Clinical Commissioning Policy
Tocilizumab for the treatment of adult-onset Still's disease refractory to second-line therapy (adults) [210801P] (URN: 1609)

First published: June 2018 **Updated:** August 2021 **Version number:** 2.0

Commissioning position

Summary

Tocilizumab is recommended to be available as a routine commissioning treatment option for adult-onset Still's disease within the criteria set out in this document.

Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Executive summary

Plain language summary

About adult-onset Still's Disease

Adult-onset Still's disease (AOSD) is a relatively rare multisystem autoinflammatory disorder of unknown cause. Typically, patients have symptoms of high spiking fever, arthritis in multiple joints, enlarged lymph nodes, rashes, sore throat, an elevated white blood cell count and raised blood markers for inflammation.

There are a number of other recognised clinical symptoms of AOSD including swollen spleen and liver (hepatosplenomegaly), weight loss, muscle pain (myalgia) and swelling around the heart (pericarditis). Diagnosis is difficult due to the wide range of possible diagnoses and lack of specific diagnostic tests.

Still's disease in children is subject to a separate clinical commissioning policy as there are significant differences in the course of the illness and its treatment.

About current treatments

Treatment for AOSD consists of the prescribing of anti-inflammatory medicines such as non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids. Once the diagnosis is confirmed, patients are initially treated with corticosteroids. Methotrexate, an immune system suppressant, can be added to treatment for patients who fail to achieve remission or are dependent on steroids for symptom control.

In patients that fail to achieve remission after use of corticosteroids, methotrexate and disease modifying anti-rheumatic drugs (DMARDS), the use of anakinra through NICE Technology Appraisal (TA) 685 published on 31st March 2021 and tocilizumab through this clinical commissioning policy have been suggested as alternative treatments.

Tocilizumab has also been suggested as a treatment in AOSD patients with chronic arthritis that does not respond to methotrexate or DMARDS. Tocilizumab is a monoclonal antibody that attaches to the receptor for interleukin-6 (IL-6) which is also part of the process that leads to inflammation. Tocilizumab is not licensed for use in AOSD.

Clinical outcomes following treatment of AOSD include decreased severity of the disease or remission, normalisation of white blood cell count and decreased blood markers for inflammation and improvement in quality of life.

What we have decided

NHS England has carefully reviewed the evidence to treat adult-onset Still's disease with tocilizumab, where the disease does not respond to methotrexate, corticosteroids and DMARDs. We have concluded that there is enough evidence to make the treatment available at this time.

Links and updates to other policies

The following documents have informed this policy:

- B09/S/a NHS Standard Contract for Specialised Immunology (All Ages)
- A13/S/a NHS Standard Contract for Specialised Rheumatology Services (Adult)
- https://cks.nice.org.uk/dmards
- Anakinra for treating Still's disease Technology appraisal guidance [TA685] Published date: 31 March 2021

Overview of condition and treatments

AOSD is a relatively rare multisystem autoinflammatory disorder of unknown aetiology with an incidence of approximately 1-2 per million. It is estimated there are between 55-110 incident cases per year and an estimated prevalence of between 400-800 patients in England. Typically, patients present with high spiking fever, polyarthritis, lymphadenopathy, evanescent rash, sore throat and a prominent leucocytosis. Acute phase markers such as C-Reactive Protein (CRP), erythrocyte sedimentation rate (ESR) and serum ferritin are often raised.

There are a number of other recognised clinical manifestations of AOSD including hepatosplenomegaly, weight loss, myalgia and pericarditis. Diagnosis is difficult due to the wide range of differential diagnoses and lack of specific diagnostic tests.

Various diagnostic criteria have been developed, but the Yamaguchi classification (Yamaguchi 1992) criteria are most frequently used. Five or more criteria are required of which two or more must be major:

Major criteria

- Fever >39 °C, lasting 1 week or longer
- Arthralgia or arthritis, lasting 2 weeks or longer
- Typical rash
- Leucocytosis >10,000/mm^3 with >80% polymorphonuclear cells

Minor criteria

- Sore throat
- Recent development of significant lymphadenopathy

- Hepatomegaly or splenomegaly
- Abnormal liver function tests
- Negative tests for antinuclear antibody (IF) and rheumatoid factor (IgM)

Exclusion criteria

- Infections
- Malignancies (mainly malignant lymphoma)
- Other rheumatic disease (mainly systemic vasculitides).

