GUIDELINES AND AUDIT
IMPLEMENTATION NETWORK

Regional Audit of Biologic Usage in Arthritis

February 2014

Foreword

The introduction of biologic agents, towards the end of the 1990's, to the treatment of a number of conditions including rheumatoid arthritis has been life changing for patients.

There are a number of National Institute for Health and Care Excellence (NICE) products relating to rheumatoid arthritis guidance. The technology appraisal TA195 which was published in August 2010 was used as the basis of this work. Northern Ireland is committed to using therapies and treatments in line with NICE guidance.

These are powerful agents and for patients who respond they will be taking the medication for lengthy periods, potentially life long. They are also expensive agents with the costs accumulating over time. At the end of December 2014, there were 3,779 patients on treatment for rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis. The recurrent funding available for these therapies at the end of 2013/14 was £30.5m.

NICE guidance has been updated and the current extant guidance in use are TA130, TA186, TA220, TA224, TA225, TA233 and TA280. It is important for patients and the service that they are receiving their treatment in accordance with current guidance and that it is administered in the most cost effective way. An important component of compliance with NICE is to undertake a post implementation evaluation.

It would also be of benefit to have information systems to allow ongoing real time monitoring rather than relying on occasional audits which by the time of completion are often out of date.

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1. INTRODUCTION

1.1 Policy Context

The biologic and Anti -Tumour Necrosis Factor (Anti –TNF) therapies became available from the end of the 1990s.

In March 2002 NICE published guidance on the use of biologic or Anti-TNF therapies for the treatment of severe arthritis. The Department of Health, Social Services and Public Safety (DHSSPS) Priorities for Action 2006/07 introduced a target to ensure that all patients with severe arthritis who were on the waiting list for treatment with biologic therapies on March 2006 would commence their treatment by 31 March 2008. This target was fully achieved and in subsequent years, further targets have seen an ongoing reduction in regional waiting times to 13 weeks. Maintaining the progress that has been made in terms of the timeliness of access to biologic therapies remains a priority for the Minister.

The numbers of patients accessing treatment for this range of conditions has increased year on year and as treatment is long the costs are increasing annually putting increased demands on resources at a time of financial constrain. Clinical staff have a key role in managing the resources associated with biological therapies for severe inflammatory arthritis not only to ensure that therapies continue to be provided to support effective outcomes but also to ensure that appropriate arrangements are in place in instances where continued therapeutic care is assessed as ineffective.

The monitoring of clinical effectiveness should be in keeping with NICE guidance including adherence to the NICE guidance on biologic drugs for the treatment of Rheumatoid Arthritis (RA) (January 2013).and Trusts should undertake a post implementation evaluation of adherence to guidance extant at the time.

As the number of patients increase costs of treatment are also increasing. The circumstances of each patient can be different and lead to temporary suspension from treatment for a number of patients. As the cohort of patients is large and increasing Trusts need to assure themselves that they are making the best use of the entirety of the funds for biologic therapies for severe inflammatory arthritis for all patients.

Where patients are already on treatment outwith NICE guidance, Trusts are required to put in place a system to review this cohort of patients, at least on an annual basis. This process should support a rationale to either continue or cease treatment, depending on the degree of clinical benefit derived for the individual patient.

1.2 Methodology Selection

At 31 March 2010 there were 1,660 patients on biologic therapies. Guidance was sought on the appropriate sample size and a recognised sample calculator was used. This generated a sample size of 360 which was to be distributed proportionately to the patient numbers on treatment in each unit. An audit proforma was designed to reflect extant NICE guidance for the arthropothies at the time (TA 195). The data collection was undertaken in 2012 based on the above sample of patients on treatment. A total of 359 completed audit proformas were analysed by the GAIN staff. Throughout the audit report the population size (N) may change in relation to each of the questions being asked due to a variation in the subgroup. On occasion due to rounding rule the total percentage may not equal 100%

1.3 Audit Design

The audit proforma was developed by the Audit Project Team. The team included representation from the five Health and Social Care (HSC) Trusts (Appendix 1) all of whom provide biologic therapies to patients. The audit proforma was piloted using 15 patient charts (i.e. 3 per Trust). Minor amendments were made to the audit proforma following the pilot and the final audit proforma was agreed. (See Appendix 2).

1.4 Data Collection

Data was collected across the five HSC Trusts in Northern Ireland during February to May 2012. The audit proformas were completed by specialist nursing staff and clinicians in each of Trusts.

2. RESULTS

The following results from the audit are based on 359 completed forms.

2.1 Demographic Information

Table 1: Forms completed by HSC Trusts

Trust	(n=359)
Belfast Trust	155 (43%)
Northern Trust	104 (29%)
Southern Trust	53 (15%)
Western Trust	31 (9%)
South Eastern Trust	16 (4%)

The distribution of patient forms completed by Trusts reflects the distribution of patients treated by Trust.

Table 2: Gender

Gender	(n=359)
Male	86 (24%)
Female	251 (70%)
Not Recorded	22 (6%)

The gender distribution reflects the gender distribution of these conditions.

