# Drug Safety Update

## Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

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## Contents



The Medicines and Healthcare products Regulatory Agency is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

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An EU-wide review of the latest safety data on mirabegron (Betmiga▼), a beta 3-adrenoceptor agonist used in the management of urinary frequency, urgency, and incontinence in overactive bladder syndrome, has led to new measures to help reduce the risks of severe hypertension. It is already known that mirabegron can increase blood pressure. However, cases of severe hypertension have been reported, which include hypertensive crisis associated with reports of cerebrovascular and cardiac events (mainly transient ischaemia attack or stroke)—some with a clear temporal relation to mirabegron use.

Mirabegron is now contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg, or both). Regular monitoring of blood pressure is important, especially in patients with pre-existing hypertension—see article 1.

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## 1 **Mirabegron (Betmiga▼): risk of severe hypertension and associated cerebrovascular and cardiac events**

Mirabegron is now contraindicated in patients with severe uncontrolled hypertension; advice about regular monitoring is being introduced because of cases of serious hypertension.

**Key updated safety advice for healthcare professionals:**

- Mirabegron is contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg, or both)
- Blood pressure should be measured before starting treatment and monitored regularly during treatment, especially in patients with hypertension
- Please report suspected side effects to mirabegron on a Yellow Card

Mirabegron (Betmiga▼) is a beta 3-adrenoceptor agonist used in the management of urinary frequency, urgency, and incontinence in overactive bladder syndrome. Approximately 700 000 packs of mirabegron have been dispensed in the UK since it was first licensed in December 2012.*

*Data derived from IMS Health IMS MIDAS 07/2012 to 06/2015, by the MHRA.

### Risks of severe hypertension

An EU-wide review of the latest safety data for mirabegron has led to new measures to help reduce the risks of severe hypertension. It is already known that mirabegron can increase blood pressure. However, cases of severe hypertension have been reported, which include hypertensive crisis associated with reports of cerebrovascular and cardiac events (mainly transient ischaemia attack or stroke)—some with a clear temporal relation to mirabegron use.

### New contraindication

Mirabegron is now contraindicated in patients with severe uncontrolled hypertension (systolic blood pressure ≥180 mm Hg or diastolic blood pressure ≥110 mm Hg, or both). Regular monitoring of blood pressure is important, especially in patients with pre-existing hypertension.

### Use in stage 2 hypertension

Data are limited regarding use of mirabegron in patients with stage 2 hypertension (ie, systolic blood pressure ≥160 mm Hg or diastolic blood pressure ≥100 mm Hg) and it should therefore be used with caution in this group.

### Reminder of use in some other patient subgroups

Mirabegron is not recommended in patients with severe renal impairment (ie, GFR 15–29 mL/min/1.73 $m^2$) or in those with moderate hepatic impairment (ie, Child-Pugh Class B) who are also taking strong inhibitors of cytochrome P450 3A such as itraconazole, ketoconazole, ritonavir, or clarithromycin.

The dose of mirabegron in patients with mild to moderate renal impairment (ie, GFR 30–89 mL/min/1.73 $m^2$) or those with mild hepatic impairment (ie, Child-Pugh Class A) who are also taking strong inhibitors of cytochrome P450 3A should be reduced to 25 mg once daily.

**Further information**

Mirabegron summary of product characteristics

Letter sent to healthcare professionals 7 September 2015

*Article citation: Drug Safety Update volume 9 issue 3 October 2015: 1*

## 2 Letters sent to healthcare professionals in September 2015

In September 2015, a letter was sent to relevant healthcare professionals for mirabegron to inform of a risk of severe hypertension and associated cerebrovascular and cardiac events. Further information is also provided in our article on page 2.

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