Based on the predominant symptoms, disease activity and evolution, two phenotypes of AOSD have been described. One is a systemic form which has an acute onset. These patients tend to be highly symptomatic with fevers, weight loss and other systemic manifestations (Group 1). In patients with the systemic predominant form, the course of the disease might be self-limiting, intermittent. The current literature suggests that on average 30% of patients develop a self-limiting course, 30% an intermittent course, and 40% a chronic course.

The other disease type is the arthritis predominant form of AOSD. This usually has an indolent onset (Group 2). Systemic symptoms are less well defined and a subset of patients develop a chronic erosive arthritis.

Current treatments

First line treatment for AOSD consists of NSAIDs and corticosteroids. NSAIDs can be used for symptomatic control during diagnostic work-up. Once the diagnosis is confirmed, patients are initially treated with corticosteroids (0.8-1.0 mg/kg/day). Methotrexate (MTX) (7.5-20 mg/week) can be added for patients who fail to achieve remission or are dependent on steroids for symptomatic control.

Under NICE TA 685, anakinra is recommended as an option for treating Still's disease with moderate to high disease activity, or continued disease activity after non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids. It is only recommended for AOSD disease that has responded inadequately to 2 or more conventional disease-modifying antirheumatic drugs (DMARDs).

Clinical outcomes following treatment of AOSD include resolution of disease flare, clinical remission, normalisation of biochemical markers, improved serum amyloid levels and improvement in quality of life.

New treatment

Tocilizumab has been suggested as a treatment in AOSD patients with the chronic arthritis predominant form (Group 2) refractory to MTX and patients in Group 1 who have failed to respond to MTX and anakinra.

Tocilizumab is a monoclonal antibody that attaches to the receptor for interleukin-6 (IL-6) which is important on the pathway that leads to inflammation. Tocilizumab in combination with MTX, is licensed for the treatment of severe, active and progressive rheumatoid arthritis in adults not previously treated with MTX and the treatment of moderate to severe active rheumatoid arthritis in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.

Tocilizumab is also licensed for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients over 2 years, who have responded inadequately to previous therapy with NSAIDs and systemic corticosteroids.

Tocilizumab can be given as monotherapy or in combination with MTX. NICE has not reviewed tocilizumab for use in AOSD. It has published a technology appraisal guidance (TA238) recommending tocilizumab as a treatment for some children and young people with systemic juvenile idiopathic arthritis that is refractory to standard treatment (NICE, 2011).

NICE has recommended tocilizumab in combination with methotrexate for treating rheumatoid arthritis if the disease activity scores (DAS28) is greater than 5.1 and has not responded to intensive therapy with a combination of conventional DMARDs.

Epidemiology and needs assessment

There is no consensus on the incidence and prevalence of AOSD overall and in Groups 1 and 2 in the English population. Fautrel (2004) states the estimated incidence of AOSD in France is between 1 – 2 cases per million population per year.

Therefore, it can be estimated that in England, approximately 55-110 new cases of AOSD could be expected every year, assuming the French and English populations are similar. There is insufficient epidemiological information to make estimates of incidence for each AOSD sub-group.

Fautrel (2004) reports the prevalence of AOSD disease at around 10 per million (range 7.3 to 14.7) in Japan. Asanuma et.al (2015) estimated the prevalence of AOSD disease at 3.9 per 100,000 in a Japanese study. Based on extrapolated estimates for England, approximately 600-800 cases of AOSD could be estimated to be prevalent in the population. Applying this epidemiology should be interpreted with caution given the significant differences in the ethnic and age profiles between the Japanese and English populations. There is insufficient epidemiological information to make estimates of prevalence for each AOSD sub-group.
No evidence was available as regards the proportion of patients thought to be refractory to methotrexate and corticosteroids with AOSD in the evidence review. Gerfaud-Valentin et al (2014) estimated between a quarter and a third of patients with AOSD are thought to be refractory to DMARDs and could require biologicals.