Table 3: Age categories

Age (Years)	(n=359)
18 – 24	1 (1%)
25 – 34	8 (2%)
35 – 44	26 (7%)
45 – 54	80 (22%)
55 – 64	119 (33%)
65 – 74	101 (28%)
75 + years	21 (6%)
Not Recorded	3 (1%)

Table 4: Date of Rheumatoid Arthritis diagnosis

Year	(n=359)
1950 - 1960	1 (1%)
1961 - 1970	5 (1%)
1971 – 1980	10 (3%)
1981 – 1990	38 (10%)
1991 – 2000	90 (25%)
2001 – 2010	161 (45%)
Not Recorded / Not Known	54 (15%)

The length of time patients had been diagnosed with rheumatoid arthritis reflects the chronicity of the condition and the fact that the biologic therapies were beginning to be introduced in 1999.

2.2 Assessment for Treatment

Table 5: Year of first assessment for biologic treatment

Year	(n=359)
2000	1 (1%)
2001	3 (1%)
2002	3 (1%)
2003	7 (2%)
2004	9 (3%)
2005	7 (2%)
2006	12 (3%)
2007	55 (15%)
2008	95 (26%)
2009	109 (30%)
2010	14 (4%)
Not Recorded	44 (12%)

The date of the first assessment for biologic treatment again reflects the timing of the introduction of the therapies.

Table 6: Disease Activity Score in 28 joints (DAS28 Score)

Score		(n=359)
3 – 4	moderate	1 (1%)
4 - 5	moderate	2 (1%)
5 – 6	high	139 (38%)
6 – 7	high	124 (34%)
7 – 8	high	38 (11%)
8 - 9	high	8 (2%)
Not Recorded		47 (13%)

NICE recommendations use the DAS28 score as a method of quantifying disease activity based on numbers of swollen and tender joints, general health as assessed by the patient and circulatory inflammatory markers. Eighty-five percent (n=309) of patients were classed as having a high score on initial assessment.

Table 7: Timeframe of second assessment for biologic treatment

Year	(n=359)
Before and including 2003	13 (4%)
2004	9 (3%)
2005	8 (2%)
2006	8 (2%)
2007	42 (12%)
2008	98 (27%)
2009	127 (35%)
2010	25 (7%)
Not Recorded	29 (8%)

Table 8: DAS28 Score

Score	(n=359)
5 – 6	127 (35%)
6 – 7	132 (37%)
7 – 8	54 (15%)
8 - 9	6 (2%)
Not Recorded	40 (11%)

On second assessment 89% of patients were recorded as having a high score.

2.3 Commencement of Treatment

At the time of the audit the DHSSPS Priorities for Action target (PFA target) was that no patient should wait longer than 9 months to commence specialist drug therapies for the treatment of severe arthritis. The information in the table below outlines that actual time taken to commence treatment for 329 patients. Please note 30 patients were excluded as the relevant information to calculate the date between assessment and commencement of treatment was not recorded.

Table 9: PFA target (2006/07)

PFA Target (2006/7) (9 months or less)	(n=329)
9 months or less	127 (39%)
10 mths – 15 mths	82 (25%)
16 mths – 20 mths	68 (21%)
21 mths – 25 mths	35 (10%)
> 25 mths	17 (5%)

Table 10: Date of initiation of biologic therapy

Year	(n=359)
2000	1 (1%)
2001	0 (0%)
2002	1 (1%)
2003	3 (1%)
2004	4 (1%)
2005	3 (1%)
2006	7 (2%)
2007	15 (4%)
2008	22 (6%)
2009	140 (39%)
2010	160 (44%)
2011	1 (1%)
Not Recorded	2 (1%)

Table 11: DAS28 Score

Score	(n=359)
2 – 3	3 (1%)
3 – 4	15 (4%)
4 – 5	37 (10%)
5 – 6	107 (30%)
6 – 7	119 (33%)
7 – 8	37 (10%)
8 – 9	8 (2%)
Not Recorded / Not Available	33 (9%)

At the time of commencement on therapy 76% were recorded as having a high score (Score rating of 5 -9)

Table 12: Was the person receiving?

Receiving	(n=359)
Adalimumab	169 (47%)
Etanercept	118 (33%)
Infliximab	21 (6%)
Rituximab	41 (11%)
Other (Certolizumab)	8 (2%)
Not recorded	2 (1%)

Table 13: Does the person have active rheumatoid arthritis as measured by DAS28 greater than 5.1 confirmed on at least two occasions, 1 month apart?

Active Rheumatoid Arthritis	(n=359)
Yes	302 (84%)
No	24 (7%)
Not Recorded	33 (9%)

Table 14: Has the person had trials of two Disease-modifying Antirheumatic Drugs (DMARDs)?

Trials	(n=359)
Yes	343 (96%)
No	8 (2%)
Not Recorded	8 (2%)

Table 14a: If yes, was one of them methotrexate?

Methotrexate	(n=343)
Yes	337 (98%)
No	6 (2%)

Table 14b: If no, was methotrexate contraindicated?

Contraindicated	(n=8)
Yes	3 (38%)
No	0 (0%)
Not Recorded	5 (62%)

Table 15: Is the person taking a TNF-a. inhibitor in combination with methotrexate?

TNF-a Inhibitor	(n=359)
Yes	206 (58%)
No	130 (36%)
Not Recorded	23 (6%)

Table 15a: If no, was the patient intolerant of methotrexate?

Intolerant	(n=130)
Yes	74 (57%)
No	51 (39%)
Not Recorded	5 (4%)

Table 15b: If no, was methotrexate treatment considered to be inappropriate?

