Royal Cornwall Hospitals
NHS Trust

# Isoprenaline Infusion for the Management of Life-Threatening Bradycardia Policy

## V2.0

## July 2024

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**Data Protection Act 2018 (UK General Data Protection Regulation – GDPR) Legislation.**

The Trust has a duty under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed, and documented. We cannot rely on opt out, it must be opt in.

Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the Data Protection Act 2018 and UK General Data Protection Regulations 2016/679 please see the Information Use Framework Policy or contact the Information Governance Team.

Royal Cornwall Hospital Trust rch-tr.infogov@nhs.net

# 1. Introduction

1.1. Isoprenaline is a non-selective β-adrenergic agonist. It has positive inotropic and chronotropic effects, increasing cardiac output by increasing the heart rate and cardiac contractility. Isoprenaline also decreases diastolic blood pressure by lowering peripheral vascular resistance. The aim of an isoprenaline infusion is to maintain end-organ perfusion whilst waiting definitive pacing for life-threatening bradycardia.

1.2. Bradycardia is a common finding which requires careful and thorough assessment to correctly establish the underlying diagnosis and determine the appropriate therapy. Bradycardia is often a benign condition requiring no intervention, but when it gives rise to symptoms or results from conduction abnormalities that are associated with an adverse prognosis, cardiac pacing may be required unless a reversible and remediable cause can be identified. In daily medical practice, bradycardia is a common finding that ranges from the usually benign sinus bradycardia to sinus arrest and complete atrioventricular block. Before suitable therapy can be chosen for the individual patient, it is essential to perform a thorough diagnostic work-up to establish the type of bradycardia, to evaluate associated symptoms, to identify potentially reversible causes, and to estimate the risk of severe consequences.

1.3. This version supersedes any previous versions of this document.

1.4. Basic points on the cardiac conduction system:

- Baseline heart rate is balance between parasympathetic and sympathetic nervous systems.
- ‘Normal’ heart rate is 60-100 beats per minute.
- Normal range depends on age, gender, training status and time of day.
- At rest or during sleep, rates as low as 40bpm may be normal in healthy subjects.
- Heart rate should fluctuate physiologically during respiration, Valsalva manoeuvre and other vagal manoeuvres.

1.5. Important points on bradycardias and conduction disorders:

- Symptoms depend on cardiac output, defined as the product of left ventricular stroke volume and heart rate.
- Changes in stroke volume can compensate for reduced heart rate, and even patients with profound bradycardia may remain asymptomatic and it is common to see associated high systolic blood pressure.
- Most dramatic symptom is syncope or near syncope. *Cardiac standstill of > 6 sec is generally required before complete loss of consciousness.*
- Usual symptoms can be non-specific and chronically recurring; transient dizziness, light-headedness or confusional states (reflecting cerebral

hypoperfusion), episodes of fatigue or muscular weakness with exercise intolerance.

- More overtly, there can be symptoms and signs of heart failure, reflecting the reduced cardiac output, with breathlessness at rest or on exercise, especially if there is pre-existing left ventricular dysfunction.

1.6. Atrioventricular blocks:

First-degree AV block: (Figures 1, 2):

- Prolonged PR interval to > 200msec.
- If QRS narrow, delay is usually in AV node.
- If QRS wide, delay may be either in AV node or in the His-Purkinje system.
- Does not cause bradycardia unless it progresses intermittently to higher degree block.

