

## Perindopril arginine

### Switching from Coversyl® Arginine products (perindopril arginine) to perindopril erbumine tablets

This is one of a number of bulletins providing further information on medicines contained in the PrescQIPP DROP-List (DRugs of IOW Priority). This bulletin focuses on different perindopril formulations (salts) which are not directly equivalent. It provides the rationale for new patients to be commenced on generic perindopril erbumine, also known as tert-butylamine.<sup>1</sup> Current patients can be considered for a switch from Coversyl® Arginine (perindopril arginine) to perindopril erbumine. Options for dose conversion in support of the switch, potential switch savings and information on perindopril adverse effects are provided.

Further bulletins, including the full DROP-List are available on the PrescQIPP website:<sup>2</sup>

<http://www.prescqipp.info/resources/viewcategory/171-drop-list>

### Recommendations

- Commence new patients on perindopril erbumine, where perindopril is an appropriate angiotensin converting enzyme (ACE) inhibitor choice according to your local formulary.
- Review all patients on Coversyl® Arginine and Coversyl® Arginine Plus preparations for suitability for switching to generic perindopril erbumine. Switch all suitable patients to perindopril erbumine. As with all switches, these should be tailored to the individual patient.
- Caution is needed when selecting treatment on clinical prescribing systems to prevent inadvertent selection of perindopril arginine instead of perindopril erbumine.<sup>3</sup>

### Background

Perindopril arginine (Coversyl® Arginine and Coversyl® Arginine Plus preparations) features in the PrescQIPP DROP-List.<sup>2</sup> The DROP-List is an accumulation of medicines that are regarded as low priority, poor value for money or medicines for which there are safer alternatives.

The manufacturer (Servier) discontinued the original brand Coversyl® when they brought out Coversyl® Arginine.<sup>3</sup> Therefore any branded prescriptions written just as Coversyl® could also mean the branded product, Coversyl® Arginine is dispensed.

In the PrescQIPP membership area (20.3 million patients, Dec 2013) £681,528 was spent on perindopril arginine and branded Coversyl® (including Coversyl®, Coversyl® Arginine and Coversyl® Arginine Plus) over the course of a year (ePACT Dec 13). Perindopril/Coversyl® Arginine accounts for only 3% of total perindopril usage, but a disproportionate 15% of costs. Switching to perindopril erbumine could save up to £458,801 annually across the PrescQIPP membership. As with all switches, individual patient circumstances need to be borne in mind. However, with tight switching criteria, assistance from practice nurses, support from your local CCG prescribing teams and the experiences of CCGs/GPs that have already undertaken this work, it is hoped that GPs will participate in realising the cost savings.

## Rationale for switching to perindopril erbumine

- National Institute for Health and Care Excellence (NICE) hypertension guidelines advise prescribing non-proprietary drugs of low acquisition cost as first line choices of drug therapy.<sup>4</sup>
- Coversyl® Arginine (perindopril arginine) has no clinical benefit over generic perindopril erbumine and is more costly.<sup>5</sup>
- In view of the substantial difference in cost between perindopril arginine (Coversyl® Arginine, Coversyl® Arginine Plus) and generic perindopril erbumine the preferred choice is generic perindopril erbumine.<sup>6</sup>
- The principal reason for the change in the Coversyl® Arginine formulation originally (from erbumine to arginine salt) was improved stability which makes it better suited to extremes of (the Australian) climate.<sup>7</sup> The improved stability increases shelf life from two to three years.<sup>8</sup> This is of minor consequence in the UK.

All switches should be tailored to the individual patient.

## Adverse effects of perindopril

Perindopril erbumine has the same side-effect profile as perindopril arginine, asthenia (weakness), mood and sleep disturbances. This is in addition to the main side-effects for angiotensin-converting-enzyme (ACE) inhibitors: persistent dry cough, angioedema, renal impairment, gastro-intestinal effects, altered liver function tests, pancreatitis, and blood disorders. See BNF for more details.<sup>1</sup>

## Costs

There is a significant difference in cost between Coversyl® Arginine products and perindopril erbumine. Table 1 below illustrates the cost differences.

**Table 1: Price comparison of perindopril products<sup>6</sup>**

Product (tablets)	Cost per 30 days
Perindopril erbumine 2mg	£1.43
Perindopril erbumine 4mg	£1.51
Perindopril erbumine 8mg	£1.65
Coversyl® Arginine 2.5mg	£4.43
Coversyl® Arginine 5mg	£6.28
Coversyl® Arginine Plus (Perindopril 5mg/indapamide 1.25mg)	£9.51
Coversyl® Arginine 10mg	£10.65

## Switching options

The potential switch options from perindopril/Coversyl® Arginine to perindopril erbumine are shown in table 2, overleaf. Clinicians may wish to choose other options according to the clinical need of the patient. This could include a trial of discontinuing treatment gradually, if antihypertensive medication

is no longer needed for people whose blood pressure has been well controlled for years and who have favourable factors. These include:

- Where only one antihypertensive drug has been needed
- Younger age
- Lower blood pressure
- Person has successfully adopted lifestyle measures such as losing weight, not misusing alcohol, exercising regularly, and restricting salt consumption.

Follow the manufacturer's guidance on withdrawing the antihypertensive gradually. Follow-up the patient carefully (e.g. at about 4-week intervals for 6 months, then 2 or 3 times a year) to detect any recurrence of hypertension. This is most likely to happen in the first 6 months, although it can happen later.<sup>9</sup>

**Table 2: Recommended dose equivalence<sup>3, 10-13</sup>**

Current treatment	Switch to
Coversyl® Arginine 2.5mg once daily	Perindopril erbumine 2mg once daily
Coversyl® Arginine 5mg once daily	Perindopril erbumine 4mg once daily
Coversyl® Arginine 10mg once daily	Perindopril erbumine 8mg once daily

For patients receiving Coversyl® Arginine Plus which contains perindopril arginine 5mg and indapamide 1.25mg, there is not a direct switch.<sup>14</sup> However prescribing perindopril erbumine 4mg plus an appropriate diuretic as a separate component is the best option.<sup>3</sup> This provides greater flexibility of dosing.

