IQWiG Reports – Commission No. V17-01

Guideline synopsis for a DMP "rheumatoid arthritis"[1]

Extract

[1] Translation of Chapters 1 to 6 of the rapid report V17-01 *Leitliniensynopse für ein DMP Rheumatoide Arthritis* (Version 1.0; Status: 24 November 2017). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

Publishing details

Publisher:
Institute for Quality and Efficiency in Health Care

Topic:
Guideline synopsis for a DMP “rheumatoid arthritis”

Commissioning agency:
Federal Joint Committee

Commission awarded on:
20 April 2017

Internal Commission No.:
V17-01

Address of publisher:
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The rapid report was subject to an external review.

The responsibility for the contents of the report lies solely with IQWiG.

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IQWiG thanks the external experts for their collaboration in the project.

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Keywords: arthritis – rheumatoid, disease-management-program, methodological guideline appraisal

Overview

Research question

The aim of the present investigation is to identify current evidence-based guidelines, summarize their recommendations as key statements and specify those key statements that are suitable for a disease management programme (DMP) “rheumatoid arthritis”.

The following research question should be answered:

- For which health care aspects can (particularly) suitable key statements be identified?

Key results

The guideline synopsis is based on the analysis of 13 guidelines; a total of 242 recommendations were included. Table 1 provides an overview of the health care aspects covered in the respective guidelines.

Table 1: Overview of the health care aspects for which the guidelines contain recommendations

	Health care aspect												
Guideline	**Definition of rheumatoid arthritis[a]**	**Diagnostics**	**Treatment goals**	**Therapeutic measures – general aspects and cardiovascular risk management**	**Non-drug therapy and general measures**	**Drug therapy**	**Disease-modifying drugs[b]**	**Pregnancy[b]**	**Symptomatic and anti-inflammatory therapy[b]**	**Monitoring**	**Rehabilitation**	**Cooperation of health care sectors**	**Patient training**
ACR 2017	–	–	–	–	–	X	X	–	–	–	–	–	–
ACR 2015	X	–	X	–	–	X	X	–	X	–	–	–	–
BSR 2017	–	X	–	–	–	X	X	–	X	–	–	X	X
BSR 2013 TCZ	X	–	–	–	–	X	X	X	–	–	–	–	–
CRA 2012 Safety	–	–	–	–	–	X	X	–	–	–	–	–	–
DGRh 2012	–	–	X	–	–	X	X	–	X	–	–	X	–
EULAR 2017	–	–	X	X	–	X	X	–	X	X	–	X	–
EULAR 2016	–	–	X	–	–	X	X	X	–	–	–	X	–
EULAR 2016 CV	–	–	–	X	X	X	X	–	X	X	–	X	–
EULAR 2015	–	–	X	X	–	–	–	–	–	X	–	–	X
EULAR 2014	–	–	–	–	–	–	–	–	–	–	–	–	X
EULAR 2013 Imaging	–	X	–	–	–	–	–	–	–	X	–	–	–
NICE 2015	–	–	–	–	X	–	–	–	–	–	–	–	–
Guideline sum	2	2	5	3	2	9	9	2	5	4	0	5	3

a: In general, the definitions provided in the guidelines are not recommendations that have a GoR and/or an LoE.
b: “Disease-modifying drugs”, “pregnancy” and “symptomatic and anti-inflammatory therapy” are partial aspects of drug therapy.
GoR: grade of recommendation; LoE: Level of Evidence

Key statements rated as particularly suitable or as suitable for a new DMP were identified for 7 health care aspects (diagnostics, treatment goals, non-drug therapy and general measures, drug therapy, monitoring, cooperation of health care sectors, patient training). Table 2 additionally shows the number of key statements per health care aspect for which further evaluation is proposed, for which the suitability for a new DMP could not be assessed, or which were assessed as less suitable. Furthermore, the number of key statements per health care aspect is presented for which IQWiG designations were included.

