NICE National Institute for Health and Care Excellence

Putting NICE guidance into practice

Resource impact report:
Dapagliflozin for treating chronic heart failure with reduced ejection fraction (TA679)

Published: March 2021

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Summary

NICE has recommended dapagliflozin, as an option for treating symptomatic chronic heart failure with reduced ejection fraction in adults, only if it is used as an add-on to optimised standard care with:

- angiotensin-converting enzyme (ACE) inhibitors or angiotensin-2 receptor blockers (ARBs), with beta blockers, and, if tolerated, mineralocorticoid receptor antagonists (MRAs), or
- sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

Based on current practice:

- 70% of the eligible population receive optimised standard care based on ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs and
- 30% receive optimised standard care based on sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

In the absence of dapagliflozin, the uptake of sacubitril valsartan is expected to increase to 50% by year 5. In the future it is expected that 25% of the eligible population will receive dapagliflozin as an add-on to optimised standard care with sacubitril valsartan, with beta blockers, and, if tolerated, MRAs by year 5 and 50% people to receive dapagliflozin as an add-in to optimised standard care based on ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs.

We estimate that:

- 75,000 people with symptomatic chronic heart failure with reduced ejection fraction are eligible for treatment with dapagliflozin, and
- 56,250 people will have dapagliflozin as an add-on treatment from year 2024/25 onwards once uptake has reached 75%. See table 1 for further details. 50% of this is as an add-on optimised standard care with ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs and 25% is as an add-on to optimised standard care with sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

The estimated annual cost of implementing this guidance for the population of England based on the uptake in the resource impact assumptions is shown in table 1. Based on the assumptions used for England, this is equivalent to a cost of around £7,000 per 100,000 population.

This report is supported by a resource impact template (see resource impact information) which may be used to calculate the resource impact of implementing the guidance by amending the variables.

This technology is commissioned by clinical commissioning groups. Providers are NHS hospital trusts and primary care.

Table 1 Estimated uptake and annual costs of implementing the guidance for England

	World without dapagliflozin					World with dapagliflozin				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
People receiving ACEi or ARBs (standard care)	70%	65%	60%	55%	50%	65%	50%	40%	30%	20%
People receiving optimised standard care based on sacubitril valsartan or people receiving sacubitril valsartan as an add-on to ACEi or ARBs	30%	35%	40%	45%	50%	15%	15%	10%	10%	5%
People receiving dapagliflozin as an add-on to sacubitril valsartan	0%	0%	0%	0%	0%	5%	10%	15%	20%	25%
People receiving dapagliflozin as an add-on to ACEi or ARBs	0%	0%	0%	0%	0%	15%	25%	35%	40%	50%
Change in costs (£'000s)										
People receiving ACEi or ARBs (standard care)						-£163	-£490	-£653	-£816	-£979
People receiving optimized standard care based on sacubitril valsartan or people receiving sacubitril valsartan as an add-on to ACEi or ARBs						-£13,407	-£17,877	-£26,816	-£31,284	-£40,223
People receiving dapagliflozin as an add-on to sacubitril valsartan						£6,190	£12,380	£18.570	£24,760	£30,950
People receiving dapagliflozin as an add-on to ACEi or ARBs						£5,667	£9,447	£13,227	£15,115	£18,894
Total change in drug costs (£'000s)						**-£1,713**	**£3,460**	**£4,328**	**£7,775**	**£8,642**
Savings from hospitalisations avoided (£'000s)						**-£813**	**-£2,119**	**-£2,942**	**-£3,774**	**-£4,597**
Total resource impact (£'000s)						**-£2,526**	**£1,341**	**£1,386**	**£4,001**	**£4,045**

1 Dapagliflozin

1.1 NICE has recommended dapagliflozin as an option for treating symptomatic chronic heart failure with reduced ejection fraction in adults, only if it is used as an add-on to optimised standard care with:

- ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs, or
- Sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

1.2 Heart failure with reduced ejection fraction (HFrEF) is a chronic condition that affects survival and quality of life. Clinical expert submissions to NICE confirmed that HFrEF is associated with high rates of death and hospitalisation and that there is an unmet need for new treatment options.

1.3 Standard care includes an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin 2 receptor blocker (ARB), with beta blockers and, if tolerated, a mineralocorticoid receptor antagonist (MRA). Alternatively, people may be offered sacubitril valsartan, with beta blockers and, if tolerated, MRAs if symptoms continue on ACE inhibitors or ARBs.

1.4 Current treatments aim to manage symptoms and stabilise the disease to prevent further decline in quality of life and to keep people alive longer. The committee heard from clinical experts that despite optimising therapies, many people still have symptoms, including breathlessness.

1.5 People whose symptoms continue or worsen on optimised doses of standard care based on ACE inhibitors or ARBs can only start sacubitril valsartan under the supervision of a specialist with access to a multidisciplinary team. So dapagliflozin should only be started

on advice from a heart failure specialist in primary, secondary or community care.

