Pwyllgor Gwasanaethau Iechyd Arbenigol Cymru (PGIAC)
Welsh Health Specialised Services Committee (WHSSC)

Specialised Services Policy:
CP92
Extracorporeal Photophoresis (ECP) for the Treatment of Cutaneous T-cell Lymphoma

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Implementation Date:	1st November 2015
Review Date:	2024
Document No:	CP92

Document History

Revision History			
Version No.	Revision date	Summary of Changes	Updated to version no.:
0.1		New draft Commissioning Policy	0.1
0.2		Revised draft following consultation	0.2
0.2	29.10.15	Approved by Management Group	1.0
Date of next revision			

Consultation		
Name	Date of Issue	Version Number
Members of WHSSC Cancer CEEG	11.11.14	0.1
Members of WHSSC Cancer and Blood Programme Team	11.11.14	0.1
NHS England Blood and Transplant	11.11.14	0.1
Medical Directors, HBs and VCC	11.11.14	0.1
Members of WHSSC Management Group	11.11.14	0.1
Consultant BMT Transplant Physicians, C&V UHB, BCUHB, The Christie and RLBG	11.11.14	0.1
Management Group	29.10.15	0.2

Approvals		
Name	Date of Issue	Version No.
WHSSC Corporate Directors Group	19.10.15	0.2
Management Group	29.10.15	1.0

Distribution – *this document has been distributed to*			
Name	By	Date of Issue	Version No.

Policy Statement

Background	**Extracorporeal photphoresis (ECP)** is a form of apheresis and photodynamic therapy in which blood is treated with a photosensitizing agent and subsequently irradiated with specified wavelengths of light to achieve an effect. Specifically, buffy coat (white blood cells plus platelets) is separated from whole blood, chemically treated with 8-methoxypsoralen, exposed to ultraviolet light, and returned to the patient. **Cutaneous T-cell lymphoma** is a class of non-Hodgkin's lymphoma of the skin. Unlike most non-Hodgkin's lymphomas (which are generally B-cell related), CTCL is caused by a mutation of T cells. The malignant T cells in the body initially involve the skin, causing itchy red patches which may thicken to become plaques or tumours or spread all over the body to develop widespread redness of the skin termed 'erythroderma'. Spread to lymph nodes or metastasis may occur, with a poor prognosis. **Mycosis Fungoides** is the most common form of cutaneous T-cell lymphoma. **Sezary's Disease** is a leukaemic type of cutaneous lymphoma presenting with erythroderma.
Summary of Access Criteria	Following a review of the evidence for clinical and cost effectiveness, the Welsh Health Specialised Services Committee (WHSSC) will fund extracorporeal photophoresis (ECP) for the treatment of cutaneous T-cell lymphoma on a prior approval basis only.
Responsibilities	NHS Blood and Transplant must ensure patients are treated in accordance with this Policy. The referring clinician must use the Policy to advise patients of their treatment options and submit IPFR requests where appropriate.

Table of Contents

1. Aim

1.1 Introduction

The document is the commissioning policy for Extracorporeal Photophoresis (ECP) for the treatment of Cutaneous T-Cell Lymphoma for Welsh patients. The policy applies to residents of all seven Health Boards in Wales and English residents with a Welsh GP.

The purpose of this document is to:

- Set out the commissioning policy for ECP for the treatment of cutaneous T-cell lymphoma.

1.2 Relationship with other Policies and Service Specifications

This document should be read in conjunction with the following documents:

- All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR).

2. Scope

2.1 Definition

Extracorporeal Photophoresis (ECP) ECP is a form of apheresis and photodynamic therapy in which blood is treated with a photosensitizing agent and subsequently irradiated with specified wavelengths of light to achieve an effect. Specifically, buffy coat (white blood cells and platelets) is separated from whole blood, chemically treated with 8-methoxypsoralen, exposed to ultraviolet light, and returned to the patient.

The mode of action of ECP in cutaneous T-cell lymphoma (CTCL) involves the activation of dendritic cells against the tumoural population. (Atta et al., 2012).

Peripheral T-cell lymphoma (PTCL) consists of a group of rare and usually aggressive non-Hodgkins lymphomas (NHLs) that develop from mature T-cells. Most T-cell lymphomas are PTCLs, which collectively account for about 10 percent to 15 percent of all NHL cases in the UK. PTCLs are sub-classified into various subtypes, each of which are typically considered to be separate diseases based on their distinct clinical differences. Most of these subtypes are very rare. The three most common subtypes of PTCL are peripheral T-cell lymphoma not otherwise specified (PTCL-NOS), anaplastic large-cell lymphoma (ALCL), and angioimmunoblastic T-cell lymphoma (AITL).

Cutaneous T-Cell Lymphoma (CTCL) is a rare manifestation of PTCL and usually affects people aged 40-60. It is caused by T-cells in the skin growing in an uncontrolled way. The malignant T-cells in the body initially involve the skin, causing itchy red patches which may thicken to become plaques or tumours or spread all over the body to develop widespread redness of the skin termed 'erythroderma'. Spread to lymph nodes or metastasis may occur, with a poor prognosis. CTCL is more common in men than in women.