**Figure 1 (1st degree AV block)**

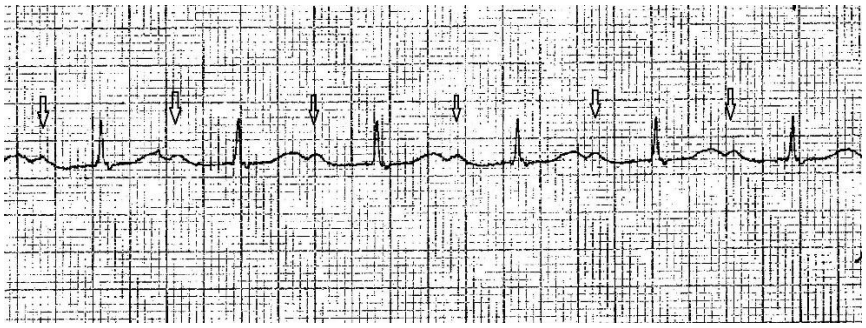
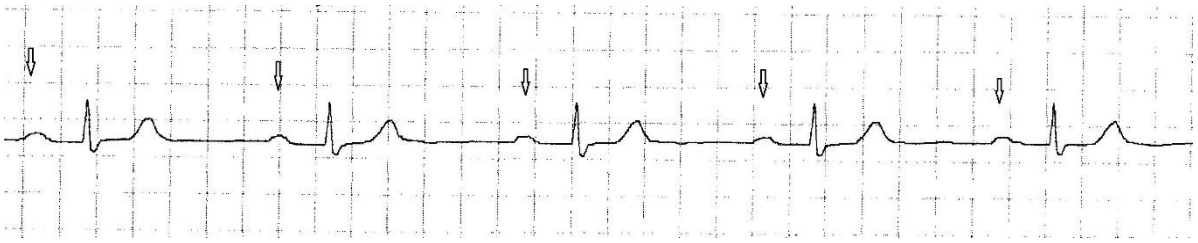


**Figure 2 (1st degree AV block)**

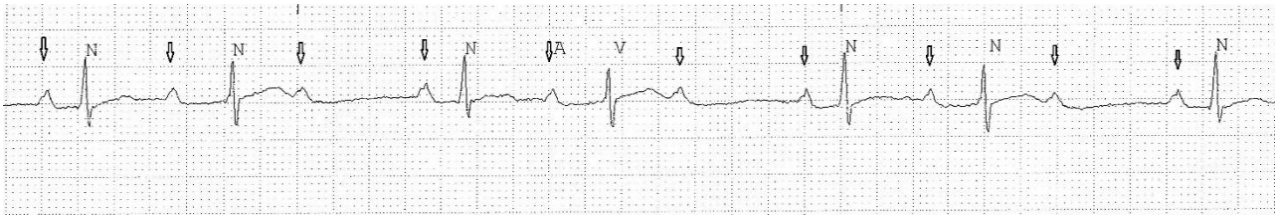


1.7. Second degree AV block, Mobitz I (Weckenbach): (Figure 3)

- Progressive increase in PR intervals until a P wave is not conducted.
- P-P interval relatively stable in cycle.
- R-R interval progressively shortens.
- Cycles of P:QRS groups repeat in ratios of 3:2 or 4:3 or 5:4.
- Usually originates in AV node – progressive fatigue of dysfunctional cells.
- Deterioration to higher degree AV block is uncommon.

- Can be non-pathological vagal response in young, healthy and fit individuals, when the PR at the start of the cycle is normal.
- May represent significant conduction disorder in older individuals and when PR interval already prolonged at beginning of cycle or wide QRS.
- Usually not indication for pacing, unless red flag symptoms (see Table 1).

**Figure 3 (2nd degree AV block, Mobitz I / Weckenbach)**




1.8. Second degree AV block, Mobitz II: (Figures 4 to 7)

- Abrupt conduction failure with non-conducted P waves.
- Can have a regular pattern 2:1, 3:1 etc. but not always.
- PR interval is constant before and after the blocked P wave.
- If QRS narrow, origin is usually in the bundle of His.
- If QRS broad, origin is infra-Hisian ('bilateral bundle branch block').
- Often progresses to complete AV block.
- Usually structural, rather than functional problem.
- Associated with ischaemia (MI involving septum), fibrosis, inflammatory conditions (myocarditis, Lyme), autoimmune disease (SLE, systemic sclerosis), infiltrative disease (cardiac amyloidosis, sarcoidosis, haemochromatosis).
- Requires pacing.

