



Dear Colleague

METOPROLOL 50MG AND 100MG TABLETS – SUPPLY ISSUE

28 February 2019

Summary

1. This Circular provides information for NHS Boards, Prescribers and community pharmacy contractors on the current supply issue with Metoprolol 50mg and 100mg tablets.

Addresses

For action

Chief Executives, NHS Boards
Medical Directors, NHS Boards
NHS Directors of Pharmacy
Primary Care Leads, NHS
Boards
General Practitioners
Community Pharmacists

Background

2. We have been made aware of an ongoing supply issue with the following two products:
 - Metoprolol 50mg tablets
 - Metoprolol 100mg tablets
3. The issue has been caused because some manufacturers discontinuing the products and others having supply difficulties. Milpharm/Aurobindo, are currently the **sole supplier of both presentations to the UK market.**
4. Supplies of both presentations are currently available but may be limited, further stock is arriving over the coming weeks however supply is likely to be intermittent for a number of months.
5. If patients are having difficulty obtaining metoprolol, they may need to be switched to an appropriate alternative treatment.

For information

Prescribing Advisors, NHS
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Details

6. See **Annex A** which has been produced by UK Medicine Information with input from national experts, which advises on management options for patients affected by this supply issue, including the use of alternative beta blockers,

dosing information for these alternative beta blockers and monitoring requirements.

7. Suppliers of alternative, beta blockers have been contacted to determine if they can meet any additional demand and currently, the manufacturer of carvedilol has indicated that it 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** additional demand on their products.
8. We continue to work with Department of Health and Social Care who are working with the manufacturers Milpharm/Aurobindo, to accelerate future deliveries. We will continue to monitor the overall situation.

Action

9. You are asked to note the content of this circular and Annex and bring to the attention of all relevant healthcare professionals and team members

Yours sincerely

A handwritten signature in cursive script, reading "Rose Marie Farr".

Chief Pharmaceutical Officer and
Deputy Director, Pharmacy & Medicines Division

Metoprolol 50mg and 100mg tablets

Description of product affected

Metoprolol is a cardioselective beta-blocker, licensed for use in adults for the following indications¹:

- Hypertension
- Angina pectoris
- Tachyarrhythmias, in particular supraventricular tachycardia
- Maintenance treatment after a myocardial infarction
- Prophylaxis of migraine

Doses across the various indications range from 50mg to 200mg, in single or divided doses (usually twice daily).

Background

There are intermittent supply issues affecting metoprolol 50mg and 100mg as some manufacturers have recently discontinued these products and others are having supply difficulties. Supplies of both strengths are currently available but may be limited; further stock is arriving over the coming weeks however supply is likely to be intermittent for a number of months. Suppliers of alternative beta blockers have been contacted to determine if they can meet any additional demand and currently, the manufacturers of carvedilol 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.

Alternative agents and management options

There is no robust evidence to suggest metoprolol is the beta blocker of choice in certain patient groups. The following table provides an overview of the licensed uses of metoprolol and some of the other commonly used beta-blockers. The choice of beta-blocker will depend on co-morbidities, local recommendations, and cost. Where possible, prescribe a drug that is taken only once a day and prescribe generically².

Table 1: Licensed indications of the more commonly used beta-blockers

Indications Drugs	Hypertension	Heart failure	Angina	Arrhythmias	Post-Myocardial infarction^a	Migraine prophylaxis
Metoprolol ^{1e}	√	Used off-label ^b	√	√	√	√ ^c
Bisoprolol ^{3e}	√	√	√	-	-	-
Carvedilol ^{4,d}	√	√	√	-	-	-
Atenolol ^{5e}	√	-	√	√	√	
Propranolol ⁶	√	-	√	√	√	√

- a. In their clinical guideline on the secondary prevention of myocardial infarction, NICE makes no recommendations on choice of beta-blocker⁷. CKS have however recommended metoprolol (standard release), propranolol (standard release), timolol, or atenolol because these are licensed for long-term prophylaxis following myocardial infarction in people without left ventricular dysfunction⁸.
- b. Whilst metoprolol is not licensed for management of heart failure, it is sometimes used for this indication based on evidence from the MERIT-HF trial which used metoprolol succinate.
- c. Although metoprolol is licensed for migraine prophylaxis, the NICE clinical guideline on the management of headaches recommends propranolol as the beta-blocker of choice⁹.
- d. Manufacturer of carvedilol cannot support the market with the additional demand.
- e. Considered cardioselective, therefore have less effect on the beta2 receptors and may be more suitable for patients with asthma or COPD.

Dose equivalence and conversion

There is no definitive guidance for dose conversion between beta-blockers and clinical judgement will be required in considering where the metoprolol 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. The following table provides dose ranges for some commonly used beta-blockers described above.

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

	Metoprolol ¹	Atenolol ⁵	Bisoprolol ³	Carvedilol ⁴	Propranolol ⁶
Hypertension	100-200mg daily (single or divided doses)	25-100mg OD	5-20mg OD	12.5mg to 50mg OD	40mg BD or TDS, max 320mg per day
Heart failure	Used off-label ^{b(above)}	-	Initially 1.25mg OD, titrated upwards to 10mg OD	3.125mg BD increased at 2-weekly intervals to max 25mg BD	-
Angina	50-100mg BD	50-100mg OD or 50mg BD	5-20mg OD	12.5mg BD increased at 2-weekly intervals to max 50mg BD	40mg BD or TDS, max 240mg per day
Arrhythmias	100-200mg per day	50-100mg OD	-	-	10-40mg TDS or QDS

Post-Myocardial infarction	100mg BD	50-100mg OD	-	-	40mg QDS followed by 80mg BD after 2 days (initiated between days 5 and 21 after myocardial infarction)
Migraine prophylaxis	50-100mg BD	-	-	-	40mg BD or TDS, to max of 160mg daily

References

1. Metoprolol Tartrate 50 mg tablets SPC (Accord Healthcare Ltd); DOR = 20/10/2017
2. NICE. Clinical Knowledge Summaries: Hypertension - not diabetic (Last revised in January 2018): <https://cks.nice.org.uk/hypertension-not-diabetic#!prescribingInfoSub:37>
3. Bisoprolol 10mg film-coated tablets SPC (Accord Healthcare Ltd); DOR = 31/05/2014
4. Carvedilol 6.25mg film-coated tablets SPC (Aurobindo Pharma - Milpharm Ltd); DOR = 03/02/2018
5. Atenolol Tablets BP 25mg SPC (Accord-UK Ltd); DOR = 14th April 2017
6. Propranolol 40mg film-coated tablets SPC (Accord Healthcare Limited); DOR = 14/06/2018
7. NICE. Myocardial infarction: cardiac rehabilitation and prevention of further cardiovascular disease. Clinical Guideline 172 (November 2013): <https://www.nice.org.uk/guidance/cg172#>
8. NICE. Clinical Knowledge Summaries: MI – Secondary prevention (October 2015): <https://cks.nice.org.uk/mi-secondary-prevention#!prescribingInfoSub:8>
9. NICE. Headaches in over 12s: diagnosis and management. Clinical Guideline 150 (November 2015): <https://www.nice.org.uk/guidance/cg150>