Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: Secukinumab (juvenile Psoriasis-Arthritis) und Secukinumab (Enthesitis-assoziierte Arthritis)

Stand: Mai 2019

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA

„Zur Behandlung der aktiven juvenilen Psoriasis-Arthritis (JPsA) bei Patienten ab 2 Jahren.“

Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	*Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“*
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	„nicht angezeigt“
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Im vorliegenden Anwendungsgebiet liegen keine Beschlüsse über die Nutzenbewertung nach § 35a SGB V vor.
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	*Siehe systematische Literaturrecherche*

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Secukinumab L04AC10 Cosentyx®	
Klassische synthetische krankheitsmodifizierende Antirheumatika (csDMARD)	
Methotrexat L01BA01 generisch	– Polyarthritische Formen der schweren aktiven juvenilen idiopathischen Arthritis (JIA) ab dem 3. Lebensjahr bei mangelndem Ansprechen auf NSAIDs.
Biologische krankheitsmodifizierende Antirheumatika (bDMARD)	
TNF-alpha-Inhibitoren	
Etanercept L04AB01 Enbrel® 10 mg für Kinder und Jugendliche	*Juvenile idiopathische Arthritis* Behandlung der Polyarthritis (Rheumafaktorpositiv oder -negativ) und der erweiterten (extended) Oligoarthritis bei Kindern und Jugendlichen ab dem Alter von 2 Jahren, die unzureichend auf eine Methotrexat-Behandlung angesprochen haben oder eine Methotrexat-Behandlung nicht vertragen. **Behandlung der Psoriasis-Arthritis (Arthritis psoriatica) bei Jugendlichen ab dem Alter von 12 Jahren, die unzureichend auf eine Methotrexat-Behandlung angesprochen haben oder eine Methotrexat-Behandlung nicht vertragen.** Behandlung der Enthesitis-assoziierten Arthritis bei Jugendlichen ab dem Alter von 12 Jahren, die unzureichend auf eine konventionelle Therapie angesprochen haben oder eine konventionelle Therapie nicht vertragen. Enbrel wurde nicht bei Kindern unter 2 Jahren untersucht.

II. Zugelassene Arzneimittel im Anwendungsgebiet

nicht-konventionelle Wirkstoffe	
Abatacept L04AA24 Orencia®	*Polyartikuläre juvenile idiopathische Arthritis* ORENCIA ist in Kombination mit Methotrexat indiziert zur Behandlung der mäßigen bis schweren aktiven polyartikulären juvenilen idiopathischen Arthritis (pJIA) bei pädiatrischen Patienten ab 2 Jahren, wenn das Ansprechen auf eine vorherige DMARD Therapie, einschließlich MTX, nicht ausreichend war. Orencia kann als Monotherapie angewendet werden, wenn eine Intoleranz gegenüber Methotrexat besteht oder wenn eine Behandlung mit Methotrexat nicht angezeigt ist.
Systemische steroidale Antirheumatika (Glucokortikoide) (beispielhafte Aufzählung)	
Prednisolon H02AB06 generisch	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: o Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke (DS b, c), Arthritis psoriatica (DS c, d), enteropathische Arthropathie mit hoher Entzündungsaktivität (DS a) o Reaktive Arthritiden (DS: c) • Juvenile idiopathische Arthritis mit schwerer systemischer Verlaufsform (Still-Syndrom) oder mit lokal nicht beeinflussbarer Iridozyklitis (DS: a)
Prednison H02AB07 generisch	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: o Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke (DS b, c), Arthritis psoriatica (DS c, d), enteropathische Arthropathie mit hoher Entzündungsaktivität (DS a) o Reaktive Arthritiden (DS: c) • Juvenile idiopathische Arthritis mit schwerer systemischer Verlaufsform (Still-Syndrom) oder mit lokal nicht beeinflussbarer Iridozyklitis (DS: a)
Triamcinolon H02AB08 Volon®	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: o Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke, Arthritis psoriatica, enteropathische Arthropathie mit hoher Entzündungsaktivität); o Reaktive Arthritiden; • Juvenile idiopathische Arthritis mit schwerer systemischer Verlaufsform (Still-Syndrom) oder mit lokal nicht beeinflussbarer Iridozyklitis.
Nichtsteroidale Antirheumatika (NSAR oder NSAID)	

II. Zugelassene Arzneimittel im Anwendungsgebiet	
z.B. Acemetacin M01AB11 generisch	Symptomatische Behandlung von Schmerz und Entzündung bei – akuten Arthritiden (einschließlich Gichtanfall) – chronischen Arthritiden, insbesondere bei rheumatoider Arthritis (chronische Polyarthritis) Kinder und Jugendliche Eine Anwendung von Acemetacin Heumann bei Kindern und Jugendlichen wird nicht empfohlen, da für diese Altersklasse keine ausreichenden Daten zur Wirksamkeit und Sicherheit vorliegen.
z.B. Ibuprofen generisch	Symptomatische Behandlung von Schmerz und Entzündung bei – akuten Arthritiden (einschließlich Gichtanfall) – chronischen Arthritiden, insbesondere bei rheumatoider Arthritis (chronische Polyarthritis)

Quellen: AMIS-Datenbank, Fachinformationen, Lauer-Fischer-Taxe®

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA

„Behandlung der Enthesitis-assoziierte Arthritis (ERA) bei Patienten ab dem Alter von 2 Jahren“

Kriterien gemäß 5. Kapitel § 6 VerfO	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	*Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“*
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	„nicht angezeigt“
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Im vorliegenden Anwendungsgebiet liegen keine Beschlüsse über die Nutzenbewertung nach § 35a SGB V vor.
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	*Siehe systematische Literaturrecherche*