Mycosis fungoides is the most common form of cutaneous T-cell lymphoma. It generally affects the skin, but may progress internally over time. Symptoms include rash, tumors and very itchy skin. While the cause remains unclear, most cases are not genetic or hereditary. Most cases are in people over 20 years of age, and it is

more common in men than women. Treatment options are wide and may be initially directed at controlling symptoms with sunlight exposure, ultraviolet light, topical steroids and radiotherapy. Advanced disease requires immunotherapy or chemotherapy to control disease.

Sézary's disease (often called **Sézary syndrome**) is a type of cutaneous lymphoma where the patient is red all over (erythroderma) and has blood involvement. Sézary's disease is sometimes considered advanced stage CTCL.

2.2 Codes

ICD-10 Codes

Code	Description
C84.0	Mycosis fungoides
C84.1	Sezary's disease
C84.8	Cutaneous T-cell lymphoma

3. Access Criteria

Following a review of the evidence of clinical and cost effectiveness, the Welsh Health Specialised Services Committee (WHSSC) will fund extracorporeal photophoresis (ECP) for the treatment of cutaneous T-cell lymphoma on a prior approval basis only.

A summary of the evidence review is found in Annex i.

3.1 Exceptions

If the referring clinician believes that there are exceptional grounds for treatment, an Individual Patient Funding Request (IPFR) can be made to WHSSC under the *All Wales Policy for Making Decisions on Individual Patient Funding Requests (IPFR)*.

Guidance on the IPFR process is available at www.whssc.wales.nhs.uk

3.2 Responsibilities

NHS Blood and Transplant

NHSBT must ensure patients are treated in accordance with the Policy.

Referring Clinicians

The referring clinician must use the Policy to advise patients of their treatment options and to refer patients in accordance with the Policy.

4. Putting Things Right: Raising a Concern

Whilst every effort has been made to ensure that decisions made under this policy are robust and appropriate for the patient group, it is acknowledged that there may be occasions when the patient or their representative are not happy with decisions made or the treatment provided. The patient or their representative should be guided by the clinician, or the member of NHS staff with whom the concern is raised, to the appropriate arrangements for management of their concern:

- When a patient or their representative is unhappy with the decision that the patient does not meet the criteria for treatment further information can be provided demonstrating exceptionality. The request will then be considered by the All Wales IPFR Panel.
- If the patient or their representative is not happy with the decision of the All Wales IPFR Panel the patient and/or their representative has a right to ask for this decision to be reviewed. The grounds for the review, which are detailed in the All Wales Policy: Making Decisions on Individual Patient Funding Requests (IPFR), must be clearly stated. The review should be undertaken, by the patient's Local Health Board;
- When a patient or their representative is unhappy with the care provided during the treatment or the clinical decision to withdraw treatment provided under this policy, the patient and/or their representative should be guided to the LHB for NHS Putting Things Right. For services provided outside NHS Wales the patient or their representative should be guided to the NHS Trust Concerns Procedure, with a copy of the concern being sent to WHSSC.

5. Equality Impact and Assessment

The Equality Impact Assessment (EQIA) process has been developed to help promote fair and equal treatment in the delivery of health services. It aims to enable Welsh Health Specialised Services Committee to identify and eliminate detrimental treatment caused by the adverse impact of health service policies upon groups and individuals for reasons of race, gender re-assignment, disability, sex, sexual orientation, age, religion and belief, marriage and civil partnership, pregnancy and maternity and language (welsh).

This policy has been subjected to an Equality Impact Assessment. The Assessment demonstrates the policy is robust and there is no potential for discrimination or adverse impact. All opportunities to promote equality have been taken.

Annex (i) Summary of Evidence

Abbreviations
CTLC – Cutaneous T-Cell Lymphoma
ECP – Extracorporeal Photophoresis
MF – Mycosis fungoides
SS – Sézary Syndrome

Clinical Effectiveness
Overall, there was low-quality evidence that ECP improves response rates and survival in patients with refractory erythrodermic CTCL. There was significant heterogeneity in the studies assessed including different treatment regimens; a variety of forms of CTCL (and not necessarily treatment resistant) including MF, erythrodermic, MF, SS; SS with peripheral blood involvement with considerable uncertainty as to the role of T cell clonality reporting. Most studies had small sample sizes with response criteria that were not clearly defined or consistent; it was unclear how concomitant therapy contributed to responses with significant variation in definitions of concomitant therapy in the published studies. Comparison was made to historical controls with some patients excluded from analysis because of progression of disease, toxicity and other reasons. Unclear or unusual statistical approaches were adopted in some of the studies assessed and quality of life was not reported as an outcome of interest in most of the studies assessed.

The reported complete response range was between 16% to 23% and the overall reported CR/PR range is from 33% to 80%. The wide range in reported responses to ECP appeared to be due to the variability of the patients treated and the way in which the data were presented and analysed. Many patients, in mostly retrospective case series, were concurrently on other therapies and were not assessed for comparability of diagnosis or disease stage (MF versus SS; erythrodermic versus not erythrodermic). Blood involvement in patients receiving ECP (e.g. T cell clonality) was not consistently reported, especially in earlier studies. The definitions of partial and complete response also are not standardized or consistent between studies.

Quality of life was reported in one study, however the scale was developed by the authors and was not a standard validated scale. Adverse events associated with ECP appear to be uncommon and

most involve catheter-related infections and hypotension caused by volume depletion.

Cost Effectiveness

No data on cost effectiveness was found. ECP is a costly therapy.