2 Resource impact of the guidance

2.1 Based on current practice:

- 70% of the eligible population receive optimised standard care based on ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs and
- 30% receive optimised standard care based on sacubitril valsartan, with beta blockers, and, if tolerated, MRAs.

In the absence of dapagliflozin, the uptake of sacubitril valsartan is expected to increase to 50% by year 5. In the future it is expected that 25% of the eligible population will receive dapagliflozin as an add-on to optimised standard care with sacubitril valsartan, with beta blockers, and, if tolerated, MRAs by year 5 and 50% people to receive dapagliflozin as an add-in to optimised standard care based on ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs.

2.2 We estimate that:

- 75,000 people in England with symptomatic chronic heart failure with reduced ejection fraction are eligible for treatment with dapagliflozin each year.
- 56,250 people will have dapagliflozin as an add-on treatment from year 2024/25 onwards once uptake has reached 75%. See table 1 for further details. 50% of this is as an add-on optimised standard care with ACE inhibitors or ARBs, with beta blockers, and, if tolerated, MRAs and 25% is as an add-on to optimised standard care with sacubitril valsartan, with beta blockers, and, if tolerated, MRAs. See table 2 for further details.

2.3 The current treatment and future uptake figure assumptions are based on company estimates and clinical expert opinion and are shown in the resource impact template.

2.4 The estimated annual cost of implementing this guidance for the population of England based on the uptake in the resource impact assumptions is shown in table 2. The cost from year 2024/25 once steady state is reached is equivalent to £7,000 per 100,000 population (see table 3 for further details).

Table 2 Estimated uptake and annual costs of implementing the guidance for England

	World without dapagliflozin					World with dapagliflozin				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
People receiving ACEi or ARBs (standard care)	70%	65%	60%	55%	50%	65%	50%	40%	30%	20%
People receiving optimized standard care based on sacubitril valsartan or people receiving sacubitril valsartan as an add-on to ACEi or ARBs	30%	35%	40%	45%	50%	15%	15%	10%	10%	5%
People receiving dapagliflozin as an add-on to sacubitril valsartan	0%	0%	0%	0%	0%	5%	10%	15%	20%	25%
People receiving dapagliflozin as an add-on to ACEi or ARBs	0%	0%	0%	0%	0%	15%	25%	35%	40%	50%
Change in costs (£'000s)										
People receiving ACEi or ARBs (standard care)						-£163	-£490	-£653	-£816	-£979
People receiving optimized standard care based on sacubitril valsartan or people receiving sacubitril valsartan as an add-on to ACEi or ARBs						-£13,407	-£17,877	-£26,816	-£31,284	-£40,223
People receiving dapagliflozin as an add-on to sacubitril valsartan						£6,190	£12,380	£18.570	£24,760	£30,950
People receiving dapagliflozin as an add-on to ACEi or ARBs						£5,667	£9,447	£13,227	£15,115	£18,894
Total change in drug costs (£'000s)						**-£1,713**	**£3,460**	**£4,328**	**£7,775**	**£8,642**
Savings from hospitalisations avoided (£'000s)						**-£813**	**-£2,119**	**-£2,942**	**-£3,774**	**-£4,597**
Total resource impact (£'000s)						**-£2,526**	**£1,341**	**£1,386**	**£4,001**	**£4,045**

Table 3 Estimated uptake and resource impact of implementing the guidance per 100,000 population

	World without dapagliflozin					World with dapagliflozin				
	Year 1	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
People receiving ACEi or ARBs (standard care)	70%	65%	60%	55%	50%	65%	50%	40%	30%	20%
People receiving optimized standard care based on sacubitril valsartan or people receiving sacubitril valsartan as an add-on to ACEi or ARBs	30%	35%	40%	45%	50%	15%	15%	10%	10%	5%
People receiving dapagliflozin as an add-on to sacubitril valsartan	0%	0%	0%	0%	0%	5%	10%	15%	20%	25%
People receiving dapagliflozin as an add-on to ACEi or ARBs	0%	0%	0%	0%	0%	15%	25%	35%	40%	50%
Change in costs (£'000s)										
People receiving ACEi or ARBs (standard care)						£0	-£1	-£2	-£2	-£2
People receiving optimized standard care based on sacubitril valsartan or people receiving sacubitril valsartan as an add-on to ACEi or ARBs						-£24	-£31	-£48	-£55	-£72
People receiving dapagliflozin as an add-on to sacubitril valsartan						£11	£22	£33	£44	£55
People receiving dapagliflozin as an add-on to ACEi or ARBs						£10	£16	£25	£27	£34
Total change in drug costs (£'000s)						**-£3**	**£6**	**£8**	**£14**	**£15**
Savings from hospitalisations avoided (£'000s)						**-£1**	**-£4**	**-£5**	**-£7**	**-£8**
Total resource impact (£'000s)						**-£4**	**£2**	**£3**	**£7**	**£7**

2.5 This report is supported by a resource impact template (see resource impact information) which may be used to calculate the resource impact of implementing the guidance by amending the variables.