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Secukinumab L04AC10 Cosentyx®	
Klassische synthetische krankheitsmodifizierende Antirheumatika (csDMARD)	
Methotrexat L01BA01 generisch	– Polyarthritische Formen der schweren aktiven juvenilen idiopathischen Arthritis (JIA) ab dem 3. Lebensjahr bei mangelndem Ansprechen auf NSAIDs.
Sulfasalazin A07EC01 Pleon RA	[…] **Behandlung der aktiven juvenilen idiopathischen Oligoarthritis (Enthesitis-assoziierte Arthritis) ab dem 6. Lebensjahr, die unzureichend auf nichtsteroidale Antiphlogistika (nonsteroidal antiinflammatory drugs, NSAID) und/oder Glukokortikoidinjektionen angesprochen hat.** Behandlung der aktiven juvenilen idiopathischen Polyarthritis und Spondyloarthropathie mit peripherer Arthritis bei Patienten ab 6 Jahren, die nicht ausreichend auf NSAIDs angesprochen haben. Sulfasalazin medac ist nicht angezeigt bei Patienten mit systemischer juveniler idiopathischer Arthritis oder Patienten mit juveniler Spondyloarthropathie ohne periphere Arthritis.
Biologische krankheitsmodifizierende Antirheumatika (bDMARD)	
TNF-alpha-Inhibitoren	
Etanercept L04AB01 Enbrel® 10 mg für Kinder und Jugendliche	*Juvenile idiopathische Arthritis* Behandlung der Polyarthritis (Rheumafaktorpositiv oder -negativ) und der erweiterten (extended) Oligoarthritis bei Kindern und Jugendlichen ab dem Alter von 2 Jahren, die unzureichend auf eine Methotrexat-Behandlung angesprochen haben oder eine Methotrexat-Behandlung nicht vertragen. Behandlung der Psoriasis-Arthritis (Arthritis psoriatica) bei Jugendlichen ab dem Alter von 12 Jahren, die unzureichend auf eine Methotrexat-Behandlung angesprochen haben oder eine Methotrexat-Behandlung nicht vertragen.

II. Zugelassene Arzneimittel im Anwendungsgebiet

	Behandlung der Enthesitis-assoziierten Arthritis bei Jugendlichen ab dem Alter von 12 Jahren, die unzureichend auf eine konventionelle Therapie angesprochen haben oder eine konventionelle Therapie nicht vertragen. Enbrel wurde nicht bei Kindern unter 2 Jahren untersucht.
Adalimumab L04AB04 Humira®	*Juvenile idiopathische Arthritis* *Polyartikuläre juvenile idiopathische Arthritis* Humira ist in Kombination mit Methotrexat indiziert zur Behandlung der aktiven polyartikularen juvenilen idiopathischen Arthritis bei Patienten ab dem Alter von 2 Jahren, die nur unzureichend auf ein oder mehrere krankheitsmodifizierende Antirheumatika (DMARDs) angesprochen haben. Humira kann im Falle einer Unvertraglichkeit gegenüber Methotrexat oder, wenn die weitere Behandlung mit Methotrexat nicht sinnvoll ist, als Monotherapie angewendet werden (zur Wirksamkeit bei der Monotherapie siehe Abschnitt 5.1). Bei Patienten, die jünger als 2 Jahre sind, wurde Humira nicht untersucht. *Enthesitis-assoziierte Arthritis* **Humira ist zur Behandlung der aktiven Enthesitis-assoziierten Arthritis bei Patienten indiziert, die 6 Jahre und älter sind und die nur unzureichend auf eine konventionelle Therapie angesprochen haben oder die eine Unverträglichkeit gegenüber einer solchen Therapie haben (siehe Abschnitt 5.1).**
nicht-konventionelle Wirkstoffe	
Abatacept L04AA24 Orencia®	*Polyartikuläre juvenile idiopathische Arthritis* ORENCIA ist in Kombination mit Methotrexat indiziert zur Behandlung der mäßigen bis schweren aktiven polyartikulären juvenilen idiopathischen Arthritis (pJIA) bei pädiatrischen Patienten ab 2 Jahren, wenn das Ansprechen auf eine vorherige DMARD Therapie, einschließlich MTX, nicht ausreichend war. Orencia kann als Monotherapie angewendet werden, wenn eine Intoleranz gegenüber Methotrexat besteht oder wenn eine Behandlung mit Methotrexat nicht angezeigt ist.
Systemische steroidale Antirheumatika (Glucokortikoide) (beispielhafte Aufzählung)	
Prednisolon H02AB06 generisch	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: o Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke (DS b, c), Arthritis psoriatica (DS c, d), enteropathische Arthropathie mit hoher Entzündungsaktivität (DS a)

II. Zugelassene Arzneimittel im Anwendungsgebiet	
	○ Reaktive Arthritiden (DS: c) • Juvenile idiopathische Arthritis mit schwerer systemischer Verlaufsform (Still-Syndrom) oder mit lokal nicht beeinflussbarer Iridozyklitis (DS: a)
Prednison H02AB07 generisch	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: ○ Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke (DS b, c), Arthritis psoriatica (DS c, d), enteropathische Arthropathie mit hoher Entzündungsaktivität (DS a) ○ Reaktive Arthritiden (DS: c) • Juvenile idiopathische Arthritis mit schwerer systemischer Verlaufsform (Still-Syndrom) oder mit lokal nicht beeinflussbarer Iridozyklitis (DS: a)
Triamcinolon H02AB08 Volon®	• andere entzündlich-rheumatische Arthritiden, sofern die Schwere des Krankheitsbildes es erfordert und nicht-steroidale Antirheumatika (NSARs) nicht angewandt werden können: ○ Spondarthritiden (Spondylitis ankylosans mit Beteiligung peripherer Gelenke, Arthritis psoriatica, enteropathische Arthropathie mit hoher Entzündungsaktivität); ○ Reaktive Arthritiden; • Juvenile idiopathische Arthritis mit schwerer systemischer Verlaufsform (Still-Syndrom) oder mit lokal nicht beeinflussbarer Iridozyklitis.
Nichtsteroidale Antirheumatika (NSAR oder NSAID)	
z.B. Acemetacin M01AB11 generisch	Symptomatische Behandlung von Schmerz und Entzündung bei – akuten Arthritiden (einschließlich Gichtanfall) – chronischen Arthritiden, insbesondere bei rheumatoider Arthritis (chronische Polyarthritis) Kinder und Jugendliche Eine Anwendung von Acemetacin Heumann bei Kindern und Jugendlichen wird nicht empfohlen, da für diese Altersklasse keine ausreichenden Daten zur Wirksamkeit und Sicherheit vorliegen.
z.B. Ibuprofen generisch	Symptomatische Behandlung von Schmerz und Entzündung bei – akuten Arthritiden (einschließlich Gichtanfall) – chronischen Arthritiden, insbesondere bei rheumatoider Arthritis (chronische Polyarthritis)

