North West Coast
Strategic Clinical Networks

Guidelines for the Administration of Intravenous and Subcutaneous diuretics for Heart Failure Patients in the Ambulatory and Community Setting

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Background

Heart Failure (HF) is a growing problem and incurs high cost to both patient and the NHS. Globally, it is increasingly common to live with heart failure, due to an ageing population and improving medical care (Savarese et al., 2023). In the United Kingdom, heart failure accounts for 5% of all emergency admissions and consumes 2% of the total NHS budget (Duffy, 2023; NICE 2023) and around 200,000 new diagnoses of heart failure are made annually (NHS England, 2022).

The prevalence of HF is expected to continue to rise, through a combination of improved survival of patients with ischaemic heart disease and acute coronary syndromes, more efficacious therapy for heart failure and the effects of an ageing population.

Heart failure is characterised by episodes of decompensation often requiring hospitalisation. A proportion of admissions are due to rapid deterioration resulting in shortness of breath and pulmonary oedema which inevitably results in hospitalisation. However, many are due to a more steady deterioration with increasing peripheral oedema.

Use of intravenous (IV) and subcutaneous (SC) diuretics has been piloted in several areas of the UK and found to be effective in treating fluid overload and symptoms in HF patients and resulted in reduced hospitalisations, the largest being the British Heart Foundation (2014). The programme was led by heart failure specialist nurses (HFSNs) working within existing HF teams. This builds on existing evidence that HF patients under the care of an HFSN are five times less likely to be hospitalised compared to all HF patients. It collected evidence showing both cost-saving and improvement in quality of life in heart failure patients who were treated with parenteral diuretics in the community. The main outcomes for patients included:

- Reduced hospital admissions
- Supported early discharge
- Provided a better experience for patients and carers
- Supporting people when their condition becomes more advanced
- Enable people to have choice to remain at home during end of life care

Purpose of Guidelines

These guidelines have been developed to provide a template in the Mersey and Cheshire region to facilitate the administration of parenteral diuretics in an out of hospital setting or as a day case. The guidelines are intended to be adapted locally to reflect local services and resources available.

This protocol aims to offer patients an option for parenteral diuretics via two routes of administration

Section 1: Guidelines for the administration of ambulatory and community intravenous (IV) diuretics for patients with heart failure:

- Prevention of hospital admission, facilitation of early discharge and for symptomatic management of palliative patients.

Section 2: Guidelines for the administration of subcutaneous (SC) diuretics to patients with heart failure who are approaching the end of life:

- when a person is judged by the multi professional clinical team to be approaching the end of life they may be considered for SC diuretics at home or within the Hospice setting to aid symptom control.

SECTION 1: Guidelines for the administration of ambulatory and community intravenous (IV) diuretics for patients with Heart Failure

1.1 Guidelines for provision of community IV diuretics in decompensated heart failure

Consider patient groups that may be suitable for ambulatory and community IV diuretics for:

- Prevention of acute hospital admission
- To facilitate early discharge

1.2 Patient Selection

1. Suitable patients should be identified following assessment by an appropriate Heart Failure Specialist.
2. The Heart Failure team will assess the patient and ensure oral medication has been optimised. If there is an insufficient response to oral diuretics, a referral will be made to your local service.
3. The community or hospital-based Heart Failure team will assess, prescribe and organise IV administration. This may involve liaising with other appropriate health care professionals for administration purposes.
4. Patients treated in the ambulatory unit or community to prevent admission to hospital would receive IV diuretics if they meet the appropriate criteria. These groups of patients are likely to have had previous episodes of decompensating heart failure and previously known to the Heart Failure service.

1.3 Route of Administration

Patients requiring administration of IV furosemide will require intravenous access. The peripheral cannula can remain in place for up to 7 days unless Visual infusion Phlebitis score (VIP) is > 0. If infusion is to continue over 7 days, long term venous access should be considered e.g. peripheral inserted central catherter(PICC) line.

Consideration should be given to:

- Device availability (requires an appropriate device to deliver a one hour metered dose), this could include an elastomeric pump, which is preferential in the community setting where available.
- Availability of frequent cannulation.
- Patient's condition/age/diagnosis/vascular condition.
- Type and duration of therapy (-including frequency of administration, volume and other concomitant IV therapy).
- Potential complications.
- Patient preference.