Inappropriate	(n=130)
Yes	45 (35%)
No	80(62%)
Not Recorded	5 (4%)

Table 15c: If no, alternative explanation, e.g. Other DMARD substituted?

Alternative Explanation	(n=130)
Yes	26 (20%)
No	99 (76%)
Not Recorded	5 (4%)

Alternative Explanation (n=26):

- Arava x3
- Heflainomide x4
- Humax x1
- Infection x1
- Leflunomide x3
- Low WCC x1
- MTX Ineffective x2
- Sulfasalazine x3
- Unresponsive x1
- Yes, but with no explanation x7

Table 16: Steroids used in year before first assessment for anti-TNF

Steroids Used	(n=359)
Oral	127 (35%)
Injections im or intra-articular	167 (47%)
Not Recorded	65 (18%)

Table 16a: Average Dose for Oral

Average Dose	(n=127)
1 – 5 mgs	23 (18%)
6 – 10 mgs	72 (57%)
11 – 15 mgs	10 (8%)
16 – 20 mgs	7 (6%)
20 – 25 mgs	0 (0%)
26 – 30 mgs	2 (2%)
31 mgs +	4 (3%)
Not Recorded	9 (7%)

Table 16b: Total Dose for injections

Total Dose	(n=167)
<100 mgs	44 (26%)
101 – 200 mgs	67 (40%)
201 – 300 mgs	22 (13%)
301 – 400 mgs	10 (6%)
401 – 500 mgs	1 (1%)
501 mgs +	2 (1%)
Not Recorded	21 (13%)

Table 17: Steroids used in period AFTER first assessment for anti-TNF whilst on waiting list

Steroids Used	(n=359)
Oral	144 (40%)
Injections im or intra-articular	147 (41%)
Not Recorded	68 (19%)

Table 17a: Average Dose for Oral

Average Dose	(n=144)
1 – 5 mgs	29 (20%)
6 – 10 mgs	80 (55%)
11 – 15 mgs	18 (13%)
16 – 20 mgs	5 (3%)
20 – 25 mgs	0 (0%)
26 – 30 mgs	1 (1%)
31 mgs +	0 (0%)
Not Recorded	11 (8%)

Table 17b: Total Dose for injections

Total Dose	(n=147)
<100 mgs	45 (31%)
101 – 200 mgs	48 (33%)
201 – 300 mgs	29 (20%)
301 – 400 mgs	4 (3%)
401 – 500 mgs	5 (3%)
501 mgs +	4 (3%)
Not Recorded	12 (8%)

Table 18a: Unexpected event - Additional hospital admission

Unexpected Events	(n=359)
Additional hospital admissions (RA related)	20 (6%)
Number:	**(n=20)**
1	17 (85%)
2	1 (5%)
Not Recorded	2 (10%)

Table 18b: Unexpected event – Additional outpatients

Unexpected Events	(n=359)
Additional outpatient visits (beyond 2 appointments)	48 (13%)
Number:	**(n=48)**
1	22 (46%)
2	14 (29%)
3	3 (6%)
3+	3 (6%)
Not Recorded	6 (13%)

Table 18c: unexpected event – telephone calls

Unexpected Events	(n=359)
Telephone calls (recorded in case notes/ office nursing notes)	38 (11%)
Number:	**(n=38)**
1	17 (45%)
2	13 (34%)
3	3 (8%)
3+	4 (11%)
Not Recorded	1 (3%)

Tables 18 a, b and c indicate that 106 individuals or 30% of the respondents experienced a hospital admission, additional outpatient visits or telephone contact. The 20 individuals requiring hospitalisation accounted for a fifth of those with complications.

Table 19: Steroids used in year AFTER commencing anti-TNF

Steroids Used	(n=359)
Oral	115 (32%)
Injections im or intra-articular	58 (16%)
Not Recorded	186 (52%)

Table 19a: Average Dose for Oral

Average Dose	(n=115)
1 – 5 mgs	47 (41%)
6 – 10 mgs	50 (43%)
11 – 15 mgs	3 (3%)
16 – 20 mgs	3 (3%)
20 mgs +	1 (1%)
Not Recorded	11 (10%)

Table 19b: Total Dose for injections:

Total Dose	(n=58)
<100 mgs	22 (38%)
101 – 200 mgs	21 (36%)
201 – 300 mgs	3 (5%)
301 – 400 mgs	2 (3%)
Not Recorded	10 (17%)

2.4 Efficacy Assessments

First efficacy assessment

Table 20: Was there documented evidence that the DAS28 score had fallen by 1.2 or more in the 6 months after starting treatment?

Documented Evidence	(n=359)
Yes	252 (70%)
No	89 (25%)
Not Recorded	18 (5%)

Table 21: Year

Year	(n=344)
< 2000	1 (1%)
2001	2 (1%)
2002	0 (0%)
2003	0 (0%)
2004	1 (1%)
2005	6 (2%)
2006	4 (1%)
2007	12 (3%)
2008	9 (3%)
2009	67 (19%)
2010	146 (42%)
2011	84 (24%)
2012	5 (1%)
Not Recorded	7 (2%)

This was recorded as N/A for 15 patients

Table 22: DAS28 Score

Score	(n=342)
0 – 1	3 (1%)
1 – 2	19 (6%)
2 – 3	68 (19%)
3 – 4	89 (26%)
4 - 5	68 (20%)
5 – 6	52 (15%)
6 – 7	14 (4%)
7 – 8	3 (1%)
8 - 9	1 (1%)
Not Recorded	25 (7%)

This was recorded as N/A for 17 patients

Table 23: If an adequate response (i.e. fall in DAS28 score of > 1.2) was not achieved, was treatment stopped?