Quellen: AMIS-Datenbank, Fachinformationen, Lauer-Fischer-Taxe®

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: Secukinumab

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	4. April 2019

Inhaltsverzeichnis

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
DMARD	Krankheitsmodifizierende Antirheumatika
ERA	Enthesitis-assoziierte Arthritis
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
HR	Hazard Ratio
IL-17i	Interleukin-17 Inhibitor
IL-12/23i	Interleukin-12/23 Inhibitor
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
JIA	Juvenile idiopathische Arthritis
jPsA	Juvenile Psoriasis-Arthritis
KI	Konfidenzintervall
LoE	Level of Evidence
NICE	National Institute for Health and Care Excellence
NSAR/ NSAID	Nicht-steroidale Antirheumatika
OR	Odds Ratio
OSM	Oral Small Molecules (z.B. Methotrexat, Sulfasalazin, Cyclosporin, Leflunomid, Apremilast)
PsA	Psoriasis-Arthritis
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
TNFi	Tumornekrosefaktor-Inhibitoren
WHO	World Health Organization

1 Indikation

„…juvenile idiopathische Arthritis bei Kindern ab 2 und bei Erwachsenen mit Fokus auf ERA und jPsA.“

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zu den Indikationen *juvenile idiopathische Arthritis (jiA)* und *aktive Enthesitis-assoziierten Arthritis (ERA*) durchgeführt. Der Suchzeitraum wurde auf die letzten 5 Jahre eingeschränkt und die Recherche am 11.03.2019 abgeschlossen. Die Suche erfolgte in den aufgeführten Datenbanken bzw. Internetseiten folgender Organisationen: The Cochrane Library (Cochrane Database of Systematic Reviews), MEDLINE (PubMed), AWMF, G-BA, GIN, NICE, TRIP, SIGN, WHO. Ergänzend erfolgte eine freie Internetsuche nach aktuellen deutschen und europäischen Leitlinien. Die detaillierte Darstellung der Suchstrategie ist am Ende der Synopse aufgeführt.

Die Recherche ergab 834 Quellen, die anschließend in einem zweistufigen Screening-Verfahren nach Themenrelevanz und methodischer Qualität gesichtet wurden. Zudem wurde eine Sprachrestriktion auf deutsche und englische Quellen vorgenommen. Insgesamt ergab dies 8 Quellen, die in die synoptische Evidenz-Übersicht aufgenommen wurden.

3 Ergebnisse

3.1 G-BA Beschlüsse/IQWiG Berichte

G-BA, 2019 [1].

Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie (AM-RL): Anlage XII - Beschlüsse über die Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V –Tofacitinib (neues Anwendungsgebiet: Psoriasis-Arthritis) vom 21. Februar 2019

Neues Anwendungsgebiet

a) Erwachsene Patienten mit aktiver Psoriasis-Arthritis, die auf eine vorangegangene krankheitsmodifizierende antirheumatische (DMARD-) Therapie unzureichend angesprochen oder diese nicht vertragen haben.

b) Erwachsene Patienten mit aktiver Psoriasis-Arthritis, die unzureichend auf eine vorhergehende Therapie mit krankheitsmodifizierenden biologischen Antirheumatika (bDMARD) angesprochen oder diese nicht vertragen haben.

Zweckmäßige Vergleichstherapie

a) ein TNF-alpha-Antagonist (Adalimumab oder Certolizumab Pegol oder Etanercept oder Golimumab oder Infliximab) ggf. in Kombination mit Methotrexat

b) der Wechsel auf ein anderes biologisches krankheitsmodifizierendes Antirheumatikum (Adalimumab oder Certolizumab Pegol oder Etanercept oder Golimumab oder Infliximab oder Secukinumab oder Ustekinumab) ggf. in Kombination mit Methotrexat

Ausmaß des Zusatznutzens

a) Ausmaß und Wahrscheinlichkeit des Zusatznutzens von Tofacitinib in Kombination mit Methotrexat gegenüber Adalimumab in Kombination mit Methotrexat:

   Anhaltspunkt für einen geringen Zusatznutzen.

b) Ausmaß und Wahrscheinlichkeit des Zusatznutzens von Tofacitinib in Kombination mit Methotrexat gegenüber der zweckmäßigen Vergleichstherapie:

   Ein Zusatznutzen ist nicht belegt.

G-BA, 2018 [4].

Richtlinie über die Verordnung von Arzneimitteln in der vertragsärztlichen Versorgung (AM-RL); Anlage XII: (Frühe) Nutzenbewertung nach § 35a SGB V; Geltende Fassung zum Beschluss vom 16. August 2018 - Ixekizumab (neues Anwendungsgebiet: Psoriasis-Arthritis)

Anwendungsgebiet

Taltz, allein oder in Kombination mit Methotrexat, ist angezeigt für die Behandlung erwachsener Patienten mit aktiver Psoriasis-Arthritis, die unzureichend auf eine oder mehrere krankheitsmodifizierende Antirheumatika (DMARD) angesprochen oder diese nicht vertragen haben.

a) Erwachsene Patienten mit aktiver Psoriasis-Arthritis, die für eine andere klassische DMARD-Therapie außer Methotrexat infrage kommen
b) Erwachsene Patienten mit aktiver Psoriasis-Arthritis, die bDMARD-naiv sind und für die eine erstmalige Therapie mit bDMARDs angezeigt ist
c) Erwachsene Patienten mit aktiver Psoriasis-Arthritis, die unzureichend auf eine vorhergehende Therapie mit krankheitsmodifizierenden biologischen Antirheumatika (bDMARDs) angesprochen oder diese nicht vertragen haben

Zweckmäßige Vergleichstherapie

a) Leflunomid
b) ein TNF-alpha-Hemmer (Adalimumab oder Certolizumab Pegol oder Etanercept oder Golimumab oder Infliximab) ggf. in Kombination mit Methotrexat
c) der Wechsel auf ein anderes biologisches krankheitsmodifizierendes Antirheumatikum (Adalimumab oder Certolizumab Pegol oder Etanercept oder Golimumab oder Infliximab oder Secukinumab oder Ustekinumab) ggf. in Kombination mit Methotrexat

Ausmaß des Zusatznutzens gegenüber der zweckmäßigen Vergleichstherapie

a) Ein Zusatznutzen ist nicht belegt.
b) Ausmaß des Zusatznutzens gegenüber Adalimumab: Anhaltspunkt für einen geringen Zusatznutzen.
c) Ein Zusatznutzen ist nicht belegt.

