



BSPAR ECS 'Event of Special Interest' (ESI) Questionnaires

These forms are used when a participant experiences an adverse event that has been classed by the BSPAR ECS study team as being of special interest.

This list currently includes:

- Aplastic anaemia/pancytopenia/neutropenia
- Tuberculosis
- Serious infection (any pathogen including viral)
- Pregnancy
- Malignancy (non haematological)
- Lymphoproliferative malignancy
- Significant immunologic reaction
- GI Ulcer/Bleed/Perforation
- IBD
- Demyelination/optic neuritis
- Congestive Heart Failure
- Lupus/Lupus-like reaction
- Uveitis

An ESI form has been developed for each of the above events; these forms ask very specific questions relating to the event, and are used for validation purposes. If we are informed that a participant has experienced an ESI, the relevant ESI form will be sent to the clinician or nurse for completion.

Further to the ESIs, a generic information request letter has been developed to collect information about serious adverse events that do not fall into an ESI category. A letter has also been drafted to collect information on participants who have passed away.

Not all Serious Adverse Events (SAEs) are Events of Special Interest (ESIs), but all ESIs are SAEs, with the exception of pregnancy, which is classed as a non-serious event of special interest.

BSPAR ECS Event of Special Interest (ESI) Report Inflammatory Bowel Disease (IBD)

BSPAR ECS ID:

HRN:

Event Details (please annotate with any additional information including complications such as peritonitis, bowel necrosis, etc)

Biologic at time of event (if any):

Date of Event:

Date of Endoscopy or surgery:

Medical History

 IBD in first degree relative ☐ YES (please specify: _____) ☐ NO ☐ DON'T KNOW

Please tick as appropriate: YES NO DON'T KNOW

Please tick as appropriate: YES NO DON'T KNOW

Symptoms ≥ 4 weeks			
Abdominal Pain			
Rectal Bleeding			
Anorexia			
Weight loss			
Growth retardation			

Symptoms ≥ 2 episodes in 6 months			
Cramps			
Tenesmus			
Vomiting			
Constipation			
Diarrhoea			

 Extra-intestinal Symptoms ☐ YES (please specify: _____) ☐ NO ☐ DON'T KNOW

Specific tests performed related to IBD

Please tick as appropriate:

YES NO DON'T
KNOWYES NO DON'T
KNOW

Infectious causes of enteritis or colitis excluded			
Lab tests performed			
Small bowel follow through			
CT Scan			

Gadolinium-enhanced MRI/MRI enteroclysis/MR enterography			
Capsule Endoscopy			
Upper gastrointestinal Endoscopy			
Colonoscopy performed			

 What was the outcome? ☐ Resolved ☐ Not Resolved
☐ Resolved with sequelae ☐ Fatal (Date: _____)

 Has a yellow card been submitted? ☐ YES ☐ NO ☐ UNKNOWN

Form completed

 By: _____
 On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft Way, Manchester Science Park, M15 6SZ, or fax to 0161 2751640.

**BSPAR ECS Event of Special Interest (ESI)
Report
APLASTIC ANAEMIA,
PANCYTOPAENIA / NEUTROPAENIA**

BSPAR ECS ID:

HRN:

Event Details

Biologic at time of event:

Date of Event:

What was thought to be the cause?**How was this confirmed?**Please provide the **lowest Hb value:** _____**lowest neutrophil value:** _____**lowest platelet value:** _____

- Did the patient have any cytopaenic history prior to starting therapy? ☐ YES ☐ NO
- Was a bone marrow aspiration / biopsy performed? ☐ YES ☐ NO

(If yes, please send a copy of the results)

Please indicate all **concomitant medications** taken:-----
-----Were there any complications as a direct result of cytopaenia? (**E.g. infection or bleeding**)**What was the outcome?**☐