An appropriate diuretic would be chlortalidone (12.5mg – 25mg once daily) or indapamide (1.5mg modified release once daily or 2.5mg once daily) according to the NICE clinical guideline for hypertension.<sup>4</sup>

Chlortalidone is only available as 50mg tablets (28 tablet pack is £1.64).<sup>1,7</sup> They may be difficult to obtain.<sup>1</sup> These tablets would also need to be quartered or halved by the patient which requires a certain level of dexterity.

Indapamide is not available as a 1.25mg tablet. Modified release 1.5mg tablets are available and cost from £3.40 for a 30 tablet pack. The most cost-effective brands are Tensaid XL® (Mylan) and Natrilix SR® (Servier) which are also £3.40 for a 30 tablet pack.<sup>1,6,15</sup>

## Switch savings

Table 3 below illustrates the savings that can be made by switching from perindopril/Coversyl® Arginine to perindopril erbumine.

**Table 3: Cost savings due to switching from branded to generic perindopril<sup>6</sup>**

Perindopril switch	Annual switch savings per 100,000 patients per year across PrescQIPP membership
Switch from perindopril/Coversyl® Arginine products to perindopril erbumine	£2,258

There is a significant difference in cost between perindopril/Coversyl® Arginine and perindopril erbumine. In the PrescQIPP membership area, £681,528 is spent on perindopril/Coversyl® Arginine per year. **Switching from perindopril/Coversyl® Arginine to perindopril erbumine could release savings of up to £458, 801 annually across the total PrescQIPP membership.**

## Summary

- **Perindopril arginine has no clinical benefit over perindopril erbumine<sup>5</sup> and no difference in safety profile.<sup>1</sup>**
- **Prescribing advice is to switch from Coversyl® Arginine products to generic perindopril erbumine, to realise substantial cost savings.**

## References

1. Joint Formulary Committee. British National Formulary. 66th ed. London: BMJ Publishing Group and Royal Pharmaceutical Society. January 2014 update. Available via NICE BNF app.
2. PrescQIPP DROP-List <http://www.prescqipp.info/resources/viewcategory/171-drop-list>
3. Potential for confusion with new formulation of Coversyl®. 18th April 2008. NPC Rapid Review [www.npc.nhs.uk/rapidreview](http://www.npc.nhs.uk/rapidreview) Accessed 14.01.14
4. National Institute for Health and Care Excellence (NICE). Hypertension Quick Reference Guide. Aug 2011. [www.nice.org.uk/guidance/CG127/QuickRefGuide](http://www.nice.org.uk/guidance/CG127/QuickRefGuide)
5. Hughes D A, Ferner R E. New Drugs for Old: disinvestment and NICE. BMJ 2010; 340: C572
6. Drug Tariff January 2014 [www.ppa.org/ppa/edt\\_intro.htm](http://www.ppa.org/ppa/edt_intro.htm) Accessed 13.01.14
7. Kubler P. Editorial: New Drugs for Old. Aust Prescr 2006; 29: 148-9.
8. Telejko E. Perindopril arginine: benefits of a new salt of the ACE inhibitor perindopril. Curr Med Res Opin 2007 May; 23 (5): 953-60.
9. NICE Clinical Knowledge Summaries (CKS) <http://cks.nice.org.uk/hypertension-not-diabetic#!scenariorecommendation:20> Last revised April 2012. Accessed 13.01.14
10. Summary of Product Characteristics. Coversyl® Arginine 2.5mg, 5mg and 10mg tablets. Servier Laboratories. [www.medicines.org.uk](http://www.medicines.org.uk) Accessed 14.01.14
11. Summary of Product Characteristics. Perindopril 2mg tablets. Actavis UK Ltd. [www.medicines.org.uk](http://www.medicines.org.uk) Accessed 14.01.14
12. Summary of Product Characteristics. Perindopril 4mg tablets. Actavis UK Ltd. [www.medicines.org.uk](http://www.medicines.org.uk) Accessed 14.01.14
13. Summary of Product Characteristics. Perindopril 8mg tablets. Actavis UK Ltd. [www.medicines.org.uk](http://www.medicines.org.uk) Accessed 14.01.14
14. Summary of Product Characteristics. Coversyl® Arginine Plus. Servier Laboratories. [www.medicines.org.uk](http://www.medicines.org.uk) Accessed 14.01.14
15. MIMS app January 2014. Haymarket Publishing, London.

## Further resources

National Institute for Health and Care Excellence (NICE). Chronic Heart Failure Quick Reference Guide. Aug 2011. CG108. [www.nice.org.uk/nicemedia/live/13099/50526/50526.pdf](http://www.nice.org.uk/nicemedia/live/13099/50526/50526.pdf)

National Institute for Health and Care Excellence (NICE). Myocardial Infarction - Secondary Prevention. Nov 2013. CG172 full guideline. [www.nice.org.uk/nicemedia/live/14302/65691/65691.pdf](http://www.nice.org.uk/nicemedia/live/14302/65691/65691.pdf)

## Additional PrescQIPP resources



Briefing



Data pack



Audit and patient letter

Available for download here: <http://www.prescqipp.info/-perindopril-arginine/viewcategory/213>

Information compiled by Sandra Hicks, PrescQIPP Programme March 2014, and reviewed by Katie Smith, East Anglia Medicines Information Service, March 2014.

Non-subscriber publication July 2014.