NHS
Cheshire and Merseyside

Clinical Commissioning Policy

Disodium Ethylenediaminetetraacetic Acid (EDTA) in prevention of Cardiovascular Events in patients with a previous Myocardial Infarction

Category 1 Intervention - Not routinely commissioned -

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Purpose	This document is part of a suite of policies that the Integrated Care Board (ICB) uses to drive its commissioning of healthcare. Each policy in that suite is a separate public document in its own right but will be applied with reference to other policies in that suite.
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Date:	**Version Number:**	**Section and Description of Change**
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1. Introduction

1.1 This policy relates to the commissioning of interventions which optimise clinical effectiveness and represent value for money.

1.2 This document is part of a suite of policies which the Integrated Care Board (ICB) uses to drive its commissioning of healthcare. Each policy is a separate public document in its own right but should be considered alongside all the other policies in the suite as well as the core principles outlined in Appendix 1.

1.3 At the time of publication, the evidence presented per procedure/treatment was the most current available.

2. Purpose

2.1 This policy aims to ensure a common set of criteria for treatments and procedures across the region. This is intended to reduce variation of access to NHS services in different areas and allow fair and equitable treatment for all patients.

3. Policy statement

3.1 Disodium ethylenediaminetetraacetic acid (EDTA) is not routinely commissioned for the prevention of cardiovascular events in patients with a previous myocardial infarction.

4. Exclusions

4.1 None

5. Rationale

5.1 The evidence to support the use of disodium EDTA for this indication is limited.

6. Underpinning evidence

6.1 The current Cheshire CCG policy states chelation therapy is not commissioned for vascular occlusions. Two references are cited in support of this statement. The first is a national guideline on the diagnosis and management of peripheral arterial disease published by the Scottish Intercollegiate Guidelines Network (SIGN) in 2006. This was withdrawn in 2016.

6.2 The 2nd reference is the more substantive piece of work, published in the *Journal of the American Medical Association* in 2013. [1] This was a double-blind, placebo-controlled randomised trial which examined the efficacy of chelation therapy with disodium Ethylene Diamine Tetra Acetic Acid (EDTA) in reducing cardiovascular events in patients who'd had a previous a myocardial infarction (MIA).

6.3 A total of 1,708 patients aged 50 years or older who had experienced an MI at least 6 weeks before the trial were enrolled. Infusions of disodium EDTA were administered to the selected patients every week in the initial phase to a total of 40 injections. In fact, this was a 2 x 2 factorial design in which patients were also given a 28 component multivitamin, multimineral mixture. Ultimately, 4 groups were compared to each other, and these comprised EDTA + high-dose vitamin, EDTA + placebo, vitamin + placebo and placebo infusion + placebo vitamin. [2]

6.4 Effectively, the patients being studied were stable with a previous history of MI. The principal outcome was a composite index comprising mortality, recurrent MI, stroke, coronary revascularisation and hospitalisations. Secondary outcomes were the individual cardiovascular endpoints which were combined to form the principal outcome.

6.5 The principal outcome occurred in 26% of the chelation group and 30% of the placebo group. This gives a hazard ratio of 0.82 which is significant (P = 0.035) but the 95% confidence interval was 0.69 – 0.99 i.e., almost touching one which would indicate a nonsignificant change. The apparent benefit is driven largely by the rate of revascularisation procedures rather than any of the other components which were all nonsignificant. Unsurprisingly, the authors concluded that the results simply provide evidence to guide further research but were not sufficient to support the routine use of chelation therapy in patients who have had an MI. A separate study of quality-of-life measures in both intervention and control arms showed there to be no difference after 2 years of follow-up. [3]

6.6 A literature search was therefore performed to identify any additional evidence which might have surfaced since 2013. In essence, little has been published since this time.

6.7 Most of the follow-up seems to be concerned with diabetes patients. In 2014, the author of the original *JAMA* study re-presented the data which showed that the primary endpoint reduction in patients with diabetes was more pronounced.[2] He concluded that in stable post MI patients, the combination of vitamins and EDTA reduced some clinically important cardiovascular events which was significant and of potential clinical relevance.

6.8 It was subsequently postulated that the mechanism was related to the role of certain transition and toxic metals such as copper, iron, cadmium and lead which play an important role in oxidative stress pathways.[4] Around the same time, a detailed analysis of the diabetes subset (633 diabetes patients) revealed that all-cause mortality was significantly reduced by EDTA.[5] However, after adjusting for these multiple subgroup analyses, the results were no longer significant. The author concluded that the data didn't provide sufficient evidence to support the routine use of chelation therapy for all post-AMI patients with diabetes.

6.9 In conclusion, no new evidence has emerged to support the use of EDTA in post-AMI patients. The current "not routinely commissioned" policy is still appropriate

REFERENCES

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3. Mark DB, Anstrom KJ, Clapp-Channing NE, et al. Quality-of-life outcomes with a disodium EDTA chelation regimen for coronary disease: results from the trial to assess chelation therapy randomized trial. *Circulation Cardiovascular quality and outcomes* 2014;**7**(4):508-16.

4. Ouyang P, Gottlieb SH, Culotta VL, et al. EDTA Chelation Therapy to Reduce Cardiovascular Events in Persons with Diabetes. *Current cardiology reports* 2015;**17**(11):96. doi: 10.1007/s11886-015-0656-y

5. Escolar E, Lamas GA, Boineau R, et al. The Effect of an EDTA-based Chelation Regimen on Patients with Diabetes Mellitus and Prior Myocardial Infarction in the Trial to Assess Chelation Therapy (TACT). *Circulation: Cardiovascular Quality and Outcomes* 2014;**7**(1):15-24. doi: 10.1161/CIRCOUTCOMES.113.000663

7. Force

7.1 This policy remains in force until it is superseded by a revised policy or by mandatory NICE guidance or other national directive relating to this intervention, or to alternative treatments for the same condition.