1.4 Patient Review and administration

Inclusion criteria

1. Patient consents to outpatient or community management as alternative to hospitalisation
2. Diagnosis of decompensated heart failure as defined by the local Heart Failure Service
3. Patient known to or discussed with and/or under supervision of Consultant Cardiologist
4. Heart failure confirmed as ongoing / current cause of symptoms (no reversible causes identified)
5. Failure to relieve fluid overload by:
    a. Life-style measures including fluid restriction
    b. Patients on Furosemide could be considered to be switched to Bumetanide whilst considering intravenous diuretics (Bumetanide 1mg is considered to be equivalent to Furosemide 40mg)
    c. After consideration of a thiazide or thiazide-like diuretic
    d. If evidence of symptomatic hypotension, consider stopping non-heart failure (non-prognostic) antihypertensives (e.g. amlodipine, doxazosin etc.) avoiding abrupt withdrawal of beta-blockers due to the risk of rebound tachycardia
    e. Consider non-cardiac medications such as tamsulosin which may reduce blood pressure and discuss with the relevant clinician for advice
    f. Consider change in administration to night-time, split dose, temporary reduction or withdrawal of ACEi/ARB/sacubitril valsartan/MRA's if necessary for hypotension
6. Fluid retention as evidence by peripheral oedema extending above the knee/ below knee if accompanied by worsening breathlessness, orthopnoea or PND and /or weight gain of > 3kg above dry weight
7. Renal stability (eGFR ≥ 20ml/l/min) and stable for the preceding 2 months, though this may not necessarily be a deterrent to use, providing the dose is carefully titrated and monitored after discussion and agreement with a Cardiologist, unless discussed with renal team or palliative care
8. To facilitate early discharge patients must have tolerated IV furosemide (bolus or infusion) and on-going treatment is anticipated in an ambulatory patient who wishes to be discharged from hospital. Renal function must be considered as per point 6
9. Patient has sufficient and appropriate social/family /carer support
10. Patient or carer able to give informed consent to ambulatory or community IV diuretic therapy.
11. Patient able to weigh themselves / be weighed daily
12. Consideration should be made of patients with frailty and/or at risk of falls
13. Patients with pleural effusions can be considered for IV administration in the ambulatory or community setting if agreed with a cardiologist/specialist team
14. Patients with pulmonary oedema can be considered for ambulatory or community IV diuresis, if agreed by HF team to be palliative and clear discussion undertaken with patient and next of kin regarding advance care planning

Exclusion criteria

1. Difficult IV access (unless long term IV line in place or being considered)
2. Symptomatic hypotension (consider reduction or withdrawal of antihypertensive medication as per 5d, 5e and 5f of the inclusion criteria before excluding) or other features of haemodynamic instability as decided by HF team
3. Insufficient carer support
4. Pulmonary oedema with signs of uncontrolled respiratory distress and still for active HF management . If this is an expected result of on-going treatment then consideration of palliative medication to control symptoms should be considered eg opioids
5. Ongoing ACS / ventricular arrhythmias/ pulmonary oedema, other medical conditions that would warrant hospitalisation (e.g. GI bleeding, pneumonia requiring IV antibiotics etc)
6. Complex social issues that need addressing
7. Patients deemed to have a risk of falls
8. Patients with pulmonary oedema can be considered for ambulatory or community IV diuresis, if agreed by HF team to be palliative and clear discussion undertaken with patient and next of kin regarding advance care planning

1.5 Assessment, administration and monitoring

- Patient assessed as per inclusion/exclusion criteria and agreed to start IV furosemide.

Initial Assessment:

- Undertake a full clinical review of the patient including BP, HR, oxygen saturation, weight, fluid status and cardiorespiratory examination. Assess patients for signs and symptoms of heart failure
- Pending investigations such as echocardiography should not be delayed due to ambulatory or community management
- If symptomatic hypotension reduce/stop other antihypertensives (avoid stopping beta-blockers/RAASi therapy see point 5d-5f)
- Check U+E's – see table 2
- Peripheral cannula insertion - cannula can remain in place for up to 7 days unless Visual Infusion Phlebitis score (VIP) of > 0
- If the infusion site (if already in-situ) has evidence of systemic infection, admission will be required
- If localised phlebitis/infection at puncture site, cannula to be removed and the clinician to review and treat or refer accordingly
- **Advise patient to omit oral diuretics on the day of IV administration**

Initiation of Diuretics

- Commence at the equivalent dose or increase by one dose increment if clinically appropriate, no later than 4pm (see table 1)
- Maximum rate of IV furosemide administration is 4mg/min
- Dilute if necessary in lowest required volume of sodium chloride 0.9%. Glucose solutions are unsuitable
- PO diuretics have approximately 50-60% bioavailability with wide interpatient variability vs. IV diuretics which has 100% bioavailability
- Monitor more closely for hypotension and signs of ototoxicity in high doses above 240mg.