Treatment Stopped	(n=89)
Yes	45 (51%)
No	40 (45%)
Not Recorded	4 (4%)

(Please note this was only applicable to 89 patients).

Table 23a: Year of last dose of biologic

Year	(n=39)
2009	1 (3%)
2010	2 (5%)
2011	2 (5%)
2012	2 (5%)
Not Recorded	32 (82%)

(Please note the “year of last dose of biologic” was recorded as not applicable for 6 patients)

Table 24: If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment?

Treatment Continued	(n=91)
Yes	85 (93%)
No	1 (1%)
Not Recorded	5 (6%)

Table 24a: Reason documented

Reason Documented	(n=85)
Good Clinical Response	81 (95%)
Current Infection	3 (4%)
Interruption to Treatment	1 (1%)
*Other	5 (6%)

(Please note this was only applicable to 85 patients, and some patients had more than 1 reason documented).

*Other (n=5):

- DAS fell by 1.19 x2
- Reduction in oral steroids from 10mgs - 5mgs
- Tender and swollen joint
- Weight gain so dose increased to 300mgs

Table 25: Why was treatment stopped?

Why	(n=45)
An adverse event	8 (18%)
Poor response	31 (69%)
*Alternative explanation	6 (13%)

*Alternative explanation (n=6):

- Mild Bronchiectasis
- Gynae surgery
- Sensitive response
- Injection reaction <20
- Explanation not recorded x2

Table 25a: If treatment was stopped, was patient

Receiving	(n=45)
Adalimumab	8 (18%)
Etanercept	11 (24%)
Infliximab	2 (4%)
Rituximab	10 (22%)
Other - Certolizumab	4 (9%)
**Reason no other biologic used	5 (11%)
Not Recorded	5 (11%)

**Reason no other biologic used (n=5):

- Re-evaluated
- Patient Request
- Patient chose not to proceed
- Pleural effusion, gynae surgery
- Patient did not wish to have any further biologic

Second efficacy assessment

Table 26: Was treatment monitored by assessing DAS28 at least every 6 months after an initial response?

Treatment Monitored	(n=341)
Yes	303 (89%)
No	27 (8%)
Not Recorded	11 (3%)

This was recorded as N/A for 18 patients

Table 27: Year

Year	(n=359)
< 2000	1 (1%)
2001	2 (1%)
2002	0 (0%)
2003	0 (0%)
2004	1 (1%)
2005	6 (2%)
2006	4 (1%)
2007	12 (3%)
2008	9 (3%)
2009	67 (19%)
2010	146 (41%)
2011	84 (23%)
2012	5 (1%)
Not Recorded	22 (6%)

Table 28: DAS28 Score

Score	(n=335)
0 – 1	5 (1%)
1 – 2	32 (10%)
2 – 3	69 (21%)
3 – 4	72 (21%)
4 - 5	61 (18%)
5 – 6	46 (14%)
6 – 7	19 (6%)
7 – 8	9 (3%)
8 - 9	1 (1%)
Not Recorded	21 (6%)

This was recorded as N/A for 24 patients

Table 29: If an adequate response (i.e. fall in DAS28 score of > 1.2) was not maintained, was treatment stopped?

Treatment Stopped	(n=94)
Yes	42 (45%)
No	47 (50%)
Not Recorded	5 (5%)

(Please note this was only applicable to 94 patients).

Table 29a: Year of last dose of biologic?

Year	(n=36)
2010	3 (8%)
2011	4 (11%)
Not Recorded	29 (81%)

This was recorded as N/A for 6 patients

Table 29b: If treatment continued despite a documented fall in DAS28 of <1.2 was there a documented clinical reason for continuing treatment?

Treatment Continued	(n=47)
Yes	45 (96%)
No	2 (4%)

Table 29c: Reason documented

Reason Documented	(n=45)
Good Clinical Response	35 (78%)
Current Infection	0 (0%)
Interruption to Treatment	0 (0%)
Other*	10 (22%)

*Other (n=10):

- Fatigue and nausea
- Itch with Leflunomide
- Infection
- Patient had been doing well up to this point - early Rheumatoid Vasculitis (RV)
- Aches and pains
- Loss of efficacy

- Patient had sciatica
- Patient waiting for a cholecystectomy
- 2nd cycle of Rituximab was administered x2

Table 29d: Why was treatment stopped?

Why	(n=42)
An adverse event	4 (10%)
Poor response	31 (74%)
Alternative explanation	4 (10%)
Not Recorded	3 (7%)

Alternative explanation (n=4):

- Cellulihs
- Surgery to right foot
- Colposcopy
- 3/12 DAS 2.13 then increase again at 6-7 months

Table 29e: If treatment was stopped, was patient receiving

Receiving	(n=42)
Adalimumab	5 (12%)
Etanercept	6 (14%)
Infliximab	5 (12%)
Rituximab	14 (33%)
*Other	6 (14%)
**Reason no other biologic used	5 (12%)
Not Recorded	1 (2%)

*Other (n=6)

- Tocilizumab x5
- Certolizumab

**Reason no other biologic used (n=5)

- Patient developed abnormal LFTS
- Infection
- Surgery to right foot
- Patient did not wish to continue x2

Third efficacy assessment -

Table 30: Was treatment monitored by assessing DAS28 at least every 6 months after an initial response?