G-BA, 2016 [3].

Richtlinie über die Verordnung von Arzneimitteln in der vertragsärztlichen Versorgung (AM-RL); Anlage XII: (Frühe) Nutzenbewertung nach § 35a SGB V; Geltende Fassung zum Beschluss vom 02. Juni 2016 - Secukinumab

Anwendungsgebiet

Psoriasis-Arthritis (PsA)

Secukinumab (Cosentyx®), allein oder in Kombination mit Methotrexat (MTX), ist angezeigt für die Behandlung erwachsener Patienten mit aktiver Psoriasis-Arthritis, wenn das Ansprechen auf eine vorhergehende Therapie mit krankheitsmodifizierenden Antirheumatika (DMARD) unzureichend gewesen ist.

Zweckmäßige Vergleichstherapie

ein TNF-alpha-Hemmer (Etanercept oder Adalimumab oder Infliximab oder Golimumab) ggf. in Kombination mit Methotrexat

Ausmaß des Zusatznutzens

Ein Zusatznutzen ist nicht belegt.

G-BA, 2006 [2].

Beschluss des Gemeinsamen Bundesausschusses über eine Änderung der Arzneimittel-Richtlinie/AMR in Anlage 4: Therapiehinweis zu Adalimumab vom 21. November 2006

I. Die Anlage 4 nach Nummer 14 der Arzneimittel-Richtlinie wird um den folgenden Therapiehinweis zu Adalimumab ergänzt:

„Wirkstoff: Adalimumab (zum Beispiel Humira®) bei Rheumatoider Arthritis und Psoriasis-Arthritis (Arthritis psoriatica)

[…] Bei der Indikation Psoriasis-Arthritis ist der unterschiedliche Zulassungsstatus bzgl. der Hautmanifestation der Psoriasis zu beachten, insbesondere da die Zulassung von Etanercept und Infliximab die Anwendung bei Arthritis psoriatica und bei therapieresistenter mittelschwerer bis schwerer Plaque psoriasis abdeckt[…]

3.2 Cochrane Reviews

Es wurden keine Cochrane Reviews im Anwendungsgebiet identifiziert.

3.3 Systematische Reviews

Es wurden keine systematischen Reviews im Anwendungsgebiet identifiziert.

3.4 Leitlinien

Singh JA et al., 2019 [7].

American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF)

2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis

Fragestellung

To develop an evidence-based guideline for the pharmacologic and nonpharmacologic treatment of psoriatic arthritis (PsA), as a collaboration between the American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF).

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium;
- Interessenkonflikte und Finanzierung dargelegt;
- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- Systematic searches of the published English-language literature included Ovid Medline, PubMed, Embase, and the Cochrane Library (including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, and Health Technology Assessments) from the beginning of each database through November 15, 2016; we conducted updated searches on May 2, 2017 and again on March 8, 2018.

LoE and GoR

- GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology was used to rate the quality of the evidence.
- GRADE methodology specifies that panels make recommendations based on a consideration of the balance of benefits and harms of the treatment options under consideration, the quality of the evidence (i.e., confidence in the effect estimates), and patients' values and preferences.
- A recommendation could be either in favor of or against the proposed intervention and either strong or conditional. According to GRADE, a recommendation is categorized as strong if the panel is very confident that the benefits of an intervention clearly outweigh the harms (or vice versa); a conditional recommendation denotes uncertainty regarding the balance of benefits and harms, such as when the evidence quality is low or very low, or when the decision is sensitive to individual patient preferences, or when costs are expected to impact

the decision. Thus, conditional recommendations refer to decisions in which incorporation of patient preferences is an essential element of decision making.

Sonstige methodische Hinweise

- evaluated the risk of bias in primary studies using the Cochrane risk of bias tool
- Zielpopulation der LL sind erwachsene Patienten mit Psoriasis-Arthritis. Die juvenile Form ist nicht abgedeckt.

Recommendations in adult patients with active PsA

Recommendations for treatment of patients with active psoriatic arthritis despite treatment with an OSM

1. **Switch to a TNFi biologic over a different OSM** (PICO 23) **Conditional recommendation** based on moderate-quality evidence; may consider switching to a different OSM if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, if the patient prefers an oral versus parenteral therapy, or in patients without evidence of severe PsA‡ or severe psoriasis.§	Moderate (62–66, 69–86)
2. **Switch to a TNFi biologic over an IL-17i biologic** (PICO 17) **Conditional recommendation** based on moderate-quality evidence; may consider an IL-17i if the patient has severe psoriasis and/or has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, and/or a family history of demyelinating disease such as multiple sclerosis.	Moderate (62–66, 72–78, 87–97)
3. **Switch to a TNFi biologic over an IL-12/23i biologic** (PICO 16) **Conditional recommendation** based on moderate-quality evidence; may consider an IL-12/23i if the patient has severe psoriasis and/or contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, or prefers less frequent drug administration.	Moderate (62–66, 72–78, 97–102)
4. **Switch to a TNFi biologic over abatacept** (PICO 67) **Conditional recommendation** based on low-quality evidence; may consider abatacept if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.	Low (62–66, 72–78, 103, 104)
5. **Switch to a TNFi biologic over tofacitinib** (PICO 76) **Conditional recommendation** based on low-quality evidence; may consider tofacitinib if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, or prefers oral medication.	Low (62–66, 72–78, 105)
13. **Add apremilast to current OSM therapy over switching to apremilast** (PICO 22b) **Conditional recommendation** based on low-quality evidence; may consider switching to apremilast if the patient has intolerable side effects with the current OSM.	Low (83, 84, 108)
14. **Switch to another OSM (except apremilast) over adding another OSM (except apremilast) to current treatment** (PICO 22a) **Conditional recommendation** based on low-quality evidence; may consider adding another OSM (except apremilast) to current treatment if the patient has demonstrated partial response to the current OSM.	Low (83, 84, 108)
15. **Switch to a TNFi biologic monotherapy over MTX and a TNFi biologic combination therapy** (PICO 19) **Conditional recommendation** based on low-quality evidence; may consider MTX and TNFi biologic combination therapy if the patient has severe skin manifestations, has had a partial response to current MTX therapy, has concomitant uveitis (since uveitis may respond to MTX therapy), and if the current TNFi biologic is infliximab or adalimumab.	Low (109–111)

16. **Switch to an IL-17i biologic monotherapy over MTX and an IL-17i biologic combination therapy** (PICO 21) — Very low

Conditional recommendation based on very-low-quality evidence; may consider MTX and an IL-17i biologic combination therapy if the patient has severe skin manifestations, has had a partial response to current MTX therapy, or has concomitant uveitis (since uveitis may respond to MTX therapy).