**Figure 4 (2nd degree AV block, Mobitz II, 2:1 block)**

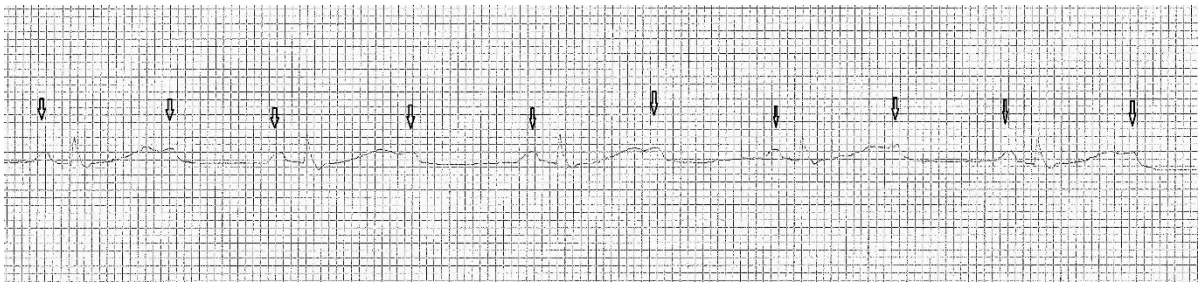


**Figure 3 (2nd degree AV block, Mobitz II, 2:1 block)**

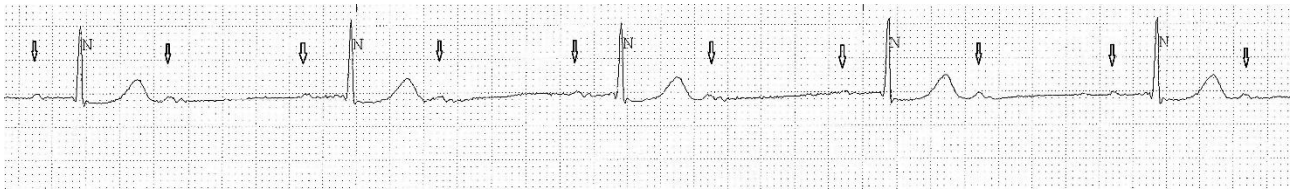


**Figure 6 (2nd degree AV block, Mobitz II, 2:1 block)**

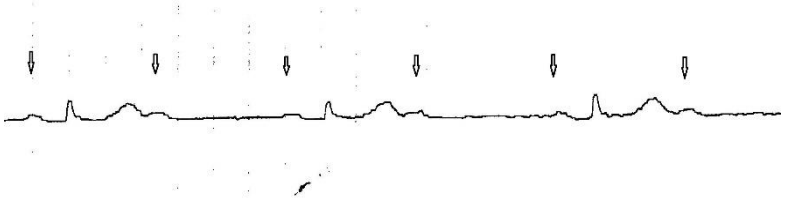
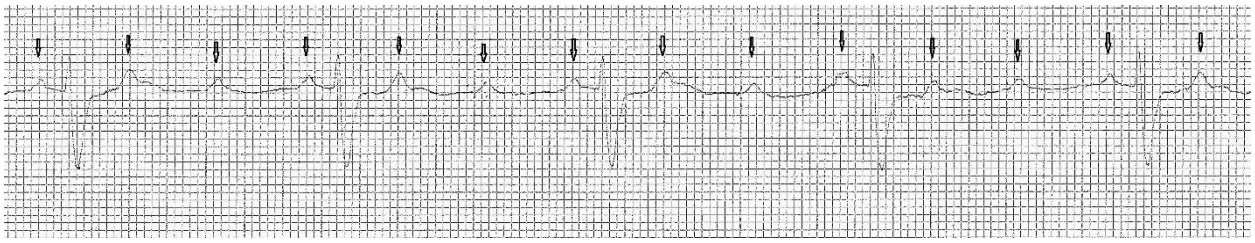


**Figure 7 2nd degree AV block, Mobitz II, 3:1 block)**



1.9. Third degree (complete) AV block: (Figures 8, 9)

- Complete dissociation of atrial and ventricular activity.
- No atrial stimulus conducted to ventricles. Ventricles depolarised by escape rhythm.
- Site of escape rhythm of major importance for patient symptom and safety.
- Supra-Hisian block gives junctional rhythm with narrow QRS, rates 40-60bpm – often better tolerated symptomatically.
- Infra-Hisian block gives wide QRS complexes with slower heart rate – therapeutic intervention needed more urgently.
- Risk of syncope, ventricular standstill, sudden cardiac death and torsade de pointes.
- Requires pacing.