Treatment Monitored	(n=299)
Yes	273 (91%)
No	17 (6%)
Not Recorded	9 (3%)

This was recorded as N/A for 60 patients

Table 31: Year

Year	(n=296)
2001	1 (1%)
2002	0 (0%)
2003	0 (0%)
2004	1 (1%)
2005	1 (1%)
2006	6 (2%)
2007	4 (1%)
2008	10 (3%)
2009	12 (4%)
2010	68 (23%)
2011	139 (47%)
2012	54 (18%)

This was recorded as N/A for 3 patients

Table 32: DAS28 Score

Score	(n=294)
0 – 1	5 (2%)
1 – 2	25 (8%)
2 – 3	73 (25%)
3 – 4	75 (26%)
4 - 5	50 (17%)
5 – 6	30 (10%)
6 – 7	11 (4%)
7 – 8	4 (1%)
8 - 9	1 (1%)
Not Recorded	20 (7%)

This was recorded as N/A for 5 patients

Table 33: If an adequate response (i.e. fall in DAS28 score of > 1.2) was not maintained, was treatment stopped?

Treatment Stopped	(n=66)
Yes	31 (47%)
No	33 (50%)
Not Recorded	2 (3%)

Table 34: Year of last dose of biologic

Year	(n=31)
2009	1 (3%)
2010	4 (13%)
2011	5 (16%)
Not Recorded	21 (68%)

Table 34a: If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment?

Treatment Continued	(n=49)
Yes	44 (90%)
No	3 (6%)
Not Recorded	2 (4%)

Reason documented	(n=44)
Good Clinical Response	33 (75%)
Current Infection	2 (5%)
Interruption to Treatment	1 (2%)
*Other	8 (18%)

*Other n=8:

- Leg ulcer + antibiotics
- 2nd cycle of Rituximab administered x4
- Joints improved when humira restarted
- Effects wearing off
- Methotrexate increased to 15mgs

Table 34b: Why was treatment stopped?

Why	(n=31)
An adverse event	9 (29%)
Poor response	22 (71%)
Alternative explanation	0(0%)

Table 34c: If treatment was stopped, was patient

Receiving	(n=31)
Adalimumab	6 (19%)
Etanercept	6 (19%)
Infliximab	1 (3%)
Rituximab	9 (29%)
*Other	3 (10%)
**Reason no other biologic used	4 (13%)
Not Recorded	2 (7%)

*Other n=3

- Tocilizumab x2
- Abatacept

**Reason no other biologic used n=4

- No longer in South Eastern Trust
- Osteomyelitis 5th MTP Joint
- Pathway followed, no further treatment
- Patient developed lung cancer

Fourth efficacy assessment

Table 35: Was treatment monitored by assessing DAS28 at least every 6 months after an initial response?

Treatment Monitored	(n=237)
Yes	212 (90%)
No	17 (7%)
Not Recorded	8 (3%)

This was recorded as N/A for 122 patients

Table 36: Year

Year	(n=235)
2001	1 (1%)
2002	0 (0%)
2003	0 (0%)
2004	0 (0%)
2005	0 (0%)
2006	5 (2%)
2007	4 (2%)
2008	7 (3%)
2009	9 (4%)
2010	31 (13%)
2011	99 (42%)
2012	77 (33%)
Not recorded	2 (1%)

This was recorded as N/A for 2 patients

Table 37: DAS28 Score

Score	(n=230)
0 – 1	3 (1%)
1 – 2	22 (10%)
2 – 3	69 (30%)
3 – 4	48 (21%)
4 - 5	40 (17%)
5 – 6	20 (9%)
6 – 7	8 (3%)
7 – 8	6 (3%)
Not Recorded	14 (6%)

This was recorded as N/A for 7 patients

Table 38: If an adequate response (i.e. fall in DAS28 score of > 1.2) was not maintained, was treatment stopped?

Treatment Stopped	(n=54)
Yes	22 (41%)
No	32 (59%)

Table 38a: Year of last dose of biologic

Year	(n=20)
2010	1 (5%)
2011	4 (20%)
2012	1 (5%)
Not Recorded	14 (70%)

This was recorded as N/A for 2 patients.

Table 38b: If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment?

Treatment Continued	(n=23)
Yes	23 (100%)
No	0 (0%)

Reason Documented	(n=23)
Good Clinical Response	19 (83%)
Current Infection	0 (0%)
Interruption to Treatment	0 (0%)
*Other	4 (17%)

*Other:

- Toe infection
- 3rd cycle of Rituximab was administered x2
- Dose increased as trial

Table 38c: Why was treatment stopped?

Why	(n=22)
An adverse event	2 (9%)
Poor response	18 (82%)
Alternative explanation / N/R	2(9%)

Table 38d: If treatment was stopped, was patient receiving;

Receiving	**(n=22)**
Adalimumab	0 (0%)
Etanercept	4 (18%)
Infliximab	0 (0%)
Rituximab	12 (54%)
* Other	4 (18%)
**Reason no other biologic used	1 (5%)
Not Recorded	1 (5%)

*Other n=4:

- Tocilizumab x2
- Certolizumab
- Orencia

**Reason no other biologic used:

- No treatment decided

Table 39: Were the following carried out by a specialist rheumatological team with experience in the use of TNF inhibitors?