Table 2: Number of key statements with assessment of the key statements on the health care aspects

Health care aspect	Assessment of suitability (number of key statements)					IQWiG designation[a]
	Particu-larly suitable	Suitable	Further evaluation proposed	No assessment possible	Less suitable	
Diagnostics	0	1	0	2	0	1
Treatment goals	0	1	0	0	0	0
Therapeutic measures – general aspects and cardiovascular risk management	0	0	0	3	0	3
Non-drug therapy and general measures	0	1	0	0	1	2
Drug therapy	1	18	0	5	19	11
▪ Disease-modifying drugs[c]	▪ 1	▪ 17	▪ 0	▪ 2	▪ 17	▪ 7
▪ Pregnancy[c]	▪ 0	▪ 0	▪ 0	▪ 3	▪ 1	▪ 3
▪ Symptomatic and anti-inflammatory therapy[c]	▪ 0	▪ 1	▪ 0	▪ 0	▪ 1	▪ 1
Monitoring	0	2	0	2	0	2
Rehabilitation	_[b]	_[b]	_[b]	_[b]	_[b]	_[b]
Cooperation of health care sectors	0	2	0	1	0	1
Patient training	0	1	0	0	0	0
Column sum	1	26	0	13	20	20

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: No assessment possible because no recommendations on this health care aspect were identified in the guidelines included.
c: “Disease-modifying drugs”, “pregnancy” and “symptomatic and anti-inflammatory therapy” are partial aspects of drug therapy.
DMP: disease management programme; IQWiG: Institute for Quality and Efficiency in Health Care

Conclusion

13 evidence-based guidelines were included in rapid report V17-01. (Particularly) suitable key statements could be generated from these for the following health care aspects:

- diagnostics
- treatment goals
- therapeutic measures
  - non-drug therapy and general measures
  - drug therapy
    - disease-modifying drugs
    - symptomatic and anti-inflammatory therapy
- monitoring
- cooperation of health care sectors
- patient training

Due to the prognostic relevance, cardiovascular risk management, for which the European League Against Rheumatism (EULAR) publishes a separate guideline, was included in the list of health care aspects in both reports (V14-02 and V17-01).

Only few recommendations were identified for the health care aspect “non-drug therapy and general measures” and no recommendations were identified for the health care aspect “rehabilitation”. This had already been the case in the final report V14-02. In contrast to the final report V14-02, the rapid report V17-01 does not contain recommendations on the topics of occupational therapy, physiotherapy, orthoses, surgical interventions and nursing management of rheumatoid arthritis. In addition, no recommendations were identified on podiatry, other autoimmune disorders, opportunistic infections and psychological care in the guidelines included in the rapid report.

The rapid report focuses on drug therapy, which plays a key role in the guidelines included. The guidelines of rapid report V17-01 only contain few recommendations on the topic of analgesics, however.

Table of contents

List of tables

Page

List of abbreviations

Abbreviation	Meaning
ACR	American College of Rheumatology
BSR	British Society for Rheumatology
DMP	disease management programme
DMP-A-RL	disease management programme requirement directive
EULAR	European League Against Rheumatism
GoR	Grade of Recommendation
IOM	Institute of Medicine
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
LoE	Level of Evidence
RA	rheumatoid arthritis
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

1 Background

Disease management programmes

Disease management programmes (DMPs) are structured treatment programmes for chronically ill people that are based on the findings of evidence-based medicine. Within these programmes, treatment methods are primarily used that correspond to the current state of scientific knowledge [1]. Patients thus receive health care that aims to prevent as far as possible the risk of late complications and acute deterioration of the disease and increase their quality of life. The goal of DMPs is, among other things, to optimize treatment, promote collaboration with service providers, and thus better interlink diagnostic and therapeutic procedures [2].

Relevant disorder

Rheumatoid arthritis (RA) is the most common chronic-inflammatory joint disorder in industrial countries with a prevalence of 0.5% to 0.8% in the adult population [3,4]. The prevalence data correspond to the data for Germany [5]. RA is attributed to the autoimmune disorders [6]. This disorder occurs in adulthood; women are more often affected than men.