Table 1: Diuretic Equivalent doses

PO furosemide	PO bumetanide	IV furosemide	Infusion time
40mg	1mg	40mg	N/A
80mg	2mg	80mg	N/A
120mg	3mg	120mg	30 mins
160mg	4mg	160mg	40 mins
200mg	5mg	200mg	50 mins
240mg	6mg	240mg	60 mins
280mg	7mg	280mg	70 mins
320mg	8mg	320mg	80 mins
400mg	10mg	400mg	100 mins
440mg	11mg	440mg	110 mins
480mg	12mg	480mg	120 mins

Ongoing monitoring

- Cardiorespiratory examination, HR, BP, SP02, weight, fluid balance and symptoms.
- If symptomatic low BP, stop or reduce other antihypertensives
- Infusion site: if evidence of systemic infection, admission will be required. If localised infection at puncture site, the clinician will need to review and treat, or refer accordingly
- Renal function and electrolytes – see table 3

Table 2: Monitoring of Renal Function and Electrolyte

Table 3: Monitoring of Renal Function and Electrolytes		
U+E	**Levels**	**Initial assessment and monitoring of renal function during IV administration**
Potassium	< 4mmol/l	Short course of oral potassium supplements and dietary advice. If continues to fall, consider an MRA and discuss with HF team/cardiology team/on-call team
	> 5.5 - < 6.0mmol/l	Stop K+ supplements, K+ sparing diuretics and consider reducing / stopping ACEi /ARBs MRA's or sacubitril/valsartan. Consider haemolysis if other results stable and repeat.
	> 6.0mmol/l	As above and arrange ECG, discuss with on call medical/ cardiology team and consider admission
Sodium	127-125mmol/l	With no symptoms of hyponatremia, consider stopping medication known to reduce sodium including MRAs/ACE inhibitors/antidepressants/PPI's.
	< 125mmol/l	As above or if symptomatic hyponatremia, discuss with on call medical/ cardiology team and admit to hospital.
Creatinine	a) Increase of up to 30% of baseline b) Increase of 30-50% c) Increases of >50% of baseline or >300umol/l	a) Acceptable particularly if patient improving with weight loss on diuretics b) May require reduction in RAASi therapy dose with plan to re-uptitrate when back on oral diuretic and renal function recovers to baseline c) Temporarily reduce / stop medictions such as RAASi therapy with a clear plan to restart if HFrEF for prognostic value. If HFpEF, RAASi may be withheld during IV diuretic therapy based on local protocol If creatinine continues to increase then discuss with cardiologist

- Point of care (POC) UEs are recommended for use in the community IV setting due to the requirement for prompt correction of electrolyte disturbances such as hypokalemia and the risks of delays in lab results or haemolysis of samples

Failure to respond to IV diuretic regime

- Increase loop diuretic by 40mg increments of furosemide (to a maximum of 480mg Furosemide daily) or 1mg increment of bumetanide (to a maximum of 12mg daily)
- Consider addition of thiazides and thiazide-like diuretic orally (if not already prescribed), either daily or on alternate days
- IV furosemide at doses >240 mg up to 480 mg can be considered in hospital ambulatory HF Units as per Table 2
- If no response i.e. improvement of symptoms and weight loss within 72 hours or locally timeframe, then consideration if hospital admission may be appropriate or to discuss with the Lead Clinician/Cardiologist or Palliative Care Team for consideration for end of life care measures

Table 3: Diuretic Equivalent doses			
PO furosemide	PO bumetanide	IV furosemide	Infusion time
280mg	7mg	280mg	70 mins
320mg	8mg	320mg	80 mins
360mg	9mg	360mg	90 mins
400mg	10mg	400mg	100 mins
440mg	11mg	440mg	110 mins
480mg	12mg	480mg	120 mins