Resolved

☐

Not Resolved

☐

Resolved with sequelae

☐

Fatal

Has a yellow card been submitted?☐

YES

☐

NO

☐

UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!**Please return to:** BSPAR ECS, Arthritis Research UK
Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft
Way, Manchester Science Park, M15 6SZ, or fax to 0161

**BSPAR ECS Event of Special Interest (ESI)
Report
UVEITIS**

BSPAR ECS ID:

HRN:

Event Details (please annotate with any additional information including **relevant clinical signs and symptoms**)

Biologic at time of event:

Date of Event:

Is this a new-onset uveitis? ☐ No ☐ Yes – please provide date of diagnosis: ____/____/____Or a relapse/worsening of uveitis? ☐ No ☐ Yes – please provide date of diagnosis: ____/____/____**Uveitis****localisation:**

- ☐ Right eye
- ☐ Left Eye
- ☐ Both sides

Uveitis type:

- ☐ anterior
- ☐ intermediate
- ☐ posterior
- ☐ panuveitis

Uveitis course

- ☐ Acute (episode characterised by sudden onset and limited duration)
- ☐ Recurrent (repeated episodes separated by periods of inactivity without treatment ≥ 3 months in duration)
- ☐ chronic (persistent uveitis with relapses in ≥ 3 months after discontinuing treatment)
- ☐ Not known

Is uveitis currently active? ☐ YES ☐ NO ☐ DON'T KNOW

• Has this patient had any Uveitis complications? (Please indicate below)?

Complication	No	Yes (please provide date)
Band keratopathy		
Cataract		
Synechiae		
Glaucoma or raised intraocular pressure		
Visual loss <0.4		
Visual loss <0.1		
Other (please specify)		

• Was additional medication necessary? No ☐ Yes ☐ details: _____• Was MTX or biologic stopped due to uveitis? No ☐ Yes ☐ details: _____

Form completed

By: _____

On: ____/____/____

Thank you for your help!

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BSPAR ECS Event of Special Interest (ESI) Report DEMYELINATION / OPTIC NEURITIS

BSPAR ECS ID:

HRN:

What was the diagnosis?

Event Details (please annotate with any additional information, including ophthalmological details). **Please provide copy letters if possible**

Biologic at time of event:

Date of Event:

What was the pattern of the disease?☐

Eye involvement

☐

Spinal involvement

☐

CNS involvement

Is this event:☐

a new onset

☐

a relapse?

Was this confirmed by a neurologist or ophthalmologist:☐ YES☐ NO● Was an **MRI** conducted?☐

YES

☐

NO

(if yes please provide copies of report)

● Was **CSF** examined?☐

YES

→

were oligoclonal bands present? **YES / NO**☐

NO

● Visual evoked potentials?

☐

YES

☐

NO

● History of any neurological disorders since baseline? ☐ YES ☐ NO

Type (please provide details): _____

● Positive family history of neurological disorders? ☐ YES ☐ NO

Type (please provide details): _____

What was the outcome?☐

Resolved

☐

Not Resolved

☐

Resolved with sequelae

☐

Fatal

Has a yellow card been submitted?☐

YES

☐

NO

☐

UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK
Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft Way,
Manchester Science Park, M15 6SZ, or fax to 0161 2751640.

BSPAR ECS Event of Special Interest (ESI) Report GI Ulcer/Bleed/Perforation

BSPAR ECS ID:

HRN:

Event Details (please annotate with any additional information including complications such as peritonitis, ileus, bowel necrosis, fistula, sepsis)

Biologic at time of event:

Date of Event:

Investigations performed

CT/ MRI ☐ Yes ☐ No ☐ Don't Know

Endoscopy ☐ Yes ☐ No ☐ Don't Know

Other ☐ Yes ☐ No ☐ Don't Know

Please give details/ attach report/histology result

Was a surgical procedure required? ☐ YES ☐ NO ☐ DON'T KNOW
If YES please give details:

