

Electrochemotherapy for metastases in the skin from tumours of non-skin origin and melanoma

Interventional procedures guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

1 Guidance

- 1.1 There is sufficient evidence of efficacy of electrochemotherapy for treating metastases in the skin from tumours of non-skin origin and melanoma to support its use as a palliative treatment. There are no major safety concerns. Therefore, in the context of palliative treatment the procedure can be used with normal arrangements for clinical governance, consent and audit.
- 1.2 Patient selection should be carried out by an appropriate specialist multidisciplinary team.
- 1.3 This procedure should only be carried out by a clinician with specific training in the technique.
- 1.4 Clinicians should submit data on all patients undergoing electrochemotherapy (including details of case selection, methods of follow-up and outcomes) to the InspECT register, an international register dedicated to electrochemotherapy, and review clinical outcomes locally.

2 The procedure

2.1 Indications and current treatments

- 2.1.1 Cutaneous and subcutaneous metastases of non-skin origin and melanoma often occur in the setting of disseminated disease and cause significant clinical problems including bleeding, pain and ulceration. The primary aim of treatment is therefore palliative and includes modalities such as regional chemotherapy, curettage, cryotherapy and radiotherapy.

2.2 Outline of the procedure

- 2.2.1 Electrochemotherapy aims to enhance the effects of chemotherapy and can be performed as an outpatient procedure. It can be used for local control of cancers that are unsuitable for surgery and resistant to radiotherapy or chemotherapy.
- 2.2.2 The procedure is performed with the patient under general or local anaesthesia with or without sedation. Chemotherapy drugs are given first, either intravenously or directly into the tumour. Drug dose is individualised based on either body surface area or tumour volume. Shortly after drug administration, brief and intense electric pulses are delivered around or directly into the tumour using either surface plates or needle electrodes. This makes the cell membranes more permeable to the chemotherapy drugs so that their cytotoxic effect is increased. Different-shaped electrodes or plates are used depending on the tumour size, extent, shape and location. Treatment duration may vary depending on the number and size of tumours. Larger tumours may need several applications to cover the entire surface. Repeated treatments can be performed if necessary (within the lifetime dose limits of the chemotherapy drugs).

2.3 Efficacy

Sections 2.3 and 2.4 describe efficacy and safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [overview](#).

- 2.3.1 A randomised controlled trial of 19 patients with melanoma metastases comparing intratumoural electrochemotherapy (in 18 tumours) with intratumoural chemotherapy alone (in 19 tumours) reported complete response in 72% (13 out of 18) of tumours treated with electrochemotherapy at end of follow-up ('average' of 21 months). On an intention-to-treat basis, objective response for electrochemotherapy was significantly greater than for chemotherapy alone (64% versus 29%, $p=0.02$).
- 2.3.2 A non-randomised comparative study of 61 patients that evaluated electrochemotherapy efficacy in 21 patients (73 tumours) with mixed non-melanoma metastases and 20 patients (98 tumours) with melanoma metastases reported an 85% objective tumour response and a 74% complete tumour response at a median follow-up of 133 days regardless of tumour histology, drug used (bleomycin or cisplatin) or route of drug administration (intravenous or intratumoural). Numbers were not reported.
- 2.3.3 A case series of 35 patients with cutaneous chest wall recurrence from breast cancer reported 54% (19 out of 35) complete response at 2 months follow-up.
- 2.3.4 A non-randomised study of 52 patients (608 tumours) including 18 patients with non-melanoma metastases of mainly breast cancer (95 tumours) and 34 patients with malignant melanoma (171 tumours) reported a significant inverse correlation between maximum tumour diameter and complete response rate: 66% for diameters less than 1.5 cm, 36% for diameters between 1.6 cm and 3 cm and 28% for diameters greater than 3 cm ($p=0.0035$).
- 2.3.5 The same study of 52 patients reported that 9% (3 out of 34) of patients with melanoma developed recurrence in the areas treated with electrochemotherapy. One patient developed recurrence at 7 months following an initial complete response.
- 2.3.6 A non-randomised comparative study of 6 patients with 26 cutaneous metastases of breast cancer origin, 12 of which were treated with electrochemotherapy, reported a median duration of response of 10 weeks in 33% (4 out of 12) of tumours that had a complete response and 5 weeks in 67% (8 out of 12) of tumours that had a partial response at up to 26 weeks of follow-up.

- 2.3.7 In the randomised controlled trial of 19 patients, 26% (5 out of 19) of patients were alive at follow-up of 37 months. The average survival of the 14 out of 19 patients (74%) who died before this follow-up was 14 months.
- 2.3.8 The study of 52 patients reported improvements in overall quality of life score (assessed in 36 patients) from a mean pretreatment score of 46 to mean scores of 52 and 55 at 1 and 2 months respectively ($p < 0.005$). These were measured using a non-validated questionnaire with scores of 0 to 60, higher scores indicating better quality of life. In the study, 94% (34 out of 36) of responding patients reported an improvement in 1 or more of the 6 parameters assessed in the questionnaire (bleeding, ulceration, aesthetics, activities of daily living, social relations and pain control).
- 2.3.9 The Specialist Advisers listed additional key efficacy outcomes as the number of procedures needed, control of bleeding and reduction in odour from fungating tumours.

2.4 Safety

- 2.4.1 Muscle spasms with myoclonus secondary to electric pulses were reported in 25% (3 out of 12) of patients treated by electrochemotherapy in a randomised controlled trial of 12 patients. These stopped immediately after the electric pulses were discontinued.
- 2.4.2 An inflammatory reaction leading to superficial necrosis and an eschar occurred in all tumours treated with electrochemotherapy in the randomised controlled trial of 19 patients. These all healed completely by 16 weeks.
- 2.4.3 Electrode marks and superficial erosions occurred in all patients after electrochemotherapy in the case series of 14 patients. The marks healed within 1 month. A mild injection site rash of grade 1 to 2 according to common toxicity criteria was reported in 8% (4 out of 52) of patients treated with electrochemotherapy in the study of 52 patients with metastatic cancer (34 of whom had malignant melanoma).
- 2.4.4 Erythema and oedema at treated areas that resolved in a 'few' days was reported

in 2% (3 out of 14) of individuals in the case series of 14 patients.

- 2.4.5 'Minimal scarring and depigmentation' of the treatment site as a late effect was reported in the non-randomised comparative study of 6 patients. This persisted for the duration of follow-up (up to 26 weeks). No further details were reported.
- 2.4.6 Other side effects attributed to the chemotherapy agent such as slight nausea, transient increase in heart rate and transient dyspnoea were also reported.
- 2.4.7 The Specialist Advisers listed additional key safety outcomes as increase in wound exudate after the procedure and chemotherapy toxicity, specifically pulmonary fibrosis.

2.5 Other comments

- 2.5.1 The Committee noted that this procedure might provide palliation and improve quality of life for patients with disease unsuitable for, or resistant to, other treatments.
- 2.5.2 The Committee noted that patients may experience pain and ulceration following treatment.

3 Further information

Sources of evidence

The evidence considered by the Interventional Procedures Advisory Committee is described in the [overview](#).

Information for patients

NICE has produced [information for the public on this procedure](#). It explains the nature of the procedure and the guidance issued by NICE, and has been written with patient consent in mind.

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Endorsing organisation

This guidance has been endorsed by [Healthcare Improvement Scotland](#).