Monitoring and follow up after completion of IV diuretics

- Patients should have IV diuretics converted to an appropriate oral dose when clinically appropriate. Careful monitoring of electrolytes and weight should continue once oral diuretics are restarted (initial U+E within a week)
- Once IV diuretics are no longer required, the oral dose of diuretic should be determined with the Heart Failure team considering the IV diuretic dose, clinical response and renal function
- The patient should be referred to the appropriate community heart failure/hospital heart failure team to arrange ongoing follow up as soon as possible
- A transfer of care letter/discharge should be completed to both GP and referrer

1.7 CONSENT

Prior to commencing community IV diuretics, a verbal explanation and information leaflet will be provided to the patient (Appendix B) and verbal consent obtained.

1.8 LOCATION

Where community services have ability and if indicated by patient need, IV furosemide should be administered in the patients home. Where there are safety concerns or clinical need, day-case administration under the above guidelines could be provided in the ambulatory setting.

1.9 INFUSION PUMP

This can be similar to that used in hospital or a portable elastomeric infusion pump (which requires training and SOP). The elastomeric portable pump does not require electricity, allows patients to easily mobilise during infusion, as it is portable. However elastromeric pumps are single -use and expensive. This is particularly beneficial for use in the community setting.

2.0 OUTCOME MEASURES

At the end of each episode, audit data should be completed to assess this service – see appendix C

- Duffy, D. The NHS must break the cycle on heart failure. 2023;https://integratedcarejournal.com/the-nhs-must-break-the-cycle-on-heart-failure/
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- Savarese, G., Becher, P. M., Lund, L. H., Seferovic, P., Rosano, G. M. C., & Coats, A. J. S. Global burden of heart failure: A comprehensive and updated review of epidemiology. *Cardiovascular Research, 2023 118*(17), 3272-3287. https://10.1093/cvr/cvac013
- NHS England. *Managing heart failure @home.2022;* Retrieved Nov 16, 2023, from https://www.england.nhs.uk/nhs-at-home/managing-heart-failure-at-home/

SECTION 2: Guidelines for the administration of subcutaneous (SC) diuretics for heart failure patients approaching end of life.

2.1 Background

Subcutaneous (SC) administration of furosemide is unlicensed in the UK but has been used with success (Dickman & Schneider 2016). Subcutaneous furosemide could be considered in end-stage heart failure patients requiring parenteral diuresis for symptom control within the hospice or community setting.

Symptomatic management of dyspnoea using opiates and/ or benzodiazepines and non-pharmaceutical measures should be initiated as necessary alongside parenteral diuretic therapy.

2.2 Patient Selection

1. Suitable patients should be identified following assessment by an appropriate Heart Failure or Palliative Care specialist, in agreement with the patient's GP.
2. The Community Heart Failure or Palliative Care team will assess and organise subcutaneous administration via a syringe driver. This will involve liaising with other health care professionals including GP, district nurses or community matrons as appropriate.
3. Consideration should be given to the practicalities of administering a diuretic for patients whom cannot transfer to a toilet or commode and do not have a catheter in situ.

Inclusion Criteria

- End stage heart failure patients who are unresponsive to high dose oral diuretics with poor or no venous access.
- End stage heart failure patients who wish to avoid hospital admission/ attendance for whom administration with IV diuretics in the community cannot be facilitated.
- End stage heart failure patients who decline/can not tolerate IV diuretic therapy.
- End stage heart failure patients in the last days of life who require ongoing administration of diuretics for symptomatic relief.

Exclusion Criteria

- No identifiable symptomatic benefit from high dose IV or SC diuretic therapy.
- Severe site reaction to SC administration of furosemide.