Relevant history of events since baseline

Upper GI ulcer ☐ Yes ☐ No ☐ Unknown Diverticulitis ☐ Yes ☐ No ☐ Unknown

Lower GI ulcer ☐ Yes ☐ No ☐ Unknown Inflammatory Bowel Disease ☐ Yes ☐ No ☐ Unknown

Other GI conditions (please give details):

What was the outcome? ☐ Resolved ☐ Not Resolved

☐ Resolved with sequelae ☐ Fatal

Has a yellow card been submitted? ☐ YES ☐ NO ☐ UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK Epidemiology Unit,
Unit 4 Rutherford House, 40 Pencroft Way, Manchester Science Park, M15
6SZ, or fax to 0161 2751640.

BSPAR ECS Event of Special Interest (ESI) Report

CONGESTIVE HEART FAILURE

BSPAR ECS ID:

HRN:

What was the diagnosis?

Event Details

Biologic at time of event:

Date of Event:

Is there a history of Congenital Heart Disease? ☐ YES ☐ NOIs this event: ☐ New onset ☐ Worsening ☐ UnknownCardiac function investigation performed? ☐ YES ☐ NO If yes, please provide details

• LV ejection fraction: ____%

• BNP Level: ____Units

Please attach a copy of ECHO performed closest to the date of the event if possible

Cardiovascular risk factors:

→ Diabetes ☐ YES ☐ NO ☐ DON'T KNOW→ Hypertension ☐ YES ☐ NO ☐ DON'T KNOW→ Hypercholesterolaemia ☐ YES ☐ NO ☐ DON'T KNOW→ Positive family history ☐ YES ☐ NO ☐ DON'T KNOWWhat was the outcome? ☐ Resolved ☐ Not Resolved☐ Resolved with sequelae ☐ FatalHas a yellow card been submitted? ☐ YES ☐ NO ☐ UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!

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**BSPAR ECS Event of Special Interest (ESI)
Report
Significant Immunologic Reaction**

BSPAR ECS ID:

HRN:

Event Details: (Please annotate with any additional information. Detail the **signs** and **symptoms** involved in the reaction)

Biologic at time of event:

Date of Event:

Did the first signs/symptoms occur within 24 hours of the infusion/injection? ☐ YES ☐ NOIf **yes**, please describe:**How long after the infusion/injection did the event occur?**☐ Within 24 hours ☐ Longer (Please state number of days: _____)Was the infusion **stopped** prematurely? ☐ YES ☐ NO**What additional medication was administered?**• **As premedication before/during infusion** (i.e, steroids, anti-histamines):• **During/after the event:**• **Other additional medication:**

Is any further treatment with the biologic agent considered to be contraindicated?

☐ YES ☐ NO**What was the outcome?**☐ Resolved☐ Not Resolved☐ Resolved with sequelae☐ Fatal**Has a yellow card been submitted?**☐ YES ☐ NO☐ UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!**Please return to:** BSPAR ECS, Arthritis Research UK
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**BSPAR ECS Event of Special Interest
(ESI) Report PREGNANCY**

BSPAR ECS ID:

HRN:

Pregnancy Details:

Last biologic therapy recorded:

Expected date of delivery:

Please provide the following details regarding this event**CONCEPTION**

Was the patient on contraceptives?

☐

Yes

☐

No

Was the pregnancy planned?

☐

Yes

☐

No

Was patient receiving biologic therapy at the time of conception?

☐

Yes

☐

No

Did the patient opt for termination of pregnancy

☐

Yes

☐

No

→ If so, what was the gestation of the pregnancy at termination? _____ weeks

Please provide details of any previous pregnancies, including any complications, outcome and year?

GESTATION

Did the patient have any complications during pregnancy?

☐

Yes

☐

No

Details:

Date of event:

Was the patient hospitalised?

☐

Yes

☐

No

Did the patient experience any infections during pregnancy?

☐

Yes

☐

No

Details:

Date of event:

Was the patient hospitalised?