Evidence summary

NHS England has concluded that there is sufficient evidence to support a policy for the routine commissioning of this treatment for the indication.

A total of four papers met the inclusion criteria determined on the basis of the research questions in the PICO. A case series published by Cipriani (2014) (n=11), a retrospective multi-centre open label study by Ortiz-Sanjuan (2014) (n=34), a prospective cohort study by Puechal (2011) (n=14) and a retrospective questionnaire based survey study by Elkayam (2014) (n=15). The papers varied significantly in the baseline characteristics of the patients included, the dosage and frequency of drug administration, the use of concurrent therapy and the previous therapies used by the patients. Patients in these studies were predominantly group 2. It was not possible to separate out the results for the two patient groups which make it challenging to make specific recommendations for each sub-group of AOSD. While most studies state that patients had refractory disease their complete treatment history is not stated, so there may be patients included in the results who may not have had refractory disease.

There were no randomised controlled trials or systematic reviews identified in literature. The design of the studies mean they may be subject to selection, publication and reporting bias and may not take account of all confounding factors. This may limit the generalisability of the studies to a larger population.

The main outcome measures included were impact on systemic disease features (Cipriani 2014), reduction in inflammatory markers (Elkayam 2014) and steroid sparing (Ortuz-Sanjuan 2014, Elkayam 2014). The retrospective nature of some of the studies also limits the range of outcomes measured and reported.

Follow up varied from 6 months (Elkayam 2014 and Puechal 2011) to 12 months (Cipriani 2014 and Ortiz-Sanjuan 2014). The variability in the follow up duration means that long term efficacy

and safety of tocilizumab cannot be fully evaluated. The studies evaluated some patients on tocilizumab as monotherapy and some for whom tocilizumab was given in combination with other drugs (for example prednisolone). However as results for all patients were pooled it is not possible to ascertain the specific effect of tocilizumab as monotherapy.

There appears to be evidence of effectiveness in the studies in modifying features of the disease such as reduction in median disease activity score, significant improvement in joint assessment ($P<0.05$) and VAS (Visual Analogue Scale) global assessment ($P<0.005$) reported (Cipriani 2014). Of the 11 patients in this study eight patients received Tocilizumab in combination with MTX and prednisolone and three had tocilizumab with prednisolone only. A statistically significant reduction in mean tender joints was reported by Elkayam (2014) ($P<0.05$). Other studies report on European League Against Rheumatism (EULAR) score remission (Cipriani 2014) (Puechal 2011) and substantial but not significant reduction in joint manifestations (Ortiz-Sanjuan, 2014). Detail was not presented on response by AOSD sub-group. Elkayam (2014) reports significant reduction in mean ESR and CRP values ($P<0.05$). Two studies reporting a statistically significant steroid sparing effect (Ortiz-Sanjuan 2014, and Elkayam 2014).

Adverse events varied in frequency and severity. The most commonly reported side effect was infection including upper respiratory tract infections (URTIs), herpes zoster, pneumonia and UTI (Ortiz-Sanjuan et.al (2014) (n=10/34), Cipriani et al (2014) n=1/11). In some cases this lead to patients discontinuing medication.

Another commonly reported side effect was injection site reaction (Cipriani et al (2014) n=2/11). Systemic flare was also reported (Cipriani et al (2014) n=3/11). Other side effects reported included single cases of hepatotoxicity.

There were no published studies evaluating the cost-effectiveness of tocilizumab and/or comparator therapies in the treatment of refractory adult-onset Still's disease.

Conclusion

The published evidence on the clinical efficacy and safety of tocilizumab in AOSD consists of case series, retrospective studies, a randomised open label study and a prospective cohort study. These studies are of variable quality. The major drawback of these studies is that they are subject to selection bias and the effect of confounding factors so it is difficult to understand the true efficacy of the intervention.

The evidence suggests that tocilizumab is associated with a positive impact on biochemical markers, systemic features and use of steroids in patients with refractory AOSD. However as drugs was administered as both monotherapy and combination therapy the exact effect cannot be ascertained. As patients received different drugs in combination with tocilizumab it is not possible to make clear recommendations on which drugs could be given in combination or at which stage of disease progression. Patients who received the drug were from Group 1 and 2 but pooled results were presented so it is not clear which group would most benefit from the therapy.