2.3 Prescribing and Administration

- Furosemide ampoules have a concentration of 10mg/ml and are available in 2ml, 5ml or 25ml ampoules.
- Use the previous oral 24 hour requirement as a continuous SC infusion over 24 hours, as a starting dose and titrate up or down according to response. Convert the bumetanide dose to furosemide as per table 1 in section 1.
- Furosemide should be used as a solitary agent in a syringe driver and should not be mixed with other medication.
- A maximum dose of 200mg in 24 hours may be administered via a single 30ml syringe driver. Smaller doses may be administered using smaller syringe sizes where necessary.
- Furosemide may be used undiluted in a syringe driver. If a diluent is required, sodium chloride 0.9% should be used. The injection is alkaline and **must not** be mixed or diluted with glucose solutions or other acidic fluids due to risk of precipitation.
- Exposure to light may cause degradation and discolouration, the solution should not be used if a yellow colour is present. Furosemide 10mg/ml in polypropylene syringes is stable at 25oC in normal light for 24 hours. Ensure that the driver is not exposed to light, by covering or using a holder.
- Reference should be made to local instructions and guidance on the general use of syringe drivers.

2.4 Recommended infusion sites for SC administration

- Upper chest.
- Upper anterior aspect of arms.
- Sites are restricted in heart failure patients because of probable oedema.
- Sites to be avoided are bony prominences and areas where tissue is damaged, thus decreasing absorption. If possible, use a site away from areas where tattoos are present as these may mask site reactions.
- If there is very poor peripheral perfusion in the terminal stage, subcutaneous absorption may be limited.

2.5 Monitoring

- Usually, careful monitoring of renal function and U+Es is required for parenteral administration of diuretics, but this may be less important when diuretics are administered for symptom control. The heart failure or palliative care team will advise regarding the appropriate frequency of blood tests and monitoring. However, during the last few days of life it is not appropriate to monitor weight or renal function.
- SC administration can be associated with pain and itching at the site of injection. This may necessitate cessation of treatment.

2.6 Contraindication and Precautions

For patients in the final days of life, while the prescriber must consider these contraindications and precautions, they may not necessarily be a deterrent to use, providing the dose is carefully titrated. The conditions include:

- Anuria
- Comatose or pre-comatose states associated with hepatic cirrhosis
- CrCl<30ml/min per 1.73m^2
- Dehydration
- Drug-induced renal failure
- Hypersensitivity to sulphonamides
- Hypovolaemia or hyponatraemia

2.7 Definitions

Palliative

Palliative care is an approach that improves the quality of life of patients and their families facing life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual……It may be done alongside treatment intended to reverse particular conditions.

WHO (2002)

End of Life

Patients are 'approaching the end of life' when they are likely to die within the next 12 months. This includes patients whose death is imminent (expected within a few hours or days).

Leadership Alliance for Care of Dying People. One chance to get it right (2014)

Care of the dying

Care needed when a person is judged by the multi professional clinical team to be within a few (2-3) days of death.

NICE Guidance on care of dying adults in the last days of life (2015)

Verma AK, da Silva JH, Kuhl DR. Diuretic effects of subcutaneous furosemide in human volunteers: a randomized pilot study. *Ann Pharmacother* 2004;**38**:544–9.

Zacharias H, Raw J, Nunn A, *et al.* Is there a role for subcutaneous furosemide in the community and hospice management of end-stage heart failure? *Palliat Med* 2011;**25**:658–63.

APPENDICES

APPENDIX A Community referral form for community IV diuretics

IV SERVICE REFERRAL FORM

A completed prescription chart MUST be received prior to acceptance

Patient Name		
D.O.B		
NHS Number		
Address:		
Telephone no:		
Hospital/Ward if applicable	Tel No	
Cardiologist		
Heart Failure Nurse		
Patients GP practice	Tel No	
Patients NOK **Name** **Relationship**	Address Tel No	
Religion		
Ethnicity		
Diagnosis		
PMH		
Allergies		
Drug Name: Furosemide	Dosage	Frequency
	Infusion time	
Type of IV line **Type of Flush required**	Date of insertion…….. Date of removal……..	
Observations	BP HR Weight NYHA Oedema score	
U&E	Na K Urea creatinine e-GFR	
Is patient known to other agencies?	Y/N Details	
Monitoring and other needs		
Any other special instructions		

APPENDIX B Patient information leaflet

Home diuretic service - Patient Information Sheet

Background
People with heart failure are often admitted to hospital because of problems with fluid retention which happens because the heart is not pumping properly. This fluid can build up in the lungs which makes you feel short of breath and in your legs or abdomen which causes swelling and can be uncomfortable. Diuretics (often known as water tablets) work on the kidneys causing you to pass more urine so your body can get rid of this extra fluid. The most common diuretics are furosemide and bumetanide Sometimes the tablets, despite increasing the dose are not effective in getting rid of the extra fluid so diuretics are then given by injection to relieve this fluid overload.