☐

Yes

☐

No

BSPAR ECS Event of Special Interest (ESI) Report PREGNANCY

• Did the patient remain on biologic therapy throughout the pregnancy? ☐ Yes ☐ No

→ If not, did they discontinue in the ☐ first ☐ second or ☐ third trimester?

• Did the patient remain on DMARD therapy throughout the pregnancy? ☐ Yes ☐ No

→ If not, did they discontinue in the ☐ first ☐ second or ☐ third trimester?

DELIVERY

What was the length of gestation? Weeks

What was the date of delivery?

• Did the patient have any complications during labour and delivery? ☐ Yes ☐ No

If yes, please provide details:

• Did the baby have any congenital abnormalities? ☐ Yes ☐ No

If yes, please provide details:

POSTPARTUM

Did the patient develop any postpartum complications? ☐ Yes ☐ No

If yes, please provide details:

Specifically, did the patient develop any postpartum infections? ☐ Yes ☐ No

If yes, please provide details:

Is the patient breastfeeding? ☐ Yes ☐ No

Did the infant develop any neonatal complications? ☐ Yes ☐ No

If yes, please provide details:

Form completed

By: _____
On: ____/____/____

Thank you for your help!

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BSPAR ECS Event of Special Interest (ESI) Report TUBERCULOSIS

BSPAR ECS ID:

HRN:

Event Details (please annotate with any additional information including relevant clinical signs and symptoms)

Biologic at time of event:

Date of Event:

SITE/S OF INFECTION:

Diagnosis based on:

☐ X-Ray / CT Scan If yes, please specify result or attach report: _____

☐ TB specific blood test If yes, please specify result: _____

☐ Acid fast bacilli If yes, please specify sample: _____

☐ Histology If yes, please specify sample: _____

Diagnosis confirmed by CULTURE? YES / NO (please circle)

If yes, please specify sample:

Pre-treatment screening measures performed on patient:

☐ PPD results ☐ mm

☐ IGRA Result (Quantiferon) ☐ Positive ☐ Indeterminate ☐ Negative

☐ Chest X-Ray → Did this indicate **latent** TB? ☐ Yes ☐ No
Please note any **relevant** family history and family risk factors for TB:

If moved to UK no of years lived here: _____

Since baseline has the patient received TB prophylaxis? ☐ YES ☐ NO ☐ UNKNOWN

If yes please provide start date: _____ and end date: _____

Please indicate which medication:

Medication prescribed to treat **active** TB:
 Has a yellow card been submitted? ☐ YES ☐ NO ☐ DON'T KNOW

Form completed

By: _____

On: ____/____/____

Thank you for your help!

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Park, M15 6SZ, or fax to 0161 2751640.

BSPAR ECS Event of Special Interest (ESI) Report

SERIOUS INFECTION (with any pathogen including viral)

BSPAR ECS ID:

HRN:

Event Details: (please provide clinical information including sequence in complex clinical scenario, organ systems involved and features of secondary HLH if present and enclose a discharge letter for the event)

Biologic at time of event:

Date of Event:

Site of infection:

Were microbiological/serological tests carried out? YES / NO / DON'T KNOW (Circle)

If yes, specify site cultured, micro-organisms / serological result: _____
(Please also state if nil grown)

Medication at time of infection and treatment of infection:

At the **TIME OF INFECTION** did the patient have?

Intubated or indwelling catheter

☐

YES

☐

NO

☐

DON'T KNOW

Central intravenous access

☐

YES

☐

NO

☐

DON'T KNOW

At **DIAGNOSIS OF INFECTION** what was the:

White cell count: _____

Neutrophil count: _____

Lymphocyte count: _____

Platelet count: _____

Haemoglobin _____

PRIOR TO THE INFECTION what was the **LAST RESULT FOR:** (TAKEN ON: _____)

White cell count: _____

Neutrophil count: _____

Lymphocyte count: _____

Platelet count: _____

Haemoglobin _____

What was the outcome?

