National Institute for Health and Clinical Excellence

368 – Extracorporeal photophoresis for Crohn's disease

Consultation Comments table

IPAC date: 12th December 2008

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Healthcare - Other Johnson and Johnson	**1**	Given the results of a recent study evaluating the safety and efficacy of ECP in 28 refractory Crohn's Disease patients we would urge the committee to consider a recommendation which stipulates "Special arrangements for consent and/or audit and/or research". This study by Abreu et al has just been accepted for publication in the Journal of Inflammatory Bowel Disease and the full manuscript has been provided to the committee in confidence.	Thank you for the sending us details of this new study. The data from it will be incorporated into our overview of evidence on this procedure and the guidance will be changed.

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2	Consultee 1 Healthcare - Other Johnson and Johnson	**2.1**	This is an accurate description of the condition in question and ranges of severity measured by CDAI score. It is suggested a reference to the significant effect this condition has on the quality of life of individuals with moderate to severely active CD would be appropriate here. In addition, a significant percentage of patients have chronic symptoms and active disease requiring chronic exposure to immunosuppressives with all the attending long term side-effects including avascular necrosis, diabetes, hypertension, cataracts from steroids, opportunistic infections and potentially an increased risk of malignancy from immunosuppressives.	Thank you for your comments. Section 2.1 is intended to be a brief description of the condition and symptoms. The potential requirement for immunosuppressant therapy is described in 2.1.3
3	Consultee 1 Healthcare - Other Johnson and Johnson	**2.1.2**	Section 2.1.2: It is advised the following definition of treatment response is included: “Clinical response is defined as greater than 100 point reduction in CDAI score. Remission is defined as a CDAI <150. A partial response to treatment is defined as >70 point reduction in CDAI score.”	Thank you for your comments. This section of the guidance is intended to be a brief summary of the procedure.
4	Consultee 1 Healthcare - Other Johnson and Johnson	**2.2**	Although this section accurate describes the procedure, there is a need to make reference to the other indications for which this therapy is widely used such as Cutaneous T-cell lymphoma (CTCL).	Thank you for your comments. The initial notification for this procedure included a range of indications including Cutaneous T-Cell Lymphoma (described as well established indication). However the literature search only focused on Crohn’s disease and not T-Cell Lymphoma. T-Cell Lymphoma may best be considered in separate guidance, and the consultee may notify this indication to the IP Programme if they believe there would be utility in developing guidance for this indication.

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5	Consultee 1 Healthcare - Other Johnson and Johnson	**2.3**	This was a severe, refractory cohort of patients, most of whom had multiple prior surgeries and few if any, medical treatments options available. The mean change from baseline (314) in the CDAI score at Week 12 was 116 points (p versus baseline < 0.001). At Week 12, 14 of 28 patients (50%) had a clinical response (defined as greater than 100 point reduction in CDAI score and or CDAI <150) and seven patients (25%) attained remission (defined as a CDAI score <150) at this time-point. A partial clinical response (>70 point reduction in CDAI score) was observed in 18 of 28 patients (64%). Quality of life was measured using the Inflammatory Bowel Disease Questionnaire (IBDQ). The mean IBDQ rose from 122 points at baseline to 154 points at Week 12 (p <0.001). Fourteen patients had a clinical response (>100 point improvement in CDAI) at Week 12, of whom 12 enrolled in the 12-week extension study and received further biweekly ECP treatments. Nine of these 12 patients (75%) maintained their clinical response at Week 24. Â Evidence from other indications such as Cutaneous T-cell lymphoma (CTCL) shows response rates of 50-73%. References have been provided separately in an email.	Thank you for your comments. The overview and efficacy section of the guidance will be changed to incorporate this new evidence.

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6	Consultee 1 Healthcare - Other Johnson and Johnson	**2.4**	Abreu et al concluded that ECP was well tolerated in patients with Crohn's Disease and was consistent with the safety profiles previously reported for this therapy in other treatment indications. Of the 28 patients enrolled only two serious adverse events (nausea and malaise) occurred in one patient. One further patient was withdrawn from the study for non-serious adverse events. The most frequent non-serious adverse events were headache and nasopharyngitis (29%), nausea (18%), pyrexia (18%) and emesis (18%). It is disputed that "fits" or skin cancer are substantiated adverse events related to ECP for Crohn's Disease or other indications or uses. Within the reported adverse events from approximately 500,000 treatments overall using ECP these have not been evident to date. For accuracy these postulated adverse events should be removed from this section. The incidence of reported adverse events across other indications is <0.003%. The most common side effects are sporadic and mild and must be balanced against the higher risks associated with oral treatment with the pharmaceutical methoxalen (8 MOP) at higher (approx 200 times) concentrations.	Thank you for your comments. The overview and Safety section of the guidance will be changed to incorporate this new evidence.

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7	Consultee 1 Healthcare - Other Johnson and Johnson	**General**	Here is a list of relevant references (there was insufficient space to include in the online submission): 1[1] Edelson R, Berger C, Gasparro F, et al. Treatment of cutaneous T-cell lymphoma by extracorporeal photochemotherapy. *N Engl J Med*. 1987;316:297-303. 1[1]Zic, et al. Long-term follow-up of paitnets with cutaneous T-cell lymphoma treated with extracorporeal photochemotherapy. Therapy. 1996 Dec; 35(6): 935-45. 1[1] Duvic M, Hester J, Lemak N Photopheresis therapy for cutaneous t-cell lymphoma Journal of the American Academy of Dermatology 1996 Oct;35(4);573-579 1[1] Scarisbrick JJ, Taylor P, Holtick U, Makar Y, Douglas K, Berlin G, Juvonen E, Marshall S. Photopheresis Expert Group.U.K.consensus statement on the use of extracorporeal photopheresis for treatment of cutaneous T-cell lymphoma and chronic graft-versus-host disease. Br J Dermatol. 2008 Apr;158(4):659-78.	These studies do not include patients with the relevant indication to this guidance and therefore will not be incorporated into the overview of evidence base.