control  
Principal Pharmacist Continuing Care Services  
Principal Pharmacist Welsh Medicines Information Centre  
CIW  
NHS Direct

**NHS Wales Shared Services Partnership to forward to:**

General Practitioners  
Dispensing General Practitioners  
Community Pharmacists  
Independent / Private clinics and hospitals and hospices throughout  
Wales

**Welsh Government:**

Chief Medical Officer  
Chief Nursing Officer  
Chief Dental Officer  
Chief Optometric Officer  
Chief Scientific Officer  
Chief Therapies Officer  
Director General Health and Social Services Group  
Emergency Planning Adviser

## CLINICAL MEMO

### Labetalol tablets all strengths

#### Description of product affected

Labetalol is a non-selective beta-blocker with additional alpha blocking properties. It is licensed for the treatment of mild to severe hypertension, hypertension in pregnancy and angina pectoris with existing hypertension.<sup>1</sup> Labetalol is primarily used for hypertension in pregnancy.

#### Background

Mylan and Recipharm are the two UK suppliers of labetalol tablets. Disruption to supply will affect all strengths of labetalol tablets:

- Labetalol 50mg tablets;
- Labetalol 100mg tablets;
- Labetalol 200mg tablets;
- Labetalol 400mg tablets.

supplies will be very limited from April until early-mid May.

Supply of labetalol IV is not affected.

#### Alternative agents and management options

##### Hypertension and angina

Other commonly used beta-blockers licensed for hypertension and angina

	Hypertension	Angina
<b>Atenolol</b>	√	√
<b>Bisoprolol</b>	√	√
<b>Propranolol</b>	√	√
<b>Carvedilol*</b>	√	√
<b>Metoprolol**</b>	√	√

\* Manufacturer of carvedilol has indicated that they cannot support the market with the additional demand.

\*\*There are current intermittent supply issues affecting metoprolol 50mg and 100mg as some manufacturers have recently discontinued these products and others are having supply difficulties.

### Hypertension in pregnancy

NICE guidelines state that where clinically appropriate, labetalol is recommended as the first line antihypertensive treatment for hypertension in pregnancy. NICE guidelines recommend nifedipine or methyldopa as alternatives to labetalol for hypertension in pregnancy taking into account the side effect profiles:<sup>2</sup>

- Nifedipine is second line choice after labetalol.<sup>2,3</sup>
- Use a modified release preparation of nifedipine, usually a twice daily (MR) preparation.<sup>3,4</sup>
- If clinically appropriate, start nifedipine on a low dose: nifedipine 10mg MR twice a day, and if necessary increase to 20mg MR twice a day, then to 30mg MR twice a day and possibly up to 40mg MR twice a day.<sup>4</sup>
- Third line treatment is methyldopa but it is less well tolerated with increased side effects such as sedation at higher doses.<sup>2,4</sup>
- Methyldopa is contraindicated in depression.<sup>5</sup>
- Nifedipine and methyldopa are not licensed specifically for hypertension in pregnancy.<sup>5,6</sup>

Expert opinion suggests that if switching from labetalol to nifedipine, labetalol 300mg tds is considered equivalent to nifedipine 20mg MR bd. Careful monitoring would be needed with escalation of dose depending on patient response, and it is important to bear in mind that non-response may represent worsening hypertension rather than a non-equivalent dose.

### Hypertension in lactation

It is important that women are managed on an individual basis in consultation with a specialist, if appropriate. Current NICE guidance suggests the following drugs may be considered: labetalol, nifedipine, enalapril, captopril, atenolol, and metoprolol<sup>2</sup>.

The UK Medicines Information (UKMi) Drugs in Lactation Advisory Service also suggests propranolol as an alternative beta-blocker<sup>7</sup>. It advises that drugs from different pharmacological sections may be used in combination with, or as a replacement for, each other for both hypertension and other cardiovascular indications. Choice of drug in a breastfeeding mother may therefore, be dependent on a number of issues, including patient-specific clinical conditions and local/national guidelines, which will impact on the choice of drug for a breastfeeding mother and the alternatives that may be considered or are appropriate.

### References

1. RPH Pharmaceuticals AB. Trandate (labetalol) 200mg film coated tablets. SPC, date of revision of the text, 8 February 2019:  
<https://www.medicines.org.uk/emc/product/9168>
2. NICE. Hypertension in pregnancy: diagnosis and management. Clinical guideline [CG107]. Last updated Jan 2011.

3. NICE CKS. Hypertension in pregnancy Oct 2016.  
<https://cks.nice.org.uk/hypertension-in-pregnancy#!prescribingInfoSub:11>
4. Personal communication, Royal College Obstetricians and Gynaecologists, 04 April, 2019.
5. Aspen. Aldomet (methyldopa) 250mg tablets. SPC, date of revision of the text, 22 Sept 2016: <https://www.medicines.org.uk/emc/product/4667>
6. Chiesi. Adipine (nifedipine) 20mg MR tablets. SPC, date of revision of the text, July 2016: <https://www.medicines.org.uk/emc/product/7801>
7. [Specialist Pharmacy Services Safety in Lactation: Drugs for hypertension - Published 9th January 2017, updated 28th November 2018](https://www.sps.nhs.uk/articles/safety-in-lactation-drugs-for-hypertension/)  
<https://www.sps.nhs.uk/articles/safety-in-lactation-drugs-for-hypertension/>

### **Acknowledgements**

Jane Bass, Senior Pharmacist, Women's Services, Guy's and St Thomas' NHS Foundation Trust.

Vanessa Chapman, Director, Trent Medicines Information Centre & the UK Drugs in Lactation Advisory Service.

Laura Kearney, Regional Principal Medicines Information Pharmacist, Trent and Leicestershire Medicines Information Centre & UK Drugs in Lactation Advisory Service.

### **Original document prepared by:**

Hina Radia and Diane Bramley, London and South East Regional Medicines Information, Guy's and St Thomas' NHS Foundation Trust, 11 April 2019.

**For all correspondence please contact:**

[Medicinesshortages@gov.wales](mailto:Medicinesshortages@gov.wales)

**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 local health boards and NHS 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 local 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.