The course of disease differs individually and cannot be predicted in individual cases [5,7,8]. The first 3 to 6 months of the disease represent a “therapeutic window” within which the immunological process can be stopped or permanently changed. Early diagnosis and initiation of treatment are thus of decisive importance for the course of disease [5,9].

RA predominantly affects the joints of the hands and feet, mostly following a symmetrical pattern [5,8]. Depending on disease severity, the chronic inflammation of the synovial membranes rapidly or insidiously leads to the destruction of cartilage and the adjoining bone, with the destruction of affected joints, which is visible in X-rays. Typical symptoms are general symptoms of disease such as pain, restriction in mobility, fatigue, as well as inflammations of tendon sheaths, blood vessels, and internal organs [5].

In order to distinguish RA from similar disorders, the classification criteria of the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) from 2010 are used; these also cover the early forms of RA and are considered in guidelines developed after 2010 (see Table 3).

Table 3: ACR/EULAR classification criteria for rheumatoid arthritis [3,6]

The precondition for the application of the criteria listed in the table below is the existence of at least one case of confirmed synovitis in at least one target joint without indications of a different cause (trauma, other inflammatory or degenerative joint disorders).

If, according to the items in the table, at least 6 points (last column) are achieved, then the disease can be classified as RA. The highest score applies in each of the columns (e.g. 4 small [3 points] and 2 large joints [1 point] 3 points).

Swollen/painful joints	**Serology**	**Acute inflammatory phase parameters**	**Symptom duration**	**Points**
≤ 1 large[a]	RF and ACPA negative	CRP and ESR normal	< 6 weeks	0
2–10 large[a]	-	CRP and/or ESR increased	≥ 6 weeks	1
1–3 small[b]	RF and/or ACPA low-positive	-	-	2
4–10 small[b]	RF and/or ACPA high-positive	-	-	3
≥ 11 including small joints	-	-	-	5

a: The definition "large joints" refers to shoulders, elbows, hips, knees and ankles. The initial definition of definitive synovitis does not have to be fulfilled for a joint to be rated as an affected joint; here it refers to any joint from the above list with swelling or tenderness.

b: The definition "small joints" refers to the first to fifth metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints, second to fifth metatarsophalangeal (MTP) joints, thumb interphalangeal joints (IP 1), and wrists. The first carpometacarpal (CMC) joints, the first metatarsophalangeal (MTP) joints, and the distal interphalangeal (DIP) joints are excluded from the assessment.

ACPA: anti-citrullinated protein antibody; ACR: American College of Rheumatology; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; EULAR: European League Against Rheumatism; RA: rheumatoid arthritis; RF: rheumatoid factor

Guidelines

For the present rapid report the term "guidelines" is used according to the definition of the Institute of Medicine (IOM): "practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances" [10] and "include recommendations intended to optimize patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options" [11].

A guideline group is expected to award a "Grade of Recommendation" (GoR) and a "Level of Evidence" (LoE). The GoR reflects the strength of a recommendation and is usually based on a weighing of the benefits and harms of a (medical) intervention in each specific health care context, as well as on the strength of the underlying evidence or the LoE. The LoE represents an assessment of the certainty of results of the studies underlying the recommendations; in this context, systematic reviews of randomized controlled trials (RCTs) are generally awarded the highest LoE. Guideline groups often use different systems to determine GoR and LoE.

2 Research question

The aim of the present investigation is to identify current evidence-based guidelines, summarize their recommendations as key statements and specify those key statements that are suitable for a disease management programme (DMP) “rheumatoid arthritis”.

The following research question should be answered:

- For which health care aspects can (particularly) suitable key statements be identified?

3 Methods

The investigation included guidelines that had been developed specifically for RA. The target population of the guideline synopsis consisted of patients with RA.

The present report is an update of the final report V14-02. For this purpose, a systematic search, in the sense of an update search, was conducted in guideline databases, as well as on the websites of multidisciplinary and specialist guideline providers.

In addition, information from enquiries to authors was included.