17. **Switch to an IL-12/23i biologic monotherapy over MTX and an IL-12/23i biologic combination therapy** (PICO 20) — Very low

Conditional recommendation based on very-low-quality evidence; may consider MTX and an IL-12/23i biologic combination therapy if the patient has severe skin manifestations, has had a partial response to current MTX therapy, or has concomitant uveitis (since uveitis may respond to MTX therapy).

In adult patients with active PsA despite treatment with a TNFi biologic monotherapy

1. **Switch to a different TNFi biologic over switching to an IL-17i biologic** (PICO 28) — Low (72, 73, 90–93, 95)

Conditional recommendation based on low-quality evidence; may consider an IL-17i if the patient had a primary TNFi biologic efficacy failure or a TNFi biologic–associated serious adverse event or severe psoriasis.‡

2. **Switch to a different TNFi biologic over switching to an IL-12/23i biologic** (PICO 27) — Low (72, 73, 99, 100)

Conditional recommendation based on low-quality evidence; may consider an IL-12/23i if the patient had a primary TNFi biologic efficacy failure or a TNFi biologic–associated serious adverse effect or prefers less frequent drug administration.

3. **Switch to a different TNFi biologic over switching to abatacept** (PICO 70) — Low (72, 73, 103, 104)

Conditional recommendation based on low-quality evidence; may consider abatacept if the patient had a primary TNFi biologic efficacy failure or TNFi biologic–associated serious adverse effect.

4. **Switch to a different TNFi biologic over switching to tofacitinib** (PICO 73) — Low (62–66, 72–78, 105)

Conditional recommendation based on low-quality evidence; may consider tofacitinib if the patient prefers an oral therapy or had a primary TNFi biologic efficacy failure or a TNFi biologic–associated serious adverse effect.

In adult patients with active PsA despite treatment with a TNFi biologic and MTX combination therapy,

14. **Switch to a different TNFi biologic + MTX over switching to a different TNFi biologic monotherapy** (PICO 33) — Very low

Conditional recommendation based on very-low-quality evidence; may consider switching to a different TNFi biologic monotherapy if the patient has demonstrated MTX-associated adverse events, prefers to receive fewer medications, or perceives MTX as a burden.

In adult patients with active PsA despite treatment with an IL-17i biologic monotherapy,

1. **Switch to a TNFi biologic over switching to an IL-12/23i biologic** (PICO 39) — Very low

Conditional recommendation based on very-low-quality-evidence; may consider switching to IL-12/23i if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, or prefers less frequent drug administration.

2. **Switch to a TNFi biologic over switching to a different IL-17i biologic** (PICO 42) — Very low

Conditional recommendation based on very-low-quality evidence; may consider switching to a different IL-17i if the patient had had a secondary efficacy failure to current IL-17i, or severe psoriasis, or contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

3. **Switch to a TNFi biologic over adding MTX to an IL-17i biologic** (PICO 41) — Very low

   Conditional recommendation based on very-low-quality evidence; may consider adding MTX to an IL-17i if the patient had had a partial response to the existing regimen or if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

4. **Switch to an IL-12/23i biologic over switching to a different IL-17i biologic** (PICO 43) — Very low

   Conditional recommendation based on very-low-quality evidence; may consider switching to a different IL-17i if the patient had had a secondary efficacy failure to current IL-17i or severe psoriasis,‡ or if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

In adult patients with active PsA despite treatment with an IL-12/23i biologic monotherapy,

6. **Switch to a TNFi biologic over switching to an IL-17i biologic** (PICO 38) — Very low

   Conditional recommendation based on very-low-quality evidence; may consider an IL-17i if the patient has severe psoriasis or contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

7. **Switch to a TNFi biologic over adding MTX to an IL-12/23i biologic** (PICO 36) — Very low

   Conditional recommendation based on very-low-quality evidence; may consider adding MTX in patients in whom the severe psoriasis is not responding to the current therapy, or if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

8. **Switch to an IL-17i biologic over adding MTX to an IL-12/23i biologic** (PICO 37). — Very low

   Conditional recommendation based on very-low-quality evidence; may consider adding MTX in patients with only partial response to the current therapy or in those who potentially have not had enough time to adequately respond.

In adult patients with active PsA and predominant enthesitis who are both OSM- and biologic treatment–naive,

5. **Start oral NSAIDs over an OSM (specifically apremilast)** (PICO 48) — Very low

   Conditional recommendation based on very-low-quality evidence; may consider starting an OSM (specifically apremilast) if the patient has active joint disease and/or skin disease or contraindications to the use of NSAIDs, including cardiovascular disease, peptic ulcer disease, or renal disease or impairment.

6. **Start a TNFi biologic over an OSM (specifically apremilast)** (PICO 48A) — Very low

   Conditional recommendation based on very-low-quality evidence; may consider starting an OSM (specifically apremilast) if the patient prefers an oral treatment as the first therapy or the patient has contraindications to TNFi biologics, including recurrent infections, congestive heart failure, or demyelinating disease.

In adult patients with active PsA and predominant enthesitis despite treatment with OSM,

8. **Switch to a TNFi biologic over an IL-17i biologic** (PICO 53) — Low (72, 73, 76, 89, 90, 92)

   Conditional recommendation based on low-quality evidence; may consider switching to an IL-117i if the patient has severe psoriasis or contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

9. **Switch to a TNFi biologic over an IL-12/23i biologic** (PICO 52) — Low (72, 73, 76, 98, 100)

   Conditional recommendation based on low-quality evidence; may consider switching to an IL-12/23i if the patient has severe psoriasis or contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease, or if the patient prefers less frequent drug administration.