Intravenously: A cannula is inserted into a vein and the diuretic is given by infusion over a few hours. You may have already received this treatment on previous admissions to hospital with your heart failure condition. It is now possible to have this treatment at home. A healthcare professional will come to your home to start the infusion and take you off the infusion when it has finished. Blood tests will be done as needed.

Subcutaneously: this is where a cannula is placed under the skin (can be inserted in different places such as the abdomen, arm or leg) and the diuretic is given by a small machine over 24 hours. Blood tests will be done as needed and a healthcare professional will monitor you at home.

What are the advantages of having this treatment at home?
The main advantage of this treatment is that it can be given to try and avoid you having to be admitted to hospital due to your heart failure or sometimes if you are in hospital you can be discharged earlier.

What are the disadvantages of having this treatment at home?
When you are in hospital there are doctors and nurses available 24 hours a day. At home you will not be as closely monitored and your family member or carer may need to be at home to help look after you.

What are the side effects?
These are the same whether diuretics are given intravenously or subcutaneously.
The most common problems are:
1) Dizziness on standing due a drop in blood pressure (postural hypotension). If this does happen then the dose may need to be reduced and your other tablets altered.
2) Passing more urine. If the diuretics work you may need go to the toilet more frequently than usual. You need to be able to get to the toilet/commode easily or have a urine bottle close to hand. If you find it difficult to get out of bed then a catheter may be needed (a tube inserted into the bladder) to make it easier for you.
3) Changes in your kidney function. Diuretics can affect your kidneys so regular blood tests may be needed so that we can monitor for any changes and alter your treatment if needed.
4) Soreness or inflammation where the cannula is inserted. The site where the cannula is inserted will be checked by the nurse every time the infusion is set up and when it has finished.
If any soreness develops at the site then it can be changed to a different area. If any infection has developed you may need antibiotic treatment.
5) Gout may occur with higher doses of any diuretics.
6) There is a small risk of hearing disorders and tinnitus (ringing in the ear). Although uncommon, deafness may occur which may not always be reversible.

What if it does not work?
If that happens then the team will discuss with you what your wishes are and what other options can be tried, they will liaise with your heart failure nurse and GP. You may need to go into hospital for more treatment or you may decide to stay at home. You may have already completed an advance care plan stating what your preferences for care are and the team can discuss this further with you.

Who provides this service?
This service will be provided by the hospital at home team. This is a group of health care professionals comprising of doctors and advanced nurse practitioners who specialize in providing care in the home.

What if there is a problem (harm, risks, complaints procedure)?
If you suffer from any adverse effect then the treatment will be reviewed and stopped following discussion with yourself and the members of the healthcare team. The treatment can also be stopped at any time at your request. You will be given the contact numbers for the team members involved in your care and out of hours contact numbers. If you have questions or concerns regarding your treatment and care you should ask to speak to the heart failure nurse who will do their best to answer your questions

You can also contact the following people for further information and advice - Local numbers would need to be included when adapted locally

APPENDIX C Audit/Outcome data

Community Intravenous Diuretic Outcome Measures

Patients Name :	**Hospital Number/ NHS Number :**
	Treatment start date:
Aim of Treatment (Please tick one box)	Treatment finish date:
Admission avoidance □	Duration of treatment:
Early discharge □	Max dose of diuretic dosage:
End of life care at home □	Route of administration: IV □

Measures	**Start Date**	**Finish Date**	**Outcome** (Please tick one box)
NYHA			Clinic/Home visit FU □
			Hospital admission □
Weight (kg)			Hospice admission □
Oedema level			Death □

PERIPHERAL OEDEMA SCORE				
0	**1**	**2**	**3**	**4**
None	Ankle only	Below knee	Above knee	Sacral /abdomen

NYHA CLASSIFICATION	
Class 1	Asymptomatic, no limitation, can perform all activities without any breathlessness or fatigue despite the presence of heart disease
Class 2	Mild, slight limitation of physical activity
Class 3	Moderate, marked limitation of physical activity, comfortable at rest, but activity results in breathlessness and fatigue
Class 4	Severe, unable to carryout physical activity without discomfort. Symptoms present even at rest