The update search was conducted for the period starting November 2015, the last time point of the literature search for report V14-02. The guidelines included in the final report V14-02 were also included in the pool of potentially relevant guidelines. Only evidence-based guidelines applicable to the German health care system and published from April 2012 onwards that were marked as valid at the time point of the update search and/or that had not exceeded the revision date mentioned were included. The recommendations had to be clearly designated as such.

The guideline recommendations relevant for the research question were extracted into tables, together with the related GoR and LoE. In order to achieve comparability of the largely different systems of the GoR and LoE used in the guidelines, the GoR and/or LoE used in the guidelines were allocated to the categories “high”, “not high” and “unclear”.

For the synthesis, the recommendations extracted were summarized as key statements.

The key statements were assessed with regard to their suitability for a new DMP. In each case, the assessment was conducted on the basis of the GoR of the recommendations underlying the key statements. Only in cases where only recommendations with unclear GoR were available for a key statement was the LoE used in addition.

The respective key statement was rated as particularly suitable, suitable or unsuitable for a DMP, or was recommended for further evaluation of suitability, or it was not possible to assess the suitability of the respective key statement.

Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to the established care of patients and may therefore be considered correspondingly in the production of a DMP, were specifically marked (Institute for Quality and Efficiency in Health Care [IQWiG] designation).

In case of (particular) suitability of key statements it was evaluated whether contradicting IQWiG reports with a publication date from April 2012 onwards existed, which could then be considered in the final evaluation of the suitability.

In addition, in the event of (particular) suitability of key statements on drugs and non-drug interventions, the approval status, the reimbursability, the billing capability, and the indication-specific prescribability in Germany were evaluated and any discrepancies were presented.

In addition to the recommendations, the respective definitions of the disease were extracted from the guidelines included and presented in the original wording.

4 Results

4.1 Results of the information retrieval

The systematic Internet search was conducted from April 2017 to May 2017. After title and abstract screening it yielded 14 potentially relevant guidelines, which were screened in full text. In addition, there were 18 guidelines included in the final report V14-02 [12]. After evaluation of the inclusion criteria, 12 relevant guidelines were included in rapid report V17-01. One further, recently published guideline was included in the rapid report after the external review.

4.2 Synthesis of recommendations

In the following tables (Table 4 to Table 17), the key statements summarized from the individual recommendations and classified by health care aspects are presented as well as their assessment regarding suitability for a DMP.

The first column contains the designation of the corresponding key statement, which also represents the name of the corresponding extraction table in Section A3.4 of the full rapid report, where the underlying recommendations can be found.

The second column shows the key statements synthesized from the extracted recommendations.

The third column contains the abbreviations of the guidelines that contain the recommendations underlying the corresponding key statement.

The fourth column presents the ratio of the number of recommendations with high GoR underlying the corresponding key statement to the total number of recommendations regarding this key statement.

The fifth column shows a methodological assessment whether the key statements are particularly suitable, suitable or less suitable for a DMP “rheumatoid arthritis”, whether further evaluation of suitability for a DMP is proposed or whether no such assessment is possible.

The sixth column can contain IQWiG designations or further notes on individual key statements.

In the key statements rated as (particularly) suitable for a DMP, there were no discrepancies between their statements on drugs or non-drug interventions, the German approval status and the indication-specific prescribability.

No contradicting IQWiG assessments were identified.

No recommendations were identified for the health care aspect “rehabilitation” for rapid report V17-01 or for the final report V14-02.

In the headings of the following sections, a numbering in line with the DMP requirement directive (DMP-A-RL) for already existing DMPs is given in brackets behind the designation of the health care aspect.

4.2.1 Definition of rheumatoid arthritis (V1.1)

The definitions provided in the guidelines are presented in Table 23 of the full rapid report; see also the classification criteria of the professional societies [6,13]. Since definitions are no recommendations, no key statements are provided here.