Adverse events were reported relatively frequently and ranged from injection site reactions to severe infections. The lack of randomised controlled trials may be due to the rarity of the disease and heterogeneous presentations which means it is difficult to make direct comparisons with standard care.

No studies have evaluated the cost-effectiveness of tocilizumab or compared its cost effectiveness with existing treatments.

Implementation

Criteria

Inclusion criteria

Tocilizumab will be routinely commissioned for the treatment of adult-onset Still's disease as a third line treatment where patients are refractory to steroid-sparing effect DMARDs.

Tocilizumab will only be commissioned for those patients who meet the following criteria:

- Patients who have failed to respond to - or are intolerant of - standard immunosuppressive therapy, including at least two of the following agents: methotrexate, cyclosporine, azathioprine, leflunomide, mycophenolate and anakinra or where standard therapies are contraindicated; AND
- Patients have been provided with information on potential adverse effects.

Response criteria

At least two of the following:

- Reduction of DAS28 by at least 1.2 points
- Reduction of ESR by at least 25%
- Reduction of CRP by at least 25%
- Reduction of corticosteroid dose by at least 25%

Dosing

Dosage can initially start at between 4mg/kg every four weeks to 8mg/kg every two weeks. This can then be titrated and reduced once the patient has started to respond. Stable patients could be considered for sub-cutaneous tocilizumab.

Stopping criteria

- Not achieving the response criteria within eight weeks.
- In patients where the response criteria are achieved but subsequently response to tocilizumab declines and loses efficacy, as judged by loss of the response criteria above over two consecutive assessments, at least three months apart.

Clinical consensus supported by NICE TA 685 suggests that tocilizumab may be chosen in preference to anakinra for patients where joint inflammation predominates and chose anakinra in preference to tocilizumab where systemic symptoms predominate. For patients where there is no response (as defined above), the clinician may consider switching to the alternative biologic, e.g. anakinra to tocilizumab. Treatments are not to be used concurrently.

Patient pathway

After an initial AOSD diagnosis using a diagnosis criterion such as Yamaguchi criteria the treatment pathway would be:

First line treatments: NSAIDS and corticosteroids: prednisolone 0.8-1 mg/kg/day for 4-6 weeks.

Second line treatments: When diagnosis is confirmed, patients treated using a selection of the following conventional steroid-sparing effect DMARDs prescribed in line with NICE Clinical Knowledge Summary (CKS) for DMARDs:

- MTX: 7.5 -25 Mg/week (oral or s/c) or
- Cyclosporine: up to 5mg/kg/day depending on tolerance/side effects
- mycophenolate 2-3g/day or
- Leflunomide 10-20 mg od, or
- Azathioprine 2-2.25mg/kg (in patients with normal thiopurine methyltransferase (TPMT) levels; 1-1.25mg.kg in patients with heterozygote level TPMT levels.)
- Corticosteroids can be used in combination with any of these regimes.

Patients that are refractory to or are intolerant of two of the above second line treatments can be considered for third line treatment.

Response criteria for DMARDS:

At least two of the following:

- Reduction of DAS28 by at least 1.2 points
- Reduction of ESR by at least 25%
- Reduction of CRP by at least 25%
- Reduction of corticosteroid dose by at least 25%

Criteria for third line treatment:

- Not achieving the response criteria within eight weeks to second line treatments.
- In patients where the response criteria are achieved to second line treatments but subsequently response declines and loses efficacy, as judged by loss of the response criteria above over two consecutive assessments, at least three months apart.

