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Medicines Optimisation

CCG briefing on Sacubitril valsartan (Entresto®) NICE technology appraisal guidance [TA388]

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Author Name	**Email Address**
Susan Turner	Susanturner4@nhs.net

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1. Purpose of the briefing

This briefing is designed to inform CCGs of the implications of NICE TAG 388 Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction.

Sacubitril valsartan is recommended as an option for treating symptomatic chronic heart failure with reduced ejection fraction, only in people:

- with New York Heart Association (NYHA) class II to IV symptoms and
- with a left ventricular ejection fraction of 35% or less and
- who are already taking a stable dose of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor-blockers (ARBs).

Treatment with sacubitril valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team.

This technology is commissioned by clinical commissioning groups (CCGs). Providers are NHS hospital trusts and GPs in primary care.

Sacubitril valsartan for treating symptomatic chronic heart failure falls within the programme budgeting category 9: problems of circulation.

Because sacubitril valsartan was made available in the NHS through the early access to medicines scheme, NHS England has indicated that this guidance will be implemented 30 days after final publication, as opposed to the usual 90 days. Sacubitril valsartan is the first drug commissioned by CCGs to be approved under the early access to medicines scheme.

This therefore means that CCGs have been obliged to fund this treatment, where a clinician and patient feel it is the correct choice for them, from the end of May 2016.

This should therefore now be incorporated into local formularies, without further review of the evidence.

2. Technology

Sacubitril/valsartan represents a new therapeutic option for patients with chronic heart failure and reduced ejection fraction and would be used instead of an ACE inhibitor or ARB. Sacubitril is the prodrug of LBQ657, a first in class neprilysin inhibitor, which enhances the protective neurohormonal systems of the heart peptides (eg natriuretic peptides). Valsartan is an established ARB.

Both sacubitril and valsartan lower blood pressure.

Sacubitril/valsartan, compared to an angiotensin-converting enzyme inhibitor, significantly reduced rates of the composite outcome of cardiovascular death and hospitalisation for heart failure, rates of the component outcomes and of all cause mortality.

The composite primary outcome of the pivotal PARADIGM-HF study included two direct health outcomes (cardiovascular death and hospitalisation due to heart failure) and there was a significant reduction with sacubitril/valsartan versus enalapril (absolute reduction of 4.7%, relative risk reduction of 20%, number needed to treat [NNT] over 27 months of 21). The reduction was significant and consistent in each of the components and considered clinically relevant: cardiovascular death (absolute reduction of 3.1%, relative risk reduction of 20%, NNT of 32) and hospitalisation due to heart failure (absolute reduction of 2.8%, relative risk reduction of 21%, NNT of 36).

The study compared sacubitril/valsartan, which included a valsartan dose equivalent to 160mg twice daily, with enalapril 10mg twice daily. Although doses of both medicines are within the target doses recommended by guidelines (valsartan 160mg twice daily and enalapril 10 to 20mg twice daily), the enalapril dose is at the lower end of the recommended target dose. However this is similar to the enalapril dose used in other heart failure studies and used in clinical practice.

Use in line with the NICE TAG is expected to reduce hospital admissions by 4 per year for a population of 100,000 at a cost per admission of £2,698 based on NICE standard assumptions.

3. Cost Impact

Nationally around 108,000 people with heart failure with reduced ejection fraction and NYHA class II to IV symptoms, with a left ventricular ejection fraction of 35% or less and taking an ACE inhibitor/ARB are likely to be eligible for sacubitril valsartan.

From year 2020/21, once uptake has reached 60%, NICE estimate that 64,500 people will have sacubitril valsartan each year. The rate of uptake is based on recognition that this is a new drug and it will be used with caution initially.

Actual uptake will depend on local implementation strategies.

Technology	**AnnualTreatment cost**
Angiotensin-converting enzyme inhibitors[a]	£32
Angiotensin II receptor blockers[b]	£87
Sacubitril valsartan[c]	£1,194
Heart failure – hospitalisation[d]	£2,698

a. Based on weighted average annual treatment costs of 4 different drugs (enalapril, ramipril, perindopril and lisinopril).
b. Based on weighted average annual treatment costs of 3 different drugs (losartan, candesartan and valsartan).
c. Based on a dosage of 200 mg twice daily.
d. 2016/17 National tariff.

The cost-effectiveness analysis for sacubitril valsartan showed benefit over ACEi on heart failure hospitalisation as well as cardiovascular and non-cardiovascular hospitalisations.

Based on the company submission the introduction of sacubitril valsartan will be expected to reduce the costs of hospital admissions because of heart failure.

Sacubitril valsartan also improves both overall mortality and cardiovascular mortality, which may lead to additional cost savings. The cost impact from prescribing, however will be a pressure on the primary care prescribing budget.

NICE estimate the resource impact to be approx. £23,000 in 2016/17 rising to approx. £127,000 per 100,000 population per year from 2020/21 (plus VAT where applicable.)

This is based on increased drug costs of £137,194 per 100,000 population offset by reduced hospital admissions of £10,791.

4. Recommendations

- Commissioners should ensure that sacubitril valsartan has been incorporated into local formularies, without further review of the evidence.
- Guidance should be produced locally in relation to the implementation of the NICE TAG and the management of patients who may be deemed suitable for treatment with this new agent. Treatment with sacubitril valsartan should be started by a heart failure specialist with access to a multidisciplinary heart failure team. Dose titration and monitoring should be performed by the most appropriate team member as defined in NICE's guideline on chronic heart failure in adults: management.
- Primary care clinicians will need to familiarise themselves with the safety advice and cautions relating to this new agent before patients are discharged back to their care. An initial briefing has been sent out to GPs by the NECS MO team.
- The impact of prescribing costs on primary care prescribing budgets will need to be noted.

References

1. NICE TAG 388 Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction. April 2016
2. Resource impact report: Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction(TA388). April 2016. https://www.nice.org.uk/guidance/ta388/resources/resource-impact-report-2479301101
3. Scottish Medicines ConsortiumSMC No. (1132/16) Feb 2016. Scottish Medicines Consortium sacubitril/valsartan (Entresto)