

Shortage of Labetalol tablets

Date: 17th April 2019

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.¹
- **Labetalol is primarily used for hypertension in pregnancy.**

Background

- Mylan and Recipharm are the two UK suppliers of labetalol tablets.
- DHSC have been informed there is going to be a supply issue affecting all strengths of labetalol tablets until early-mid May.
 - Labetalol 50mg tablets,
 - Labetalol 100mg tablets,
 - Labetalol 200mg tablets,
 - Labetalol 400mg tablets.
- Supply of labetalol IV is not affected.

Alternative agents and management options

- In the first instance the patient should be encouraged to try several pharmacies in order to fulfil the prescription. The pharmacy should support patients to ring other pharmacies in advance of attending to ascertain availability.
- Patients who do not have sufficient supplies to last until mid-May and who are unable to obtain supplies of labetalol will need to be switched to an appropriate alternative treatment during this time.
- The decision about what to do will need to be individualised to each patient.
- **The clinical management plan for pregnant and lactating patients will be different to patients who are not pregnant or lactating.**
- Prescribers should be aware that **NO NEW PATIENTS** should be commenced on labetalol during this time as there are currently very limited stocks available.

Hypertension and angina (excluding pregnancy or lactating patients)

- Table 1 demonstrates which other beta-blockers are licensed for hypertension and angina.
- The choice of beta-blocker will depend on co-morbidities, local recommendations (see below) and cost. Where possible, prescribe a drug that is taken only once a day and prescribe generically.²
- Within primary care the formulary choice which should be considered the **1st line beta-blocker** for hypertension is **Bisoprolol**.

Table 1: Other commonly used beta-blockers licensed for hypertension and angina

	Hypertension	Angina
Atenolol	√	√
Bisoprolol	√	√
Propranolol	√	√

Please note – the manufacturers of both carvedilol and metoprolol have indicated that they cannot support the market with the additional demand and so have not been included in the above table.

Dose equivalence and conversion (excluding pregnancy and breastfeeding)

- There is no definitive guidance for dose conversion between beta-blockers and clinical judgement will be required in considering where the labetalol dose sits within the dose range of the alternative beta-blocker.
- When switching patients to alternate beta-blockers, blood pressure, pulse rate, and signs and symptoms of the underlying disorder should be monitored to guide dosing. Table 2 provides dose ranges for some commonly used beta-blockers described above.
- It is important to involve any patients (and their carers, as appropriate) in the discussion regarding any planned change to their medication **BEFORE** making the change.
- If any of the recommendations are not clinically acceptable or there is any uncertainty about what to do or how to do it then management options should be discussed with the responsible consultant specialist depending on the indication.

Table 2: Licensed target dose ranges for adults for various indications (dose adjustments may be required based on clinical response, co-morbidities e.g. renal impairment and age)

	Labetalol ⁹	Bisoprolol ¹⁰	Atenolol ¹¹	Propranolol ¹²
Hypertension	100 -200mg BD, increased if necessary, to 400mg BD	5-20mg OD	25-100mg OD	40mg BD or TDS, max 320mg per day
Angina	(co-existing with hypertension) 100 -200mg BD, increased if necessary, to 400mg BD	5-20mg OD	50-100mg OD or 50mg BD	40mg BD or TDS, max 240mg per day

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 considering the side effect profiles:³
- Nifedipine is second line choice after labetalol.^{3,4}
- Use a modified release preparation of nifedipine, usually a twice daily (MR) preparation.^{4,5} **In primary care the twice daily, modified release preparation of nifedipine (MR) formulary choice is Tensipine MR which is available in a 10mg or 20mg strength (Thornton & Ross have confirmed availability).**
- 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.⁵
- Third line treatment is methyldopa but it is less well tolerated with increased side effects such as sedation at higher doses.^{3,5}
- Methyldopa is contraindicated in depression.⁶
- Nifedipine and methyldopa are not licensed specifically for hypertension in pregnancy.^{6,7}
- 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.
- When switching patients to alternate treatment, blood pressure, pulse rate, and signs and symptoms of the underlying disorder should be monitored to guide dosing.
- If any of the recommendations are not clinically acceptable or there is any uncertainty about what to do or how to do it then management options should be discussed with the responsible consultant specialist.

Hypertension in lactation

- It is important that women are managed on an individual basis in consultation with a specialist, if appropriate, considering patient-specific clinical conditions, including the health and prematurity of the infant.
- The UK Medicines Information (UKMi) Drugs In Lactation Advisory Service suggests the following potential management options⁸ for hypertension in lactation:
 - Angiotensin-converting enzyme (ACE) inhibitors: Captopril and Enalapril are considered to be compatible with breastfeeding but monitoring of infants, especially premature and newborn for hypotension if exposed to an ACE inhibitor while breastfeeding. These are also recommended by NICE.³
 - Beta-blockers: Propranolol is considered to be the beta-blocker of choice in breastfeeding. It is important to monitor breastfed infants for signs of beta blockade especially bradycardia.
 - Calcium-channel blockers: Nifedipine is considered compatible with breastfeeding and is recommended by NICE. It is important to monitor the infant for adverse effects.

- Centrally acting antihypertensives: Methyldopa is considered compatible with breastfeeding but is **NOT** recommended by NICE for use in the postnatal period due to the risk of depression.
- If any of the recommendations are not clinically acceptable or there is any uncertainty about what to do or how to do it then management options should be discussed with the responsible consultant specialist.

References

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11. Atenolol Tablets BP 25mg SPC (Accord-UK Ltd); DOR = 14th April 2017
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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

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