10. **Switch to a TNFi biologic over switching to another OSM** (PICO 49) — Low (72, 73, 76, 83–85)

    Conditional recommendation based on low-quality evidence; may consider switching to another OSM# if the patient prefers an oral medication over an injection, or if the patient has contraindications to TNFi biologics, including congestive heart failure, previous serious infections, recurrent infections, or demyelinating disease.

13. **Switch to an IL-12/23i biologic over switching to another OSM** (PICO 50) Low (83–86, 98, 100)

Conditional recommendation based on low-quality evidence; may consider switching to another OSM# if the patient prefers an oral medication over an injection, or if there are contraindications to an IL- 12/23i, such as severe recurrent infections.

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Spanish Society of Rheumatology (SER), 2018 [8].

Spanish Society of Rheumatology (SER)

Clinical practice guideline for the treatment of patients with axial spondyloarthritis and psoriatic arthritis; Update 2015.

Fragestellung

This guideline focus on the care of those patients affected by axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA). Only adult patients are included, and the clinical area being addressed is the treatment of these diseases.

Outside the scope:

- The population under 18 years of age.

- Recommendations about diagnosis, prevention, monitoring, and prognosis.

Methodik

Grundlage der Leitlinie

- Update der Leitlinie von 2015
- Repräsentatives Gremium;
- Interessenkonflikte, Finanzierung und Unabhängigkeit dargelegt;
- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- MEDLINE database (via PubMed), EMBASE (Elsevier), the Cochrane Library (Wiley Online Library), and Cinahl (EBSCOhost). The question regarding physiotherapy was researched in PEDro (Physiotherapy Evidence Database).
- Initially, all search strategies sought only to recover the primary studies in the aforementioned databases. However, if the results proved to be poor or inconsequential, then a supplemental search by hand among the bibliography in the most relevant documents was conducted. Further material was included after consulting with investigators and reviewers. This helped identify those studies published since the initial search until the current guideline were created, 2015.
- revision was completed in 2016; subsequently panelists identified some studies which had been published in 2017 and were included in the evidence corpus.

LoE

- The level of scientific evidence was evaluated using a modified version of the Oxford Centre for Evidence-Based Medicine

GoR

- The strength of each recommendation was evaluated using a modified version of CEBM

Sonstige methodische Hinweise

Zielpopulation der LL sind erwachsene Patienten mit Psoriasis-Arthritis (und axialer Spondyloarthritis). Die juvenile Form ist nicht abgedeckt.

Recommendations

7. Treatment of Psoriatic Arthritis (PsA)

Clinical Question 12 In patients with psoriatic arthritis , what is the efficacy for DMARDs in its peripheral, axial, enthesitis, dactylitis, uveitis, skin and nail domains?

Summary of Evidence

The use of Apremilast in patients with peripheral PsA after an inadequate response or intolerance to DMARD shows greater efficacy than the placebo (measured as ACR20 response increase and decrease of DAS28 (CRP)), functional capacity (HAQ-DI) and global assessment

of doctor and patient). It also improves enthesitis measured by MASES and dactylitis (200-202). However, there is no evidence Apremilast reduces radiographic progression or that it improves axial manifestations or uveitis. (LoE 1b)

Recommendation

The use of biological therapy or tsDMARD (Apremilast) is recommended in patients with PsA and enthesitis refractory to NSAID and local treatment (Grade C recommendation).

The use of biological therapy or tsDMARD (Apremilast) is recommended in patients with PsA and dactylitis refractory to NSAID and local treatment with corticoid infiltrations (Grade C recommendation, Evidence level 2b).

Clinical Question 13 In patients with psoriatic arthritis, is the combined treatment of MTX and biological therapy (BT) more efficient than treatment with BT in monotherapy?

Summary of Evidence

- In analyzing secondary subgroups (post hoc analysis, no direct comparisons), no significant differences were observed in the effectiveness biological monotherapy (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab) compared with the combined use of methotrexate and biological therapy (183, 217-219). (LoE 2b)
- When the effectiveness of ustekinumab in monotherapy (doses of 45mg and 90mg) was compared with the combined of ustekinumab and methotrexate, patient response proved quite similar (184, 185) (LoE 2b-)
- There are no differences in the safety profiles of biological monotherapy and combined use of biological therapy and methotrexate (183-185, 200, 217-219) (LoE 2b)
- Data from population registries have shown that the maintenance rate of biological therapy (adalimumab, infliximab) can be extended when used in combination with methotrexate (220-222). (LoE 2b, 4)

Recommendation

Use of biological therapy is recommended in both monotherapy and combined with csDMARD, for all peripheral manifestations of PsA. Combined therapy with MTX may increase survival of the TNFi monoclonal drugs, particularly the chimeric ones (Grade C recommendation).

Clinical Question 14 In adults with PsA with axial and/or peripheral affectation refractory to an anti-TNF, is treatment with a second biological therapy efficient?

Summary of Evidence

Favorable response rates (ACR20/50/70, EULAR and DAS28) were shown in patients when changed to a second iTNF agent, although generally with lower values than those obtained in patients not previously exposed to these drugs (125, 185, 191, 237-239). (LoE 1b)

Some studies show a slight reduction in the survival of the second biological therapy compared to the first and clearly worse in the third (221, 222, 240-243). (LoE 2b)

There are no studies comparing the usefulness of a using a second iTNF against a change in the therapeutic target (IL12/23 or anti-IL17A).

Recommendation

Switching to another biological therapies albeit another i-TNFi or a drug with a different action mechanism like i-IL12/23 or anti-IL17A or tsDMARD (Apremilast), is recommended in patients with peripheral PsA and an i-TNF failure (Grade B recommendation).

Clinical Question 15 In patient with PsA, does treatment with DMARDs or biological therapies reduce CVD mortality?