☐

Resolved

☐

Not Resolved

☐

Resolved with sequelae

☐

Fatal

Has a yellow card been submitted?

☐

YES

☐

NO

☐

UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK
Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft Way,
Manchester Science Park, M15 6SZ, or fax to 0161 2751640.

BSPAR ECS Event of Special Interest (ESI) Report Lupus/Lupus-Like Reaction

BSPAR ECS ID:

HRN:

Event Details (please annotate with any additional information including relevant clinical signs and symptoms)

Date of diagnosis:

Biologic at time of event:

Please mark which of the following diagnostic criteria were fulfilled:

- ☐ Malar Rash
 ☐ Discoid Rash
 ☐ Neurologic disorder (seizures or psychosis)
- ☐ Photo sensitivity
 ☐ Oral ulcers
 ☐ Antinuclear antibody test positive
- ☐ Arthritis
 ☐ Pleurisy / pericarditis
- ☐ Renal disorder (more than 0.5g per day protein in urine or cellular casts seen in urine under a microscope)
- ☐ Blood – haematological disorder
 ☐ Hemolytic anaemia
 ☐ Lymphopenia
- ☐ Immunologic disorder
 ☐ Leukopenia
 ☐ Thrombocytopaenia
- ☐ Immunologic disorder
 ☐ positive anti-ds-DNA
 ☐ positive anti-Smith
- ☐ antiphospholipid antibodies and/or flare positive serological test for syphilis

Was additional medication necessary?

☐ No ☐ Yes (please provide details): _____

Was medication stopped due to the event?

☐ No ☐ Yes (please provide details): _____

Relevant medical history:

Form completed

By: _____

On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft Way, Manchester Science Park, M15 6SZ, or fax to 0161 2751640.

BSPAR ECS Event of Special Interest (ESI) Report

MALIGNANCY (non- haematological)

BSPAR ECS ID:

HRN:

Event Details

Biologic at time of event:

Date of Event:

Details of Malignancy (including diagnosis, location & cell type if available)
(Please provide any histopathology/staging/ radiology reports)

Date of diagnosis: ____/____/____

Did the patient have:**Surgery**YES ☐NO ☐DON'T KNOW ☐**Radiotherapy**YES ☐NO ☐DON'T KNOW ☐**Chemotherapy**YES ☐NO ☐DON'T KNOW ☐

→ Details of chemotherapy - for example protocol number, drugs used:

Other treatment (please provide details):Is there a family history of malignancy? ☐ YES ☐ NO ☐ DON'T KNOW

→ Please provide details

Did the malignancy have associated metastases? ☐ YES ☐ NO

→ Site of metastases (please provide details)

Please provide name & hospital of doctor treating the malignancy if available:

What was the outcome? ☐ Resolved ☐ Not Resolved☐ Resolved with sequelae ☐ FatalHas a yellow card been submitted? ☐ YES ☐ NO ☐ UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK
Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft Way,
Manchester Science Park, M15 6SZ, or fax to 0161 2751640.

BSPAR ECS Event of Special Interest (ESI) Report LYMPHOPROLIFERATIVE MALIGNANCY

BSPAR ECS ID:

HRN:

Event Details

(please annotate with any additional information)

Date of Event:

Biologic at time of event:

What was the diagnosis? (Please include site)**Histopathological classification & Staging/ Radiology:** (If known, please enclose a copy of the results)**Treatment Regime:**☐

Surgery

☐

Chemo regime

☐

Radiotherapy

Please provide details:

Please provide name & hospital of doctor treating the malignancy if available:

Positive family history of cancer? ☐ YES ☐ NO ☐ DON'T KNOW**Details:****What was the outcome?**☐

Resolved

☐

Not Resolved

☐

Resolved with sequelae

☐

Fatal

Has a yellow card been submitted?☐

YES

☐

NO

☐

UNKNOWN

Form completed

By: _____

On: ____/____/____

Thank you for your help!