Initiation of TNF-inhibitor treatment	**(n=358)**
Yes	356 (99%)
No	0 (0%)
Not recorded	2 (1%)

This was recorded as N/A = 1

Follow-up of treatment response	**(n=356)**
Yes	356 (100%)
No	0 (0%)

Follow-up of adverse events	**(n=293)**
Yes	293 (100%)
No	0 (0%)

This was recorded as N/A for 63 patients.

Table 40: Was there any dose escalation beyond the starting dose?

Biologic 1	(n=358)
Yes	4 (1%)
No	353 (99%)
Not recorded	1 (1%)

This was recorded as N/A for 1 patient.

Dose escalation n=4:

- By 100mgs
- 200mgs – 300mgs
- Recorded as N/A x2

Biologic 2	(n=114)
Yes	1 (1%)
No	112 (98%)
Not recorded	1 (1%)

This was recorded as N/A for 245 patients

Dose escalation n=1:

- 200mgs – 400mgs

Biologic 3	(n=47)
Yes	0 (0%)
No	46 (98%)
Not recorded	1 (2%)

This was recorded as N/A for 312 patients

Biologic 4	(n=29)
Yes	1 (3%)
No	27 (93%)
Not recorded	1 (3%)

This was recorded as N/A for 330 patients

Dose escalation n=1:

- Not recorded

Table 41: Was it recorded that the patient was offered written information on treatment options?

Written Information	(n=359)
Yes	203 (57%)
No	156 (43%)

3. SUMMARY

The survey results show the expected gender profile for these conditions (70% female and 24% male - 6% not recorded) The condition of rheumatoid arthritis is known to be more common in women than men and national figures indicate that 69% of cases are in women.

The average age of onset of the condition is 54 years and approximately half of the prevalent population is over 55 years. The sampled group contains fewer younger individuals than might have been expected with less than 10% under the age of 45 years (Table 3). This may be partly explained by the number of years from diagnosis and the fact that the biologic agents were relatively recently available and NICE approved for the treatment of these conditions.

NICE recommends using the DAS28 score as a method of quantifying disease activity based on numbers of swollen and tender joints, general health as assessed by the patient and circulatory inflammatory markers. Eighty –four percent (84%) or The majority of patients were classed as having a DAS28 score of 5.1, one month apart, prior to commencement on treatment (Table 13). In addition 96% of patients had trials of two DMARDs and of this group 98% had been on methotrexate (Table14,14a) In the majority of cases (n=356) the initiation of biologics therapy was by a specialist rheumatology team with experience in the use of TNF inhibitors (Table 39).

In the year prior to treatment steroids were recorded as being used in 294 patients (82%) (Table 16). In the year after treatment commenced recorded use of steroids reduced in 173 patients (48%) (Table 19). Such a reduction in steroid use is often the reason of a good clinical response in patients who do not necessarily achieve the NICE indicated reduction in DAS28 score.

When individuals were awaiting treatment there were 20 unplanned hospital admissions, 48 further additional outpatient attendances and telephone support recorded for 38 patients.

Following commencement on biologics treatment 70% of patients had an initial (6 months) assessment documented DAS28 score (Table 20). Where this was documented 68% had a reduction in their severity score (Table 22).

In cases (n=40) where treatment continued in the absence of a documented fall in severity score just over 50% had documented the reason ‘’good clinical response’’ (Table 23,Table 24a). This illustrates the shortcomings of the DAS28 as a means of assessing rheumatoid

disease activity. The escalation of dose occurred in 1% of cases (Table 40). It should be noted that the use of the DAS28 score includes a degree of subjectivity.

Where treatment was stopped in 45 patients, the main reason highlighted was the patients ‘poor response’ (69%) (Table 23, Table 25).

On the second efficacy assessment the information was recorded in 84% of patients and at the third efficacy assessment information was recorded in 91% of 299 patients (Table 26, Table 30). There continued to be a number of patients for whom the severity scores had not fallen but treatment continued as there was a good clinical response.

It was recorded that 57% of patients were offered written information on treatment options (Table 41).

4. RECOMMENDATIONS

On the basis of the information provided by the audit, the following areas have been identified as important in terms of the way forward for this service area:

- Trusts should undertake a post project evaluation of NICE guidance in line with the expectations as part of investment process in these specialist therapies.

- Develop regional electronic audit tool to measure compliance against guidelines over a determined timescale

- Establish a regional information system / database that supports patient management and the ongoing evaluation of compliance and audit against guidelines in a more timely way

- Documentation should be recorded to confirm that consistent written information is provided to all patients in line with good clinical practice.

Appendix 1

Steering Group Membership

Name	Job Title	Organisation/Trust
Dr Janet Little **(Chair)**	Assistant Director, Commissioning and Screening	PHA
Dr Alistair Taggart	Consultant Rheumatologist	BHSCT
Dr Andrew Cairns	Consultant Rheumatologist	BHSCT
Ms Joyce Patton	Clinical Nurse Specialist	BHSCT
Ms Jayne Whiteman	Pharmacist	BHSCT
Dr Philip Gardiner	Consultant Rheumatologist	WHSCT
Ms Janice Carlisle	Clinical Nurse Specialist	WHSCT
Dr Anita Smyth	Consultant Rheumatologist	SEHSCT
Dr Clare Matthews	Consultant Rheumatologist	SEHSCT
Dr Michelle McHenry	Consultant Rheumatologist	NHSCT
Ms Ruth Mulligan	Clinical Nurse Specialist	NHSCT
Ms Hilary McKee	Pharmacist	NHSCT
Dr Nicola Maiden	Consultant Rheumatologist	SHSCT
Ms Elaine Wylie	Clinical Nurse Specialist	SHSCT
Dr William Moore	Consultant	PHA
Ms Veronica Gillen	Commissioning Lead	HSCB
Mrs Maggie Shilliday	Business Manager	HSCB
Mrs Dalrene Masson	Regional Clinical Audit Facilitator	GAIN

Appendix 2

GAIN Regional audit of biologic usage in arthritis
Rheumatoid Arthritis

Condition	NICE standard	Drug	Replaced
Rheumatoid Arthritis	- TA195	Adalimumab, Etanercept, Infliximab	- TA130
		Rituximab	- TA126

Complete one form for each patient.

1. Health and Social Care Trust – Hospital code: ☐☐☐

2. Patient coding reference: ☐☐☐

3. Sex: Male / Female

4. Age: 18 – 24 years ☐ 55 – 64 years ☐
   25 – 34 years ☐ 65 – 74 years ☐
   35 – 44 years ☐ 75 + years ☐
   45 – 54 years ☐

No.	Criteria	Yes	No	Additional data / response
5.1	Date of Rheumatoid Arthritis diagnosis	……/……/……		
5.2	Date of first assessment for biologic treatment	……/……/……		DAS28 score: ……
5.3	Date of second assessment for biologic treatment	……/……/……		DAS28 score: ……
6.1	**Commencement on biologic treatment** Date of initiation of biologic therapy	……/……/……		DAS28 score: ……
6.2	Was the person receiving:			
	• adalimumab	☐	☐	Starting dose …… Date ……/……/……
	• etanercept	☐	☐	Starting dose …… Date ……/……/……
	• infliximab	☐	☐	Starting dose …… Date ……/……/……
	• rituximab	☐	☐	Starting dose …… Date ……/……/……
	• other? please specify ……	☐	☐	Starting dose …… Date ……/……/……
7.	Does the person have active rheumatoid arthritis as measured by DAS28 greater than 5.1 confirmed on at least two occasions, 1 month apart?	☐	☐	

No.	Criteria			Yes	No	Additional data / response
8.1	Has the person had trials of two DMARDs?			☐	☐	
8.2	If yes, was one of them methotrexate?			☐	☐	Not documented ☐
8.3	If No, was methotrexate contraindicated?			☐	☐	Not documented ☐
9.1	Is the person taking a TNF-α inhibitor in combination with methotrexate?			☐	☐	
9.2	If No	Was the patient intolerant of methotrexate?		☐	☐	
9.3		Was methotrexate treatment considered to be inappropriate?		☐	☐	
9.4		Alternative explanation, eg. other DMARD substituted		☐	☐	Details: …… ……...
10.1	Steroids used in year before first assessment for anti-TNF:		a) Oral –	☐	☐	average dose .....
			b) Injections im or intra-articular	☐	☐	..... total dose
10.2	Steroids used in period AFTER first assessment for anti-TNF whilst on waiting list:		a) Oral –	☐	☐	average dose .....
			b) Injections im or intra-articular	☐	☐	..... total dose
10.3	Where there any unexpected events or interventations whilst on waiting list?	Additional hospital admissions (RA related)		☐	☐	Number:
		Additional outpatient visits (beyond 2 appts)		☐	☐	Number:
		Telephone calls (recorded in casenotes or team office nursing notes)		☐	☐	Number:
10.4	Steroids used in year AFTER commencing anti-TNF		a) Oral –	☐	☐	average dose .....
			b) Injections im or intra-articular	☐	☐	..... total dose

11	**First efficacy assessment** Was there documented evidence that the DAS28 score had fallen by 1.2 or more in the 6 months after starting treatment?	☐	☐	At 6 months – Date: ……/……/…… DAS score: …… *If fall in DAS28 of >1.2 (i.e. adequate response) **and** patient continued on same biologic please go to Q15.*
12.1	If an adequate response was not achieved, was treatment stopped? ☐ Not applicable	☐	☐	Date ……/……/…… Of last dose of biologic *(if recorded)*
12.2	If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment? ☐ Not applicable	☐	☐	Reason documented: ☐ Good clinical response ☐ Current infection ☐ Interruption in treatment ☐ Other: …… …… …… ……
13.1	Why was treatment stopped? ☐ Not applicable	An adverse event	☐	☐	
13.2		Poor response	☐	☐	
13.3		Alternative explanation	☐	☐	Details: …… ……
14	If treatment was stopped, was patient: a) Commenced alternative biologic, as listed below b) If no other biologic used please state reason if documented			b) reason no other biologic used: …… …… ……
	▪ adalimumab	☐	☐	Starting dose …… Date ……/……/……
	▪ etanercept	☐	☐	Starting dose …… Date ……/……/……
	▪ infliximab	☐	☐	Starting dose …… Date ……/……/……
	▪ rituximab	☐	☐	Starting dose …… Date ……/……/……
	▪ other? please specify ……	☐	☐	Starting dose …… Date ……/……/……

15	**Second efficacy assessment** Was treatment monitored by assessing DAS28 at least every 6 months after an initial response?		☐	☐	Date: ……/……/…… DAS score: *If fall in DAS28 of >1.2 (i.e. adequate response) **and** patient continued on same biologic please go to Q19.*
16.1	If an adequate response was not maintained, was treatment stopped? ☐ Not applicable		☐	☐	Date ……/……/…… Of last dose of biologic *(if recorded)*
16.2	If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment? ☐ Not applicable		☐	☐	Reason documented: ☐ Good clinical response ☐ Current infection ☐ Interruption in treatment ☐ Other: …… …… …… ……
17.1	Why was treatment stopped? ☐ Not applicable	An adverse event	☐	☐	
17.2		Poor response	☐	☐	
17.3		Alternative explanation	☐	☐	Details: …… ……
18	If treatment was stopped, was patient: a) Commenced alternative biologic, as listed below b) If no other biologic used please state reason if documented				b) reason no other biologic used: …… …… ……
	▪ adalimumab		☐	☐	Starting dose …… Date ……/……/……
	▪ etanercept		☐	☐	Starting dose …… Date ……/……/……
	▪ infliximab		☐	☐	Starting dose …… Date ……/……/……
	▪ rituximab		☐	☐	Starting dose …… Date ……/……/……
	▪ other? please specify ……		☐	☐	Starting dose …… Date ……/……/……

19	**Third efficacy assessment** ☐ Not applicable (if this is not applicable for patient please go to Q27) Was treatment monitored by assessing DAS28 at least every 6 months after an initial response?		☐	☐	Date: ……/……/…… DAS score: *If fall in DAS28 of >1.2 (i.e. adequate response) **and** patient continued on same biologic please go to Q23.*
20.1	If an adequate response was not maintained, was treatment stopped? ☐ Not applicable		☐	☐	Date ……/……/…… Of last dose of biologic *(if recorded)*
20.2	If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment? ☐ Not applicable		☐	☐	Reason documented: ☐ Good clinical response ☐ Current infection ☐ Interruption in treatment ☐ Other: …… …… …… ……
21.1	Why was treatment stopped? ☐ Not applicable	An adverse event	☐	☐	
21.2		Poor response	☐	☐	
21.3		Alternative explanation	☐	☐	Details: …… ……
22	If treatment was stopped, was patient: a) Commenced alternative biologic, as listed below b) If no other biologic used please state reason if documented				b) reason no other biologic used: …… …… ……
	▪ adalimumab		☐	☐	Starting dose …… Date ……/……/……
	▪ etanercept		☐	☐	Starting dose …… Date ……/……/……
	▪ infliximab		☐	☐	Starting dose …… Date ……/……/……
	▪ rituximab		☐	☐	Starting dose …… Date ……/……/……
	▪ other? please specify ……		☐	☐	Starting dose …… Date ……/……/……

23	**Fourth efficacy assessment** ☐Not applicable (if this is not applicable for patient please go to Q27) Was treatment monitored by assessing DAS28 at least every 6 months after an initial response?	☐	☐	Date: ……/……/…… DAS score: *If fall in DAS28 of >1.2 (i.e. adequate response) **and** patient continued on same biologic please go to Q27.*
24.1	If an adequate response was not maintained, was treatment stopped? ☐ Not applicable	☐	☐	Date ……/……/…… Of last dose of biologic *(if recorded)*
24.2	If treatment continued despite a documented fall in DAS28 of <1.2, was there a documented clinical reason for continuing treatment? ☐ Not applicable	☐	☐	Reason documented: ☐ Good clinical response ☐ Current infection ☐ Interruption in treatment ☐ Other: …… …… …… ……
25.1	Why was treatment stopped? ☐ Not applicable	An adverse event	☐	☐	
25.2		Poor response	☐	☐	
25.3		Alternative explanation	☐	☐	Details: …… ……
26	If treatment was stopped, was patient: c) Commenced alternative biologic, as listed below d) If no other biologic used please state reason if documented			b) reason no other biologic used: …… …… ……
	▪ adalimumab	☐	☐	Starting dose …… Date ……/……/……
	▪ etanercept	☐	☐	Starting dose …… Date ……/……/……
	▪ infliximab	☐	☐	Starting dose …… Date ……/……/……
	▪ rituximab	☐	☐	Starting dose …… Date ……/……/……
	▪ other? please specify ……	☐	☐	Starting dose …… Date ……/……/……

27	Were the following carried out by a specialist rheumatological team with experience in the use of TNF inhibitors?			
27.1	• initiation of TNF-inhibitor treatment	☐	☐	
27.2	• follow-up of treatment response	☐	☐	
27.3	• follow-up of adverse events	☐	☐	
28	Was there any dose escalation beyond the starting dose?			
28.1	Biologic 1	☐	☐	Dose escalation: ……
28.2	Biologic 2 ☐ Not applicable	☐	☐	Dose escalation: ……
28.3	Biologic 3 ☐ Not applicable	☐	☐	Dose escalation: ……
28.4	Biologic 4 ☐ Not applicable	☐	☐	Dose escalation: ……
29	Was patient offered written information on treatment options?	Recorded ☐	Not recorded ☐	

End of audit proforma