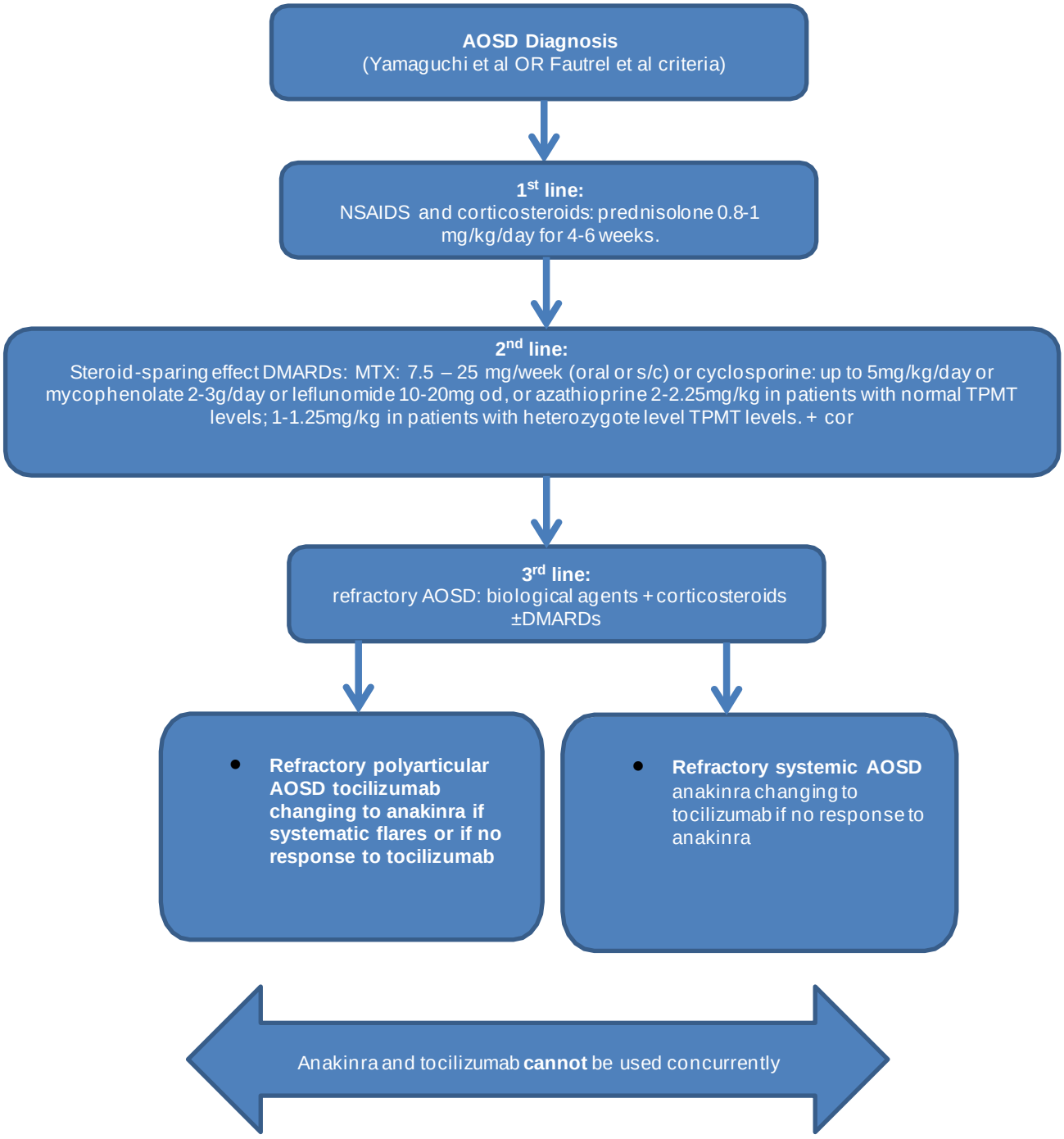
If the patient is refractory, third line treatment can be anakinra or tocilizumab plus corticosteroids ±DMARDs depending on the predominant clinical presentation:

- Polyarticular AOSD – tocilizumab changing to anakinra if systematic flares or if no response to tocilizumab.
- Refractory AOSD – anakinra changing to tocilizumab if no response to anakinra.

Anakinra and tocilizumab are not to be used concurrently.

Review period

Patients should be reviewed regularly initially to monitor response to the biologic agent, moving to 3-4 monthly as symptoms settle. It would be expected that the patient's response to biologics is reviewed annually to ensure continued efficacy.