**Figure 8 (3rd degree AV block)**

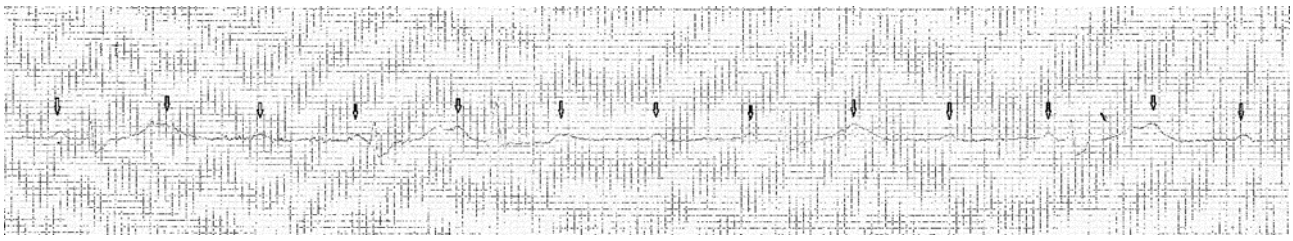
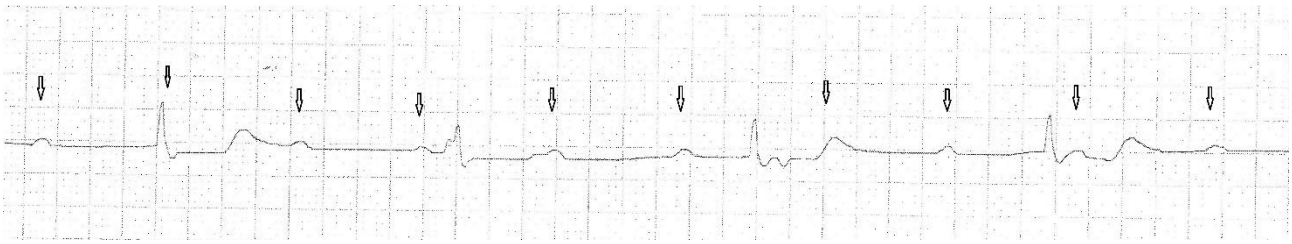


**Figure 9 (3rd degree AV block)**



| Table 1 – Red flag symptoms suggesting significant bradyarrhythmia |
| --- |
| • Abrupt syncope with little or no prodrome.<br>• Syncope or presyncope at rest (sitting or lying down).<br>• New onset exertional dyspnoea or dizziness/presyncope. |

# 2. Purpose of this Policy/Procedure

2.1. Although the gold-standard treatment for symptomatic bradycardias is the implantation of a permanent pacemaker, this is not always possible or expedient in the clinical setting in which a patient with symptomatic bradycardia presents.

2.2. There is a role for pharmacological treatment as a bridge to definitive treatment in patients who are not able to receive an emergency pacemaker implantation and are haemodynamically unstable or demonstrate signs of reduced cardiac output and reduced end-organ perfusion, as well as patients who deteriorate clinically while awaiting pacemaker implantation.

# 3. Scope

This document provides guidance for any professional involved in the clinical management of patients presenting to either primary care in the Isles of Scilly or to the Royal Cornwall Hospital NHS Trust with a life-threatening bradycardia. This will include:

- GPs.
- Specialist Nurses.
- Junior Doctors.
- Speciality Registrars.
- Consultants.

# 4. Definitions / Glossary

Life-threatening bradycardias include:

- Symptomatic second degree AV block (Mobitz type I / Weckenbach). Symptoms and signs include syncope/loss of consciousness which has abrupt onset and has no other obvious clinical explanation, dizziness, signs of reduced cardiac output. This is especially pertinent in older patients and those with already prolonged PR interval at the beginning of each cycle.
- Second degree AV block (Mobitz type II) – irrespective of symptoms.
- Third degree (complete) AV block – irrespective of symptoms.
- Sick sinus syndrome (NOT an indication for Isoprenaline).
- Episodes of ventricular standstill.