8. Coding

8.1 None

9. Monitoring And Review

9.1 This policy may be subject to continued monitoring using a mix of the following approaches:

- Prior approval process
- Post activity monitoring through routine data
- Post activity monitoring through case note audits

9.2 This policy will be kept under regular review, to ensure that it reflects developments in the evidence base regarding effectiveness and value.

10. Quality and Equality Analysis

10.1 Quality and Equality Impact Analyses have been undertaken for this policy at the time of its review.

Appendix 1 - Core Objectives and Principles

Objectives

The main objective for having healthcare commissioning policies is to ensure that:

- Patients receive appropriate health treatments
- Treatments with no or a very limited evidence base are not used; and
- Treatments with minimal health gain are restricted.

Principles

This policy aims to ensure a common set of criteria for treatments and procedures across the region. This is intended to reduce variation of access to NHS services in different areas and allow fair and equitable treatment for all patients.

Commissioning decisions by ICB Commissioners are made in accordance with the commissioning principles set out as follows:

- Commissioners require clear evidence of clinical effectiveness before NHS resources are invested in the treatment.
- Commissioners require clear evidence of cost effectiveness before NHS resources are invested in the treatment.
- Commissioners will consider the extent to which the individual or patient group will gain a benefit from the treatment.
- Commissioners will balance the needs of an individual patient against the benefit which could be gained by alternative investment possibilities to meet the needs of the community.
- Commissioners will consider all relevant national standards and consider all proper and authoritative guidance.
- Where a treatment is approved Commissioners will respect patient choice as to where a treatment is delivered, in accordance with the 'NHS Choice' framework.
- Commissioning decisions will give 'due regard' to promote equality and uphold human rights. Decision making will follow robust procedures to ensure that decisions are fair and are made within legislative frameworks.

Core Eligibility Criteria

There are a number of circumstances where a patient may meet a 'core eligibility criterion' which means they are eligible to be referred for the procedures and treatments listed, regardless of whether they meet the criteria; or the procedure or treatment is not routinely commissioned.

These core clinical eligibility criteria are as follows:

- Any patient who needs 'urgent' treatment will always be treated.
- All NICE Technology Appraisals Guidance (TAG), for patients that meet all the eligible criteria listed in a NICE TAG will receive treatment.
- In cancer care (including but not limited to skin, head and neck, breast and sarcoma) any lesion that has features suspicious of malignancy, must be referred to an appropriate specialist for urgent assessment under the 2-week rule.
- NOTE: Funding for all solid and haematological cancers are now the responsibility of NHS England.
- Reconstructive surgery post cancer or trauma including burns.
- Congenital deformities: Operations on congenital anomalies of the face and skull are usually routinely commissioned by the NHS. Some conditions are considered highly specialised and are commissioned in the UK through the National Specialised Commissioning Advisory Group (NSCAG). As the incidence of some cranio-facial congenital anomalies is small and the treatment complex, specialised teams, working in designated centres and subject to national audit, should carry out such procedures.
- Tissue degenerative conditions requiring reconstruction and/or restoring function e.g. leg ulcers, dehisced surgical wounds, necrotising fasciitis.
- For patients wishing to undergo Gender reassignment, this is the responsibility of NHS England and patients should be referred to a Gender Identity Clinic (GIC) as outlined in the Interim NHS England Gender Dysphoria Protocol and Guideline 2013/14.

Cosmetic Surgery

Cosmetic surgery is often carried out to change a person's appearance to achieve what a person perceives to be a more desirable look.

Cosmetic surgery/treatments are regarded as procedures of low clinical priority and therefore not routinely commissioned by the ICB Commissioner.

A summary of Cosmetic Surgery is provided by NHS Choices. Weblink:
http://www.nhs.uk/conditions/Cosmetic-surgery/Pages/Introduction.aspx and
http://www.nhs.uk/Conditions/Cosmetic-surgery/Pages/Procedures.aspx

Diagnostic Procedures

Diagnostic procedures to be performed with the sole purpose of determining whether or not a restricted procedure is feasible should not be carried out unless the eligibility criteria are met, or approval has been given by the ICB or GP (as set out in the approval process of the patients responsible ICB) or as agreed by the IFR Panel as a clinically exceptional case.

Where a General Practitioner/Optometrist/Dentist requests only an opinion the patient should not be placed on a waiting list or treated, but the opinion given and the patient returned to the care of the General Practitioner/Optometrist/Dentist, in order for them to make a decision on future treatment.

Clinical Trials

The ICB will not fund continuation of treatment commenced as part of a clinical trial. This is in line with the Medicines for Human Use (Clinical Trials) Regulations 2004 and the Declaration of Helsinki which stipulates that the responsibility for ensuring a clear exit strategy from a trial, and that those benefiting from treatment will have ongoing access to it, lies with those conducting the trial. This responsibility lies with the trial initiators indefinitely.

Clinical Exceptionality

If any patients are excluded from this policy, for whatever reason, the clinician has the option to make an application for clinical exceptionality. However, the clinician must make a robust case to the Panel to confirm their patient is distinct from all the other patients who might be excluded from the designated policy.

The ICB will consider clinical exceptions to this policy in accordance with the Individual Funding Request (IFR) Governance Framework consisting of: IFR Decision Making Policy; and IFR Management Policy.