AOSD Diagnosis
(Yamaguchi et al OR Fautrel et al criteria)
1st line:
NSAIDS and corticosteroids: prednisolone 0.8-1 mg/kg/day for 4-6 weeks.
2nd line:
Steroid-sparing effect DMARDs: MTX: 7.5 – 25 mg/week (oral or s/c) or cyclosporine: up to 5mg/kg/day or mycophenolate 2-3g/day or leflunomide 10-20mg od, or azathioprine 2-2.25mg/kg in patients with normal TPMT levels; 1-1.25mg/kg in patients with heterozygote level TPMT levels. + cor
3rd line:
refractory AOSD: biological agents + corticosteroids ±DMARDs
Refractory polyarticular AOSD tocilizumab changing to anakinra if systematic flares or if no response to tocilizumab
Refractory systemic AOSD anakinra changing to tocilizumab if no response to anakinra
Anakinra and tocilizumab cannot be used concurrently

Governance arrangements

Tocilizumab for AOSD must only be used for treatment in specialised Rheumatology and/or Immunology centres, or in collaboration with a specialised centre under the supervision of an expert multidisciplinary team.

Audit requirements

Treatment centres will use a prior approval system to track and audit use of tocilizumab, in order to ensure it is administered according to the criteria for commissioning.

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

Definitions

Adult-onset Still's disease	A relatively rare multisystem autoinflammatory disorder of unknown cause. Typically, patients have symptoms of high spiking fever, arthritis in multiple joints, enlarged lymph nodes, rashes, sore throat, an elevated white blood cell count and raised inflammation markers.
Biologic agent	A substance that is made from a living organism or its products andis used in the prevention, diagnosis, or treatment of diseases. Biologic agents include antibodies, interleukins, and vaccines.
Corticosteroids	A group of natural and synthetic analogues of the hormones secreted by the hypothalamic-anterior pituitary-adrenocortical (HPA) axis, more commonly referred to as the pituitary gland.
Disease modifying anti-rheumatic drugs (DMARDs)	These act by altering the underlying disease rather than treating symptoms. They are not painkillers, but they may reduce pain, swelling and stiffness over a period of weeks or months by slowing down the disease and its effects on the joints.
Inhibitors/blockers	Immunosuppressive agents which inhibit the action of interleukins.
Interleukins	A group of cytokines which are synthesized by lymphocytes, monocytes,macrophages, and certain other cells. They function especially in regulation of the immune system.

Monoclonal antibody	An antibody produced by a single clone of cells or cell line and consisting of identical antibody molecules**.**
Refractory	No improvement in symptoms, and/or inflammatory markers and/or dependence on high dose corticosteroids.

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Change form for published Specifications and Products developed by Clinical Reference Group (CRGs)
Product name: Anakinra/tocilizumab for the treatment of Adult-Onset Still's Disease refractory to second-line therapy (adults)

Publication number: formerly **170056P**

Describe what was stated in original document	Describe new text in the document	Section/Paragraph to which changes apply	Describe why document change required	Changes made by	Date change made
Anakinra/tocilizumab for the treatment of Adult-Onset Still's Disease refractory to second-line therapy (adults)	Tocilizumab for the treatment of Adult-Onset Still's Disease refractory to second-line therapy (adults)	Pages 1 and 3 Title	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
No text	Under NICE TA 685, anakinra is recommended as an option for treating Still's disease with moderate to high disease activity, or continued disease activity after non-steroidal anti-inflammatory drugs (NSAIDs) or glucocorticoids. It is only recommended for AOSD disease that has responded inadequately to 2 or more conventional disease-modifying antirheumatic drugs (DMARDs).	Page 3 Current treatment	Policy has been revised following the publication of NICE TA 685 with anakinra as a current treatment	Head of Clinical Policy Team	August 2021
NHS England will commission anakinra and tocilizumab	NHS England will commission tocilizumab	Page 5, Policy Statement	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021