Please return to: BSPAR ECS, Arthritis Research UK
 Epidemiology Unit, Unit 4 Rutherford House, 40 Pencroft Way,
 Manchester Science Park, M15 6SZ, or fax to 0161 2751640.

**BSPAR Etanercept Cohort Study
Biologic Studies Group
Arthritis Research UK Epidemiology Unit**

Unit 4 Rutherford House
40 Pencroft Way
Manchester Science Park
Manchester
M15 6SZ

Telephone: 0161 3061916

Fax: 0161 2751640

E-mail: Emily.sutton@manchester.ac.uk

<<date>>

<<Consultant name>>

<<Address>>

<<Address>>

<<Address>>

<<Address>>

Dear <<Consultant name>>

BSPAR ECS ID: <<BSPAR_ECS_ID>> Hospital number: <<HOSP_NO>>

Many thanks for your continuing support of the BSPAR Etanercept Cohort Study.

The main aim of the study is to determine the medium to long-term safety of the biologic etanercept in comparison with Methotrexate therapy in patients with Juvenile Idiopathic Arthritis. Accurate analysis of the reported adverse events is improved if we have as much information about these events as possible.

We would be most grateful if you could **provide us with any supporting information** on the following event, such as:

- Discharge summary with outcome of adverse event (i.e. whether resolved or not)
- Relevant outpatient letter
- Laboratory / Imaging / Histology reports
- Brief written summary
- Medications at time of event
- Your opinion of causality (probable/ possible/ probably not/ not related)

Event: <<Event>>

Date: <<Event Date>>

If you have no further information, please do let us know so that we do not repeatedly trouble you for information that you do not have. Many thanks once again for your ongoing assistance and support.

Yours sincerely,

Dr Kimme Hyrich
BSPAR ECS Chief Investigator

**BSPAR Etanercept Cohort Study
Biologic Studies Group
Arthritis Research UK Epidemiology Unit**

Unit 4 Rutherford House
40 Pencroft Way
Manchester Science Park
Manchester
M15 6SZ

Telephone: 0161 3061916
Fax: 0161 2751640
E-mail: emily.sutton@manchester.ac.uk

<<Date>>

«cfullname»
«caddr1»
«caddr2»
«caddr3» «caddr4»
«caddr5» «cpostc»

Dear «cfullname»

Re: BSPAR ECS ID: «studyno» HRN «phrn»

Thank you for your continued participation in the BSPAR Etanercept Cohort Study.

We have recently been informed that your patient sadly died on «date».

One of the primary objectives of the BSPAR ECS has been to study the long-term safety of biologic therapy and one of the most important outcomes has been death. All patients registered with the BSPAR ECS are flagged with the NHS Information Centre and we are, therefore, notified of all deaths and ultimately receive a copy of the death certificate.

However, this does not always contain details of every event surrounding the patient's death and we do not receive information from the NHS-IC on whether or not the patient was receiving a biologic drug at the time of death.

We would, therefore, be extremely grateful if you could provide us with more details, if you have them, about the events leading up to your patient's death. We would like to know if the death occurred in hospital and, if so, what was the initial reason for admission. In particular, we are interested in any other complications leading up to the death. We would also be grateful if you could indicate whether or not the patient was on a biologic drug at the time of death and if, in your opinion, this was in any way related to their demise.

There may be additional forms enclosed related to certain events of special interest around the time of death that have come to our notice, and we would be grateful if you could also complete these if you have the necessary details. The more information we have, the more accurately we are able to code and record important adverse events and the fewer patients we are forced to exclude from analyses, thus losing all information collected to date.

Thank you for your co-operation in this matter. Your continued help and support is much appreciated.

Yours sincerely,

Dr Kimme Hyrich
BSPAR ECS Chief Investigator