4.2.2 Diagnostics (V1.2)

Table 4: Summary assessment on the health care aspect “diagnostics” (V1.2)

Name of the extraction table in Section A3.4.2	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Clinical and laboratory tests					
V1.2/T1 – K1 (clinical and laboratory tests)	Physical examination including measurement of blood pressure and assessment of blood count, renal and liver function is recommended at the time point of diagnosis. Awareness of comorbidities is required because of their influence on the choice of drugs.	BSR 2017	2/2	Suitable	
T2: Imaging test					
V1.2/T2 – K1 (confirmation of diagnosis)	In case of diagnostic doubt imaging techniques such as conventional radiography, ultrasound and MRI can be used to improve the certainty of a diagnosis. Radiography of the hands and feet should be used as the initial imaging technique to detect joint damage. However, ultrasound and MRI can detect damage at an earlier time point.	EULAR 2013 Imaging	0/2	Not assessable	Suitable from a clinical point of view
V1.2/T2 – K2 (determination of disease activity)	Ultrasound and MRI can be more useful than clinical examination to assess signs of inflammation at the time point of diagnosis, progression and therapeutic response (monitoring during the course of the disease). Presence of bone marrow oedema on the MRI is considered to be a predictor of progression.	EULAR 2013 Imaging	0/3	Not assessable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).

DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; MRI: magnetic resonance imaging; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; T: topic; V: health care aspect

4.2.3 Treatment goals (V1.3)

Table 5: Summary assessment on the health care aspect "treatment goals" (V1.3)

Name of the extraction table in Section A3.4.3	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
V1.3 – K1 (disease control)	Patients with RA should receive the best possible treatment; the treatment decision should be based on agreement between the patients and the rheumatologist. Irrespective of the disease activity, RA patients should receive targeted treatment aimed at reaching remission or at least low disease activity as quickly as possible, thus maintaining long-term health-related quality of life. Inflammation should be reduced, disease activity measured and treatment adjusted. In pregnant women it must be ensured that the treatment does not harm the unborn child.	ACR 2015, DGRh 2012[b], EULAR 2017, EULAR 2016, EULAR 2015	5/12	Suitable	See also European standard of care for patients with RA [14]

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has expired at the time point of sending the rapid report.
DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; T: topic; V: health care aspect

4.2.4 Therapeutic measures (V1.4)

4.2.4.1 General aspects and cardiovascular risk management (V1.4.1)

Table 6: Summary assessment on the health care aspect “therapeutic measures” – general aspects and cardiovascular risk management (V1.4.1)

Name of the extraction table in Section A3.4.4	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: General aspects					
V1.4.1/T1 – K1 (general aspects)	Disease activity, existing structural damage, comorbidities and safety issues should be considered in the treatment decision. In addition, the high individual, medical and societal costs should be considered in specialist treatment.	EULAR 2017, EULAR 2015	0/3	Not assessable	Suitable from a clinical point of view
T2: Cardiovascular risk management					
V1.4.1/T2 – K1 (risk assessment)	In view of the increased risk of cardiovascular disease in RA patients, the risk assessment should be performed at least once every 5 years or according to guidelines or adapted risk scores and in case of major changes in treatment. Risk management should be conducted as in the general population. Total cholesterol and HDL cholesterol should be measured when disease activity is stable or in remission.	EULAR 2016 CV	0/8	Not assessable	Suitable from a clinical point of view

(continued)

Table 6: Summary assessment on the health care aspect “therapeutic measures” – general aspects and cardiovascular risk management (V1.4.1) (continued)

Name of the extraction table in Section A3.4.4	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T2: Cardiovascular risk management					
V1.4.1/T2 – K2 (NSAIDs and corticosteroids)	Antirheumatic drugs (NSAIDs and corticosteroids) should be used in accordance with the EULAR treatment recommendations.	EULAR 2016 CV	0/1	Not assessable	Suitable from a clinical point of view; SPCs and Pharmaceutical Directive must be taken into account, particularly in case of combination therapies

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).