Savings and benefits

2.6 Treatment with dapagliflozin may help reduce hospitalisation associated with heart failure and could save on average around £2,600 per episode. This has been included in the model.

2.7 Dapagliflozin has no titration requirements and has a favourable safety profile.

2.8 The committee concluded that there is an unmet need for heart failure with reduced ejection fraction (HFrEF) and that both patients and healthcare professionals would welcome a new treatment option.

3 Implications for commissioners

3.1 This technology is commissioned by clinical commissioning groups. Providers are NHS hospital trusts and primary care.

3.2 Dapagliflozin falls within the programme budgeting category 10X: problems of circulation.

4 How we estimated the resource impact

The population

4.1 Around 396,600 people were recorded as having heart failure in England in 2018/19 (Quality and Outcomes Framework, 2019-20). Of these people, around 56,250 are estimated to receive dapagliflozin as an add-on treatment each year from 2024/25 onwards (see table 4 for further details).

Table 4 Number of people eligible for treatment in England

Population	Proportion of previous row (%)	Number of people
Total population[1]		56,286,961
Adult population[1]		44,263,393
People with heart failure on the quality and outcomes framework register in England in 2019/20[2]	0.896	396,600
People with symptomatic chronic HF on QOF with a confirmed diagnosis[2]	80.14	317,840
People with symptomatic chronic heart failure with left ventricular systolic dysfunction (Heart failure with reduced ejection fraction: HFrEF) [2]	50.25	159,700
People with symptomatic chronic HFrEF symptomatic with NYHA class II to IV[3]	90.90	145,200
People with symptomatic chronic HFrEF with eGFR >30 mL/min per 1.73 m2[4]	79.79	115,860
People with symptomatic chronic HFrEF receiving optimised standard care[5]	83	96,160
People with symptoms continue despite receiving optimised standard care and therefore eligible for treatment[5]	78	75,000
People estimated to have dapagliflozin as an add-on treatment each year from 2024/25[5]	75	56,250

[1] Clinical Commissioning Group Mid-Year Population Estimates - Office for National Statistics.

[2] Quality and Outcomes Framework, 2019-20

[3] Company submission

[4] Thomsen et al. 2019. Elevated Potassium Levels in Patients With Congestive Heart Failure: Occurrence, Risk Factors, and Clinical Outcomes: A Danish Population-Based Cohort Study. J Am Heart Assoc. 2018;7(11): e008912

[5] Clinical expert opinion

Based on QOF data the population receiving optimised standard was 82% receiving ACEi or ARBs. This was increased to 83% to account for other treatments such as sacubitril valsartan.

Assumptions

4.2 The resource impact template assumes that:

- Standard care can be based on an ACE inhibitor or an ARB, with beta blockers and, if tolerated, an MRA or it can be based on sacubitril valsartan with beta blockers, and, if tolerated, MRAs.
- Sacubitril valsartan criteria for treatment included people with HFrEF of 35% or less. Dapagliflozin includes people with 40% or less. Therefore, an additional population with ejection fraction of between ≥35% and ≤40% will be eligible for treatment with dapagliflozin or standard care based on an ACE inhibitor, or an ARB and not standard care based on sacubitril valsartan.
- Drug treatment costs are based on a 12-month treatment duration.
- The cost for standard care is a weighted average based on the prescription cost analysis in England, 2019.
- Treatment and up-titration administration costs are not included for dapagliflozin or sacubitril valsartan. These treatments can be prescribed in primary care. However, if initiated in secondary care by a specialist in heart failure, an outpatient tariff may be incurred as part of the patient pathway.
- Treatment discontinuation rates are 7.0% for people receiving dapagliflozin as an add-on to optimised standard care based on ACE inhibitors or ARBs, 7.6% for people receiving optimised standard care based on sacubitril valsartan and 7.6% for people receiving dapagliflozin as an add-on to optimised standard care based on sacubitril valsartan. For simplicity, the model assumes discontinuation to occur at the end of the year.
- The cost-effectiveness analysis for sacubitril valsartan which showed benefit over ACEi on heart failure hospitalisations as well as cardiovascular and non-cardiovascular hospitalisations has been used to estimate potential savings associated with dapagliflozin.

- The resource impact model used all-cause hospitalisation rates as per the company. Hospitalisations based on standard care based on ACE inhibitors or ARBs are 35.52% and 31.81% for standard care based on sacubitril valsartan. Hospitalisations based on dapagliflozin as an add-on to standard care based on sacubitril valsartan are 28.01% and 31.81% for dapagliflozin add-on treatment to standard care based on ACE inhibitors or ARBs.

Other factors

4.3 Risk factors for adverse effects associated with dapagliflozin should be identified at a local level. There may be additional monitoring costs as a result and should be considered at a local level.

About this resource impact report

This resource impact report accompanies the NICE guidance on dapagliflozin for treating chronic heart failure with reduced ejection fraction and should be read with it.