# 5. Ownership and Responsibilities

This section provides a detailed overview of the strategic and operational roles responsible for the development, management, and implementation of this policy/procedure.

## 5.1. Role of the Clinical Lead in Cardiology

Reviewing this document every 3 years (or sooner if new, relevant national guidelines are published.

## 5.2. Role of the Managers

Line managers are responsible for:

- Ensuring staff are aware of, and act upon, the Trust's procedural documents.
- Implementing the procedural documents for the areas in which they apply.
- Notifying all new and existing staff on how to access both current and archived Trust procedural documents.
- Ensuring that all staff members have access to the Trust intranet site to enable access to published procedural documents.
- Ensuring that all staff members are aware of their responsibility in maintaining.

## 5.3. Role of the Cardiology speciality governance Group

The Cardiology speciality governance Group is responsible for:

- Signing off the reviewed document prior to upload to the document library.

### 5.4. Role of Individual Staff

All staff members are responsible for:

- Making themselves aware of the procedural documents that relate to their role and responsibilities.
- Complying with agreed Trust procedural documents where they apply.
- Raising any queries about implementation of Trust documents with their line manager.
- Alerting their line manager of any non-compliance with procedural documents where it is noted and represents an actual risk to the Trust, its staff, patients or the public.
- Contacting the CITS Service Desk (01209 881717) if experiencing difficulties accessing the electronic Document Library.

## 6. Standards and Practice

### 6.1. Indications

6.1.1. Heart block or bradycardia causing haemodynamic instability or organ dysfunction (i.e. reduced level of consciousness, reduced urine output):

- Symptomatic life-threatening bradycardia not responding to Atropine (e.g. hypotension / syncope / myocardial ischaemia / heart failure).
- Mobitz Type 2 Atrioventricular block.
- Complete Heart Block with broad QRS complexes.
- Ventricular pauses of > 3 seconds.
- Recent asystole.

6.1.2. Aim to maintain end-organ perfusion whilst waiting definitive pacing. **Note that the absolute heart rate alone is not an indication for isoprenaline use – most patients with complete heart block tolerate bradycardia for a variable period.**

6.1.3. Do not try to uptitrate Isoprenaline rate to achieve a heart rate target. As long as the patient is haemodynamically stable and tissue perfusion is maintained, low heart rate is acceptable.

6.1.4. Rapid uptitration of isoprenaline infusion is poorly tolerated by most of the patients and adverse effects become more pronounced.

## 6.2. Contra-indications:

- Patients with intermittent tachycardic rhythms (sick sinus syndrome, tachy-brady syndrome, recently documented tachycardias, VF arrest secondary to bradycardia).
- Bradycardia caused by digitalis toxicity.
- Relatively contraindicated in ischaemic heart disease (may precipitate or exacerbate coronary ischaemia or infarction), diabetes, hyperthyroidism.
- Use with caution in elderly patients, who are vulnerable to significant confusion or agitation.

## 6.3. Required monitoring and equipment:

- Continuous three-lead cardiac monitoring, automated blood pressure.
- Pulse oximetry.
- Confirmatory 12-lead ECG of underlying rhythm.
- High dependency area: Resus, HDU or CCU, with senior medical supervision.
- Appropriate infusion pump.

## 6.4. Pre-administration requirements:

- In working hours, please discuss with the on-call Cardiologist as urgent permanent pacing may be more suitable for some patients, and temporary pacing may be required if pharmacological therapy fails.
- Check electrolytes (potassium, magnesium, and calcium) and thyroid function. Stop negatively chronotropic drugs.
- Ensure systemic causes for bradycardia have been addressed.
- Treat any hypovolaemia.
- Ensure other causes of end organ hypoperfusion have been considered (anticipate hypoperfusion which appears ‘refractory’, e.g.: severe left ventricular failure, sepsis.

## 6.5. Dose, Infusion preparation and Conversion table

6.5.1 Isoprenaline may be difficult to obtain, and currently can only be supplied as an unlicensed product. RCHT usually stock the 5mg/5ml Isoprenaline Hydrochloride, but occasionally stock a 1mg/1ml or 0.2mg/1ml product.