DMP: disease management programme; EULAR: European League Against Rheumatism; GoR: grade of recommendation; HDL: high-density lipoprotein; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; NSAID: nonsteroidal anti-inflammatory drug; RA: rheumatoid arthritis; T: topic; V: health care aspect

4.2.4.2 Non-drug therapy and general measures (V1.4.2)

Table 7: Summary assessment on the health care aspect "therapeutic measures" – non-drug therapy and general measures (V1.4.2)

Name of the extraction table in Section A3.4.4.2	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Lifestyle					
V1.4.2/T1 – K1 (lifestyle)	Lifestyle recommendations should emphasise the benefits of a healthy diet, regular exercise and smoking cessation.	EULAR 2016 CV	0/1	Less suitable	Suitable from a clinical point of view
T2: Physiotherapy/sports					
V1.4.2/T2 – K1 (physiotherapy/ sports)	A hand exercise programme should be considered for patients with RA with pain and dysfunction of the hands and should be delivered by a trained practitioner.	NICE 2015	1/2	Suitable	From a clinical point of view, physiotherapy is not only relevant for the hands.

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).

DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; T: topic; V: health care aspect

4.2.4.3 Drug therapy (V1.4.3)

4.2.4.3.1 Disease-modifying drugs (V1.4.3.1)

4.2.4.3.1.1 Initial treatment with csDMARDs (V1.4.3.1.1)

Table 8: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – initial treatment with csDMARDs (V1.4.3.1.1)

Name of the extraction table in Section A3.4.4.3.1.1	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Basic medication					
V1.4.3.1.1/T1 – K1 (basic medication)	A conventional DMARD, MTX, should be part of the basic therapy, which is started as soon as the diagnosis of RA is made.	DGRh 2012[b], EULAR 2017	2/3	Suitable	
V1.4.3.1.1/T1 – K2 (Adaptation of basic medication)	In patients with a contraindication to MTX or early intolerance, leflunomide or sulfasalazine should be considered as part of the basic therapy.	EULAR 2017	1/2	Suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has expired at the time point of sending the rapid report.
csDMARD: conventional synthetic disease-modifying antirheumatic drug; DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; MTX: methotrexate; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; T: topic; V: health care aspect

4.2.4.3.1.2 Further treatment options (V1.4.3.1.2)

Table 9: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – further treatment options (V1.4.3.1.2)

Name of the extraction table in Section A3.4.4.3.1.2	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: csDMARD monotherapy					
V1.4.3.1.2/T1 – K1 (csDMARD monotherapy)	In treatment-naive RA patients, DMARD monotherapy, preferably with MTX, should be preferred to a combination of 2 or 3 DMARDs. If MTX cannot be administered, another DMARD, e.g. leflunomide, should be used.	ACR 2015, DGRh 2012[b]	3/10	Suitable	
T2: Combination therapy of several csDMARDs					
V1.4.3.1.2/T2 – K1 (combination therapy of several csDMARDs)	If disease activity remains moderate to high in patients with symptomatic early RA despite DMARD monotherapy, a combination therapy of conventional DMARDs or a non-TNF biologic or tofacitinib, each with or without MTX, should be given instead of continued monotherapy. If disease activity remains moderate to high in RA patients with longer disease duration despite DMARD monotherapy, a combination therapy of conventional DMARDs or, additionally, a non-TNF biologic or tofacitinib, each with or without MTX, should be given instead of continued monotherapy.	ACR 2015, DGRh 2012[b]	3/3	Particularly suitable	See also IQWiG benefit assessment A17-18 [15] for more information on tofacitinib

(continued)

Table 9: Summary assessment on the health care aspect "therapeutic measures" – drug therapy – disease-modifying drugs – further treatment options (V1.4.3.1.2) (continued)