None	NICE Technology Appraisal (TA) 685 published on 31st March 2021 covers anakinra for treating Still's disease.	Page 6, About current treatments	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
the use of anakinra and tocilizumab	the use of anakinra through NICE Technology Appraisal (TA) 685 published on 31st March 2021 and tocilizumab through this clinical commissioning policy	Page 6, About current treatments	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
About the new treatment	Removed. Text moved into current treatments	Page 6, About current treatments	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
with anakinra and tocilizumab	with tocilizumab	Page 7, What we have decided	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
Refractory polyarticular AOSD tocilizumab, OR if systemic flares or if unresponsive to anakinra	Refractory polyarticular AOSD tocilizumab changing to anakinra if systematic flares or if no response to tocilizumab	Page 8 Patient pathway flow chart	To improve clarity Incorporated the wording from page 7 on the place of Tocilizumab/Anakinra in particular AOSD and systemic OSD	Clinical Chair, Blood & Infection Programme of Care	August 2021
Refractory systemic AOSD anakinra OR if unresponsive tocilizumab	Refractory systemic AOSD anakinra changing to tocilizumab if no response to anakinra	Page 8 Patient pathway flow chart	To improve clarity Incorporated the wording from page 7 on the place of Tocilizumab/Anakinra in particular AOSD and systemic OSD	Clinical Chair, Blood & Infection Programme of Care	August 2021
In patients who fail to achieve remission after use of corticosteroids and methotrexate, the use of anakinra has been suggested	Removed from the policy as now covered by NICE TA 685	Page 9, Introduction	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021

as a follow on therapy. Anakinra is a biologic agent that blocks receptors for interleukin-1 (IL-1). IL-1 which is important on the pathway that leads to inflammation of joints and joint damage. Anakinra is licensed in combination with methotrexate by the European Medicines Agency (EMA) for use in rheumatoid arthritis (RA) and cryopyrin-associated periodic syndromes (CAPS). Anakinra is licensed for use in systemic AOSD. NICE has reviewed anakinra for use in rheumatoid arthritis and does not recommend anakinra for the treatment of rheumatoid arthritis except in the context of a controlled, long-term clinical study (NICE, 2009). The main reasons for this recommendation are that although anakinra in combination with methotrexate was effective, studies suggested that other treatments options appeared more effective and anakinra was not considered cost-effective. NICE has not reviewed anakinra for use in AOSD.					

use of anakinra and tocilizumab	use of tocilizumab	Page 11, 3 Aims and Objectives	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
Anakinra section of Evidence summary removed	Tocilizumab evidence summary section remains.	Page 12, 5 Evidence Base	Policy has been revised following the publication of NICE TA 685 and revised in line with current inclusion of evidence	Head of Clinical Policy Team	August 2021
Anakinra or tocilizumab will be routinely commissioned	Tocilizumab will be routinely commissioned	Page 14, 6 Criteria for Commissioning	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
Anakinra Anakinra will only be commissioned for those patients who meet the following criteria: • Patients who have failed to respond to – or are intolerant of - standard immunosuppressive therapy, including at least two of the following agents: methotrexate, cyclosporine, azathioprine, leflunomide, cyclophosphamide and mycophenolate or where standard therapies are contraindicated; AND • Patients have been provided with information on potential adverse effects of anakinra	No longer required, covered by NICE TA 685	Page 15, 6 Criteria for Commissioning	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021

Response criteria for anakinra: At least two of the following: • Reduction of DAS28 by at least 1.2 points • Reduction of ESR by at least 25% • Reduction of CRP by at least 25% • Reduction of corticosteroid dose by at least 25% Dosing The standard dose is 100mg/daily, but this can be increased to 200mg/daily in patients with inadequate response and also reduced to 50mg/daily in stable patients (this can be administered as 100mg on alternate days). Stopping criteria: • Not achieving the response criteria within eight weeks. • In patients where the response criteria are achieved but subsequently response to anakinra declines and loses efficacy, as judged by loss of the response criteria above					

over two consecutive assessments, at least three months apart.					
Clinical consensus suggests that tocilizumab	Clinical consensus supported by NICE TA 685 suggests that tocilizumab	Page 16, Stopping Criteria	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
Anakinra and tocilizumab for AOSD	Tocilizumab for AOSD	Page 20, 8 Governance arrangements	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
Treatment centres will use a prior approval system to track and audit use of anakinra and tocilizumab	Treatment centres will use a prior approval system to track and audit use of tocilizumab	Page 20, 10 Audit Requirements	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021
None	• Anakinra for treating Still's disease Technology appraisal guidance [TA685] Published date: 31 March 2021	Page 20, 11 Documents which have informed this Policy	Policy has been revised following the publication of NICE TA 685	Head of Clinical Policy Team	August 2021