6.5.2 To create the infusion using 5mg/5ml draw up 2ml Isoprenaline for each 500ml infusion bag.

(Note: 2.25mg Isoprenaline sulphate is equivalent to 2mg Isoprenaline hydrochloride, if this product is obtained then adjust accordingly).

6.5.3 Isoprenaline is compatible with 5% Dextrose, Normal saline and Hartmann's. Dextrose is preferable due to Isoprenaline being acidic.

6.5.4 The Trust-wide standard infusion is created by using 2mls of Isoprenaline hydrochloride 5mg/5ml drug constitution into 498mls 5% Dextrose solution. The resultant concentration is 4 micrograms per millilitre.

6.5.5 **Table 2:**

| Desired rate of Isoprenaline infusion | Pump setting (using 2mg/2ml Isoprenaline Hydrochloride in 498ml of 5% Dextrose) **(4 micrograms/ml)** |
|---|---|
| 1 microgram/min | 15ml/hr |
| 2 micrograms/min | 30ml/hr |
| 3 micrograms/min | 45ml/hr |
| 4 micrograms/min | 60ml/hr |
| 5 micrograms/min | 75ml/hr |

## 6.6. Recommendation

6.6.1. Isoprenaline should be started at a low dose (1 micrograms/min) and titrated slowly by 1-2 micrograms/min every 2-3 minutes until satisfactory response is achieved – there is no minimum heart rate target and low doses are often all that is required to prevent compromising bradycardia or asystole.

6.6.2. Maximum recommended infusion dose is 10 micrograms/min.

## 6.7. Side-Effects

- Tachycardia.
- Hypertension.
- Dysrhythmia.
- Angina.
- Increase in myocardial ischaemic area.
- Syncope.
- Confusion.
- Headache.

- Tremor.

### 6.8. General Information

- Isoprenaline is a non-selective $\beta_1$ and $\beta_2$ adrenoreceptor agonist with almost no effect on α receptors. $\beta_2$ adrenoreceptor stimulation in arteriolar smooth muscle induces vasodilation. It's inotropic and chronotropic effects elevate systolic blood pressure, while its vasodilatory effects tend to lower diastolic blood pressure. The overall effect is to decrease mean arterial pressure due to the $\beta_2$ receptors' vasodilation.
- Onset of action: Immediate.
- Duration of action (IV): 10–15 minutes.
- Plasma half-life = 2.5 to 5 minutes.
- Expect a response to a dose change within 2-3 minutes.
- Beta-blockers and Isoprenaline inhibit each other – patients on beta blockers may suffer significant hypertension.
- Arrhythmia risk is increased with use of inhaled anaesthetic agents.
- Drug interactions are possible with tricyclic and MAOi antidepressants (for a full list of interactions see Medscape reference below).
- Refer to Bradycardia ALS algorithm (Appendix 3). Isoprenaline infusion is an interim measure following failure to achieve adequate chronotropic effect with atropine whilst awaiting definitive pacing.

## 7. Dissemination and Implementation

7.1. This document will be disseminated electronically to all relevant stakeholders once published. It will also be available on the RCHT Document library.

7.2. These guidelines are widely discussed at the induction meetings of junior doctors especially in the Emergency department, Medical Assessment Unit and Cardiology Department.

7.3. User friendly posters with the guideline and pathways are displayed in all the relevant clinical areas.

## 8. Monitoring compliance and effectiveness

| Information Category | Detail of process and methodology for monitoring compliance |
|---|---|
| **Element to be monitored** | The management of life-threatening bradycardias. |
| **Lead** | Clinical lead in Cardiology. |

| Information Category | Detail of process and methodology for monitoring compliance |
|---|---|
| **Tool** | Adherence to guidelines will be monitored as part of the ongoing audit process on a Word or Excel template specific to the topic.**.** |
| **Frequency** | 12 monthly audit for monitoring the guideline, pathways and recommendations. Future reviews guided by the audit outcomes. |
| **Reporting arrangements** | The Annual report will be reviewed through the Cardiology Specialty audit and governance frameworks |
| **Acting on recommendations and Lead(s)** | The Clinical lead in Cardiology and Cardiology department will undertake subsequent recommendations and action planning for any or all deficiencies and recommendations within reasonable timeframes. |
| **Change in practice and lessons to be shared** | Required changes to practice will be identified and action will commence within 1 month of report review. A lead member of the Cardiology department will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders via the Cardiology Specialty audit and governance frameworks. |