Summary of Evidence

There are insufficient studies assessing the effects of using biological agents and other DMARDs in CVD events in patients with PsA (244, 245). (LoE 2a)

Some studies suggest TNFi and MTX acting as inflammation inhibitors may have cardioprotective effects. However, long-term quality prospective studies are required to explore the effects of said drugs on CVD morbimortality (244, 245). (LoE 2a)

Recommendation

CVD risk profile should be considered both in assessing and treating these patients. (Grade D recommendation).

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European League Against Rheumatism (EULAR)

European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update

Fragestellung

Update the recommendations of 2012

Methodik

Grundlage der Leitlinie (siehe

- Update der Version 2012;
- Repräsentatives Gremium;
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt;
- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- The search was performed in Medline, Embase and The Cochrane Central Register of Controlled Trials (Central), on 17 December 2014

LoE

- Oxford Levels of Evidence

Table 1 Categories of evidence[9]

Category	Evidence
1A	From meta-analysis of randomised controlled trials
1B	From at least one randomised controlled trial
2A	From at least one controlled study without randomisation
2B	From at least one type of quasi-experimental study
3	From descriptive studies, such as comparative studies, correlation studies or case–control studies
4	From expert committee reports or opinions and/or clinical experience of respected authorities

GoR

- GRADE

Table 2 Strength of recommendations

Strength	Directly based on
A	Category I evidence
B	Category II evidence or extrapolated recommendations from category I evidence
C	Category III evidence or extrapolated recommendation from category I or II evidence
D	Category IV evidence or extrapolated recommendation from category II or III evidence

Sonstige methodische Hinweise

- Patients were defined as adults (≥18 years old) with a clinical diagnosis of PsA
- Intervention was defined as any disease modifying antirheumatic drug (DMARD), either biological (bDMARD) or synthetic (sDMARD); comparator was any bDMARD, sDMARD, glucocorticoid, NSAID, combination of any of these or placebo (PBO).

Recommendations

	Recommendations	Level of evidence	Grade of recommendation	Level of agreement (mean±SD
5.	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, therapy with a bDMARD, usually a TNF inhibitor, should be commenced	1b	B	9.5±0.7
6.	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, in whom TNF inhibitors are not appropriate, bDMARDs targeting IL12/23 or IL17 pathways may be considered	1b	B	9.1±1.1
7.	In patients with peripheral arthritis and an inadequate response to at least one csDMARD, in whom bDMARDs are not appropriate, a targeted synthetic DMARD such as a PDE4-inhibitor may be considered	1b	B	8.5±1.4

	Recommendations	Level of evidence	Grade of recommendation	Level of agreement (mean±SD
8.	In patients with active enthesitis and/or dactylitis and insufficient response to NSAIDs or local glucocorticoid injections, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor	1b	B	9.1±1.2
9.	In patients with predominantly axial disease that is active and has insufficient response to NSAIDs, therapy with a bDMARD should be considered, which according to current practice is a TNF inhibitor	1b	B	9.6±0.6
10.	In patients who fail to respond adequately to a bDMARD, switching to another bDMARD should be considered, including switching between TNF inhibitors	1b	B	9.6±0.7

The level of evidence was determined for different parts of the recommendation (referred to as a and b) where necessary.
The level of agreement was computed as a 0–10 scale.
bDMARD, biological DMARD; CRP, C reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs, such as methotrexate, sulfasalazine or leflunomide; ESR, erythrocyte sedimentation rate; EULAR, European League Against Rheumatism; NSAIDs, non-steroidal anti-inflammatory drugs; PDE, phosphodiesterase; PsA, psoriatic arthritis; TNF, tumour necrosis factor.

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Santos MJ et al., 2016 [6].

2016 update of the Portuguese recommendations for the use of biological therapies in children and adolescents with Juvenile Idiopathic Arthritis

Fragestellung

To provide evidence-based guidance for the rational and safe prescription of biological therapies in children and adolescents with juvenile idiopathic arthritis (JIAs), considering the latest available evidence and the new licensed biologics.

Methodik

- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- Update der Versionen 2007 und 2011

Recherche/Suchzeitraum:

- literature search was performed, through November 2015, using primarily MEDLINE

LoE und GoE

- k.A.
- The level of agreement was voted online, using a 1–10 scale with a vote of 1 meaning total disagreement and 10 meaning full agreement with the recommendation.

Sonstige methodische Hinweise

- Zielpopulation juvenile idiopathische Arthritis
- „Die Leitlinie erfüllt nicht ausreichend die methodischen Anforderungen. Aufgrund fehlender höherwertiger Evidenz für die juvenile Zielpopulation, wird die LL jedoch ergänzend dargestellt."

Recommendation for the use of biological Therapy in juvenile idiopathic arthritis

General principles	Level evidence	Agreement Mean(SD)
Biological therapy for enthesitis-related arthritis		
11 Biological therapy should be considered in active polyarthritis and/or active enthesitis ERA patients with inadequate response to NSAIDs, at least one csDMARD, including MTX, and glucocorticoid injections, if appropriate	1b	9.2 (1.0)
12 TNFi are recommended for refractory ERA	1b	9.6 (0.2)
13 Assessment of response and the decision to maintain bDMARD should be performed no longer than 3 months after starting treatment in ERA patients. Biologic treatment should only be maintained in patients who achieve at least an ACRPed 50 and have documented improvement of enthesitis	1b; 5	8.9 (1.1)
Biological therapy for juvenile psoriatic arthritis		
14 Biological therapy should be considered in jPsA patients who failed at least one csDMARD, including MTX in recommended doses for at least 3 months, unless contraindication, toxicity or intolerance	1b	9.5 (0.7)
15 TNFi are recommended for refractory jPsA. Other biologics may be considered in case of inadequate response and/or major cutaneous involvement	1b	9.4 (0.8)
16 Assessment of response and the decision to maintain treatment should be performed no longer than 3 months after starting a biologic in jPsA patients. Biologic treatment should only be maintained in patients who achieve at least an ACRPed 50 and have documented improvement of extra-articular involvement (skin, dactilytis and enthesitis if applicable)	1b; 5	8.9 (0.9)

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3.5 Ergänzende Dokumente anderer Organisationen zu möglichen Komparatoren

Keine

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 3 of 12, March 2019) am 07.03.2019

