Rheumatoid arthritis high-cost drugs summary

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Norfolk and Waveney Integrated Care System

Failure of intensive therapy with 2 or more cDMARDs

- DAS score ≥ 5.1
- 3.2 ≤ DAS score < 5.1

Key	Drug	MoA	RoA	Strength	Frequency	Relative cost	C/I key	DAS score 3.2-5.1 (TA)	DAS score ≥5.1 (TA)	BioSim	MTX required?[1]	Pregnancy	BrFeed	MHRA
RTX	Rituximab	B cells/CD20	IV	2g	Every 24 weeks		2,3,5,7	-	✓ (195)	✓	-	-	-	-
ADA	Adalimumab	TNFαi	SC	40mg	Every 2 weeks[2]		1,3,4	✓ (715)	✓ (195, 375)	✓	-	T1+2	✓	-
INF	Infliximab	TNFαi	IV	3mg/kg	Every 8 weeks		2,3,4	✓ (715)	✓ (195, 375)	✓	✓	T1	-	-
FGB	Filgotinib	JAK 1&3i	PO	200mg	Once daily		1,5,9	✓ (676)	✓ (676)	✓	-	-	-	-
ETN	Etanercept	TNFαi	SC	50mg	Once weekly		1,3,4	✓ (715)	✓ (195, 375)	✓	-	T1+2	-	-
INF	Infliximab	TNFαi	SC	3mg/kg	Every 8 weeks		2,3,4	-	✓ (676)	✓	✓	T1	-	-
PAD	Upadacitinib	JAK 1i	PO	15mg	Once daily		1,5,8,9	✓ (744)	✓ (665)	-	-	-	-	✓
TFA	Tofacitinib	JAK 1&3i	PO	5mg	Twice daily		1,5,8,9	-	✓ (480)	-	-	-	-	✓
BRB	Baricitinib	JAK 1&2i	PO	4mg	Once daily		1,9	-	✓ (466)	-	-	-	-	✓
SRB	Sarilumab	IL-6i	SC	200mg	Every 2 weeks		1,5	-	✓ (485)	-	-	-	-	-
ABA	Abatacept	T cells CD80/86	IV	125mg	Once weekly		1,5	-	✓ (195, 375)	-	✓	-	-	-
ABA	Abatacept	T cells CD80/86	SC	125mg	Once weekly		1,5	-	✓ (195, 375)	-	✓	-	-	-
CZP	Certolizumab pegol	TNFαi	SC	200mg	Every 2 weeks		1,3,4	-	✓ (375, 415)	-	✓	✓	✓	-
TCB	Tocilizumab	IL-6i	SC	162mg	Once weekly		1,5	-	✓ (247, 375)	-	-	-	-	✓
GOL	Golimumab	TNFαi	SC	50mg	Every 4 weeks		1,3,4	-	✓ (225, 375)	-	✓	-	-	-
TCB	Tocilizumab	IL-6i	IV	162mg	Once weekly		1,5	-	✓ (247, 375)	-	-	-	-	✓

1 : Information regarding whether theraputic option can be initiated as monotherapy, or if methotrexate is required in combination. Rituximab can be initiated as monotherapy, as per local agreement.

Measure EULAR at 6 months
Is DAS28 response >0.6 compared to baseline?

- No → Stop treatment & wait until DAS>5.1, commence severe pathway
- Yes → **Continue treatment and review response 6 MONTHLY.** If this initial response is not maintained, stop treatment.

Measure EULAR at 6 months
Is DAS28 response >1.2 compared to baseline?

- No → Switch to alternative agent with a different mechanism of action.
- Yes → **Continue treatment and review response 6 MONTHLY.** If this initial response is not maintained, stop treatment.

2: Weekly Adalimumab dosing (local decision)

As per local agreement(TAG - May 2023), patients on the usual dose of adalimumab 40mg every 2 weeks subcutaneously, who have experienced loss of efficacy with subtherapeutic trough adalimumab levels. Note, the following exclusions apply

- patients on the originator (Humira)
- patients who have anti -drug antibodies

See Rheumatoid Arthritis High -Cost drug Treatment Pathway document for full details

Key - Contraindication

1. Hypersensitivity to active substance, or to any product excipients
2. Hypersensitivity to active substance, to other murine proteins, or to any product excipients
3. NY class 3 4 heart failure
4. Patients with/at risk of severe infections such as tuberculosis sepsis, abscesses, and opportunistic infections
5. Clinically important, active infection (e g active tuberculosis)
6. Active Crohn's disease
7. Patients in a severely immunocompromised state
8. Severe hepatic impairment
9. Pregnancy

Considerations to Support the Use of a Specific Agent

- Patient factors: Device, dexterity, adherence, dose frequency, route of administration, weight, co -morbidities, drug history
  Abatacept : High risk of infection
- **Adalimumab** : Extra articular features/co -existent eg. uveitis (TA383), psoriasis (TA146), IBD (TA 187/329).
- **Certolizumab** : Females of childbearing potential
- **Etanercept** : Risk of activation of latent TB or high risk of infection. Etanercept is less immunogenic than other TNFi, may be a suitable option for patients experiencing secondary failure.
- **Golimumab** : Patient weight >100Kg: PAS permits double dose at the same cost (??)
- **IL-6 inhibitor** : Features of IL -6 mediated disease e.g. high ESR/CRP, anaemia, high ferritin; Consider in monotherapy
- **IV Infusions** : Compliance issues, impaired manual dexterity
- **JAK inhibito** r: Needle phobia. If patient has renal impairment or on haemodialysis, consider Tofacitinib.
- **Rituximab**: Consider 1st line (off -label use) if SLE/CTD overlap, co -existing ILD, haematological malignancy or treated solid malignancy within last 5 years, history of demyelination (EULAR/ACR recommendations). Rituximab with an alternative DMARD or as monotherapy may also be considered.

Published MHRA Warnings for Specific Agents:

- **Tocilizumab** (RoActemra ®): rare risk of serious liver injury including cases requiring transplantation (July 2019)
- **All JAK inhibitors :** increased incidence of malignancy, major adverse cardiovascular events (MACE), serious infections, venous thromboembolism (VTE) and mortality (April 2023)

Specific JAK inhibitor warnings :

- **Baricitinib** (Olumiant®) : risk of venous thromboembolism (March 2020)
- **Baricitinib** (Olumiant®) : increased risk of diverticulitis, particularly in patients with risk factors (August 2020)
- **Tofacitinib** (Xeljanz®) : new measures to minimise risk of venous thromboembolism and of serious and fatal infections (March 2020)
- **Tofacitinib** (Xeljanz®) : new measures to minimise risk of major adverse cardiovascular events and malignancies (October 2021)
- **Upadacitinib** (Rinvoq ®): advice for venous thromboembolism (March 2020)