# 9. Updating and Review

9.1. This document will be updated by the Clinical lead in Cardiology every 3 years.

9.2. Revisions will be made ahead of the review date if new, relevant national guidelines are published. Where the revisions are significant and the overall policy is changed, the Clinical lead in Cardiology will ensure the revised document is taken through the standard consultation, approval and dissemination processes.

9.3. Where the revisions are minor, e.g. amended job titles or changes in the organisational structure, approval will be sought from the Executive Director responsible for signatory approval and can be re-published accordingly without having gone through the full consultation and ratification process.

9.4. Any revision activity will be recorded in the Version Control Table as part of the document control process.

# 10. Equality and Diversity

10.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the Equality Diversity And Inclusion Policy or the Equality and Diversity website.

10.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

# Appendix 1. Governance Information

| Information Category | Detailed Information |
|---|---|
| **Document Title:** | Isoprenaline Infusion for the Management of Life-Threatening Bradycardia Policy V2.0 |
| **This document replaces (exact title of previous version):** | Isoprenaline Infusion for the Management of Life-Threatening Bradycardia Policy V1.0 |
| **Date Issued / Approved:** | July 2024 |
| **Date Valid From:** | July 2024 |
| **Date Valid To:** | July 2027 |
| **Author / Owner:** | Dr. Sen Devadathan, Cardiology Consultant.<br>Dr Thisara Samrawickrama.<br>Dr. Robert Taylor, Emergency Medicine. |
| **Contact details:** | 01872 252678 |
| **Brief summary of contents:** | This document provides context and guidance to health professionals involved in the management of patients presenting in secondary or primary NHS care with life-threatening bradycardia, requiring therapeutic interventions until the time of implantation of permanent pacemaker. |
| **Suggested Keywords:** | Isoprenaline, Bradycardia, AV block, Heart block. |
| **Target Audience:** | **RCHT:** Yes<br>**CFT:** No<br>**CIOS ICB:** No |
| **Executive Director responsible for Policy:** | Chief Medical Officer |
| **Approval route for consultation and ratification:** | Cardiology Speciality Group.<br>Emergency Department Governance team. |
| **Manager confirming approval processes:** | Racheal Pearce |
| **Name of Governance Lead confirming consultation and ratification:** | Siobhan Hunter.<br>Paul Evangelista. |
| **Links to key external standards:** | None required |

| Information Category | Detailed Information |
|---|---|
| **Related Documents:** | • http://reference.medscape.com/drug/isuprel-isoproterenol-342438#3<br>• Advanced Life Support 6th edition, Resuscitation Council UK.<br>• Injectable Medicines Guide. Isoprenaline Sulphate.<br>• A. J. Camm et al, The ESC Textbook of Cardiovascular Medicine, 2nd ed., 2009, Oxford University Press. |
| **Training Need Identified:** | No additional training needs. This is formalising the clinical practice. |
| **Publication Location (refer to Policy on Policies – Approvals and Ratification):** | Internet and Intranet |
| **Document Library Folder/Sub Folder:** | Clinical / Cardiology |

**Version Control Table**

| Date | Version Number | Summary of Changes | Changes Made by |
|---|---|---|---|
| May 2020 | V1.0 | Initial issue | Dr. Sen Devadathan, Consultant Cardiologist.<br>Dr. Efstathios Magkiosis, Cardiology Registrar.<br>Dr. Robert Taylor, Consultant in Emergency Medicine.<br>Dr. Fraser Gould, Emergency Medicine Registrar. |
| May 2024 | V2.0 | Full update and transposed to new template.<br>Added section 6.1.3 and 6.1.2.<br>Section 6.6.1 amended | Dr Sen Devadathan, Cardiology Consultant |

**All or part of this document can be released under the Freedom of Information Act 2000**

**All Policies, Strategies and Operating Procedures, including Business Plans, are to be kept for the lifetime of the organisation plus 6 years.**

**This document is only valid on the day of printing.**

**Controlled Document**

This document has been created following the Royal Cornwall Hospitals NHS Trust The Policy on Policies (Development and Management of Knowledge Procedural and Web Documents Policy). It should not be altered in any way without the express permission of the author or their Line Manager.