#	Suchfrage
1	[mh “Arthritis, Juvenile“]
2	juvenile near/4 arthrit*:ti,ab,kw
3	jia:ti,ab,kw
4	(OR #1-#3)
5	#4 with Cochrane Library publication date from Mar 2014 to present

Systematic Reviews in Medline (PubMed) am 07.03.2019

#	Suchfrage
1	Arthritis, Juvenile[mh]
2	(juvenile*[tiab] OR child*[tiab]) AND arthrit*[tiab]
3	(pediatric[tiab] OR paediatric[tiab] OR child*[tiab]) AND rheumatic[tiab] AND disease*[tiab]
4	#1 OR #2 OR #3
5	(#4) AND ((Meta-Analysis[ptyp] OR ((systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND systematic review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (systematic review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])) OR Technical Report[ptyp]) OR (((((trials[tiab] OR studies[tiab] OR database*[tiab] OR literature[tiab] OR publication*[tiab] OR Medline[tiab] OR Embase[tiab] OR Cochrane[tiab] OR Pubmed[tiab])) AND systematic*[tiab] AND (search*[tiab] OR research*[tiab]))) OR ((((((((((HTA[tiab]) OR technology assessment*[tiab]) OR technology report*[tiab]) OR (systematic*[tiab] AND review*[tiab])) OR (systematic*[tiab] AND overview*[tiab])) OR meta-analy*[tiab]) OR (meta[tiab] AND analyz*[tiab])) OR (meta[tiab] AND analys*[tiab])) OR

	(meta[tiab] AND analyt*[tiab])))) OR (((review*[tiab]) OR overview*[tiab]) AND ((evidence[tiab]) AND based[tiab]))))))
6	((#5) AND ("2014/03/01"[PDAT] : "3000"[PDAT]) NOT "The Cochrane database of systematic reviews"[Journal]) NOT (animals[MeSH:noexp] NOT (Humans[mh] AND animals[MeSH:noexp]))

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#	**Suchfrage**
	Arthritis, Juvenile[mh]
2	(juvenile*[tiab] OR child*[tiab]) AND arthrit*[tiab]
3	(pediatric[tiab] OR paediatric[tiab] OR child*[tiab]) AND rheumatic[tiab] AND disease*[tiab]
4	#1 OR #2 OR #3
5	(#4) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[Title] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] *OR recommendation*[ti])*
6	(((#5) AND ("2014/03/01"[PDAT] : "3000"[PDAT])) NOT (animals[MeSH:noexp] NOT (Humans[MesH] AND animals[MeSH:noexp])) NOT ("The Cochrane database of systematic reviews"[Journal]) NOT ((comment[ptyp]) OR letter[ptyp]))

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8. **Spanish Society of Rheumatology (SER).** Clinical practice guideline for the treatment of patients with axial spondyloarthritis and psoriatic arthritis; Update 2015 [online]. Madrid (ESP): SER; 2018. [Zugriff: 11.03.2019]. URL: https://www.ser.es/wp-content/uploads/2016/06/ENGLISH_updated_GPC_Treatment_SpondyloArthritis.pdf.

Anhang

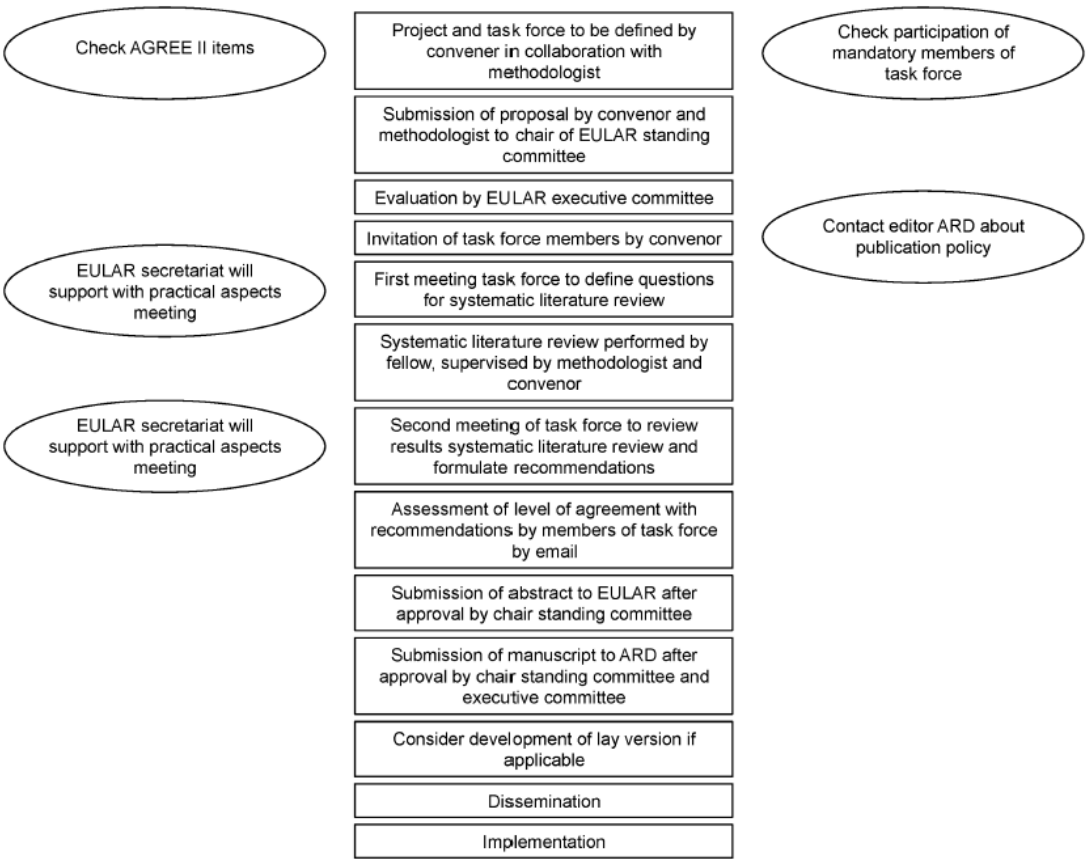

Abbildung 1: Flowchart of various steps during development of recommendations. AGREE, Appraisal of Guidelines for Research & Evaluation; ARD, Annals of Rheumatic Diseases [5]