Name of the extraction table in Section A3.4.4.3.1.2	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T3: bDMARD therapy					
V1.4.3.1.2/T3 – K1 (bDMARD therapy)	In the presence of persisting moderate to high disease activity under bDMARD monotherapy, escalated treatment with a different drug from the same drug group or with a drug from a different drug group, each with or without MTX, should be administered. Switching to a tsDMARD is also possible. In case of combination therapy with MTX, the dose can be increased when the response is inadequate. If MTX as comedication is not tolerated, IL-6 inhibitors and tsDMARDs in monotherapy may have some advantages compared with other bDMARDs.	ACR 2015, BSR 2013 TCZ, DGRh 2012[b], EULAR 2017	1/13	Suitable	See also IQWiG benefit assessments A16-70 [16] and A10-01 [17] for more information on biologics
T4: Combination therapy of csDMARDs and bDMARDs					
V1.4.3.1.2/T4 – K1 (combination therapy of csDMARDs and bDMARDs)	If the treatment goal is not achieved and unfavourable prognostic factors are present or if moderate to high disease activity persists under treatment, csDMARD monotherapy in dependence on the approval status should be combined with bDMARDs or a tsDMARD. In case of TNFi monotherapy, treatment can be switched to another TNFi or to a drug from a different drug group.	ACR 2015, EULAR 2017	2/5	Suitable	

(continued)

Table 9: Summary assessment on the health care aspect "therapeutic measures" – drug therapy – disease-modifying drugs – further treatment options (V1.4.3.1.2) (continued)

Name of the extraction table in Section A3.4.4.3.1.2	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T5: Treatment with tsDMARDs					
V1.4.3.1.2/T5 – K1 (treatment with tsDMARDs)	If a bDMARD or tsDMARD has failed, treatment with another bDMARD or tsDMARD should be considered. If one TNFi therapy has failed, another TNF inhibitor or an agent with another mode of action may be given.	EULAR 2017	1/1	Suitable	
T6: Combination therapy of csDMARDs and tsDMARDs					
V1.4.3.1.2/T6 – K1 (combination therapy of csDMARDs and tsDMARDs)	bDMARDs and tsDMARDs should be combined with a conventional DMARD in patients who do not tolerate csDMARDs as comedication. In these patients, IL-6 inhibitors and tsDMARDs may have some advantages compared with other bDMARDs.	EULAR 2017	1/1	Suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has expired at the time point of sending the rapid report.

bDMARD: biologic disease-modifying antirheumatic drug; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; IQWiG: Institute for Quality and Efficiency in Health Care; IL: interleukin; K: key statement; MTX: methotrexate; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; T: topic; TCZ: tocilizumab; TNF: tumour necrosis factor; TNFi: tumour necrosis factor inhibitor; tsDMARD: targeted synthetic disease-modifying antirheumatic drug; V: health care aspect

4.2.4.3.1.3 Conduct/monitoring and safety aspects (V1.4.3.1.3)

Table 10: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – conduct/monitoring and safety aspects (V1.4.3.1.3)

Name of the extraction table in Section A3.4.4.3.1.3	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Dose reduction if RA is in remission, low disease activity					
V1.4.3.1.3/T1 – K1 (sustained remission)	In case of sustained remission, a stepwise reduction of DMARD treatment should be considered in a shared decision between the patient and the physician.	DGRh 2012[b]	0/1	Less suitable	Suitable from a clinical point of view
V1.4.3.1.3/T1 – K2 (dose reduction)	In patients with RA in remission or with low disease activity, DMARD treatment should be reduced, but not discontinued.	ACR 2015	1/5	Suitable	
T2: Azathioprine					
V1.4.3.1.3/T2 – K1 (azathioprine)	RA patients receiving azathioprine should have baseline thiopurine methyltransferase status assessed.	BSR 2017	1/1	Suitable	**Not** suitable from a clinical point of view
T3: Therapeutic drug levels					
V1.4.3.1.3/T3 – K1 (therapeutic drug levels)	Monitoring of therapeutic drug levels should be considered for certain drugs (TCL and CSA).	BSR 2017	0/1	Less suitable	According to the SPC, TCL not approved for RA treatment in Germany [18]

(continued)

Table 10: Summary assessment on the health care aspect "therapeutic measures" – drug therapy – disease-modifying drugs – conduct/monitoring and safety aspects (V1.4.3.1.3) (continued)

Name of the extraction table in Section A3.4.4.3.1.3	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T4: Arterial blood pressure, blood-glucose levels, body weight