# Appendix 2. Equality Impact Assessment

## Section 1: Equality Impact Assessment (EIA) Form

The EIA process allows the Trust to identify where a policy or service may have a negative impact on an individual or particular group of people.

For guidance please refer to the Equality Impact Assessment Policy (available from the document library) or contact the Equality, Diversity, and Inclusion Team rcht.inclusion@nhs.net

| Information Category | Detailed Information |
|---|---|
| **Name of the strategy / policy / proposal / service function to be assessed:** | Isoprenaline Infusion for the Management of Life-Threatening Bradycardia Policy V2.0 |
| **Department and Service Area:** | Cardiology, Specialist Medicine |
| **Is this a new or existing document?** | Existing |
| **Name of individual completing EIA** (Should be completed by an individual with a good understanding of the Service/Policy): | Sen Devadathan, Cardiology Consultant |
| **Contact details:** | 01872 252678 |

| Information Category | Detailed Information |
|---|---|
| **1. Policy Aim - Who is the Policy aimed at?** (The Policy is the Strategy, Policy, Proposal or Service Change to be assessed) | To provide guidance and structure to the commencement of an Isoprenaline infusion within the Trust. |
| **2. Policy Objectives** | For medical and nursing staff to be able to safely prescribe and administer an Isoprenaline infusion when indicated. |
| **3. Policy Intended Outcomes** | Safe, timely prescription and drug administration. |
| **4. How will you measure each outcome?** | Internal audit |
| **5. Who is intended to benefit from the policy?** | Patients with life-threatening bradycardia |

| Information Category | Detailed Information |
|---|---|
| **6a. Who did you consult with?**<br>(Please select Yes or No for each category) | • Workforce: Yes<br>• Patients/ visitors: No<br>• Local groups/ system partners: No<br>• External organisations: No<br>• Other: No |
| **6b. Please list the individuals/groups who have been consulted about this policy.** | **Please record specific names of individuals/ groups:**<br>All Consultant Cardiologists.<br>Cardiology Speciality Group.<br>Emergency Department Governance team. |
| **6c. What was the outcome of the consultation?** | Approved |
| **6d. Have you used any of the following to assist your assessment?** | **National or local statistics, audits, activity reports, process maps, complaints, staff or patient surveys:**<br>No |

**7. The Impact**

Following consultation with key groups, has a negative impact been identified for any protected characteristic? Please note that a rationale is required for each one.

Where a negative impact is identified without rationale, the key groups will need to be consulted again.

| Protected Characteristic | (Yes or No) | Rationale |
|---|---|---|
| **Age** | No | |
| **Sex** (male or female) | No | |
| **Gender reassignment** (Transgender, non-binary, gender fluid etc.) | No | |
| **Race** | No | |
| **Disability** (e.g. physical or cognitive impairment, mental health, long term conditions etc.) | No | |
| **Religion or belief** | No | |

| Protected Characteristic | (Yes or No) | Rationale |
|---|---|---|
| **Marriage and civil partnership** | No | |
| **Pregnancy and maternity** | No | |
| **Sexual orientation** (e.g. gay, straight, bisexual, lesbian etc.) | No | |

**A robust rationale must be in place for all protected characteristics. If a negative impact has been identified, please complete section 2. If no negative impact has been identified and if this is not a major service change, you can end the assessment here.**

I am confident that section 2 of this EIA does not need completing as there are no highlighted risks of negative impact occurring because of this policy.

Name of person confirming result of initial impact assessment: Dr Sen Devadathan, Cardiology Consultant

**If a negative impact has been identified above OR this is a major service change, you will need to complete section 2 of the EIA form available here:**
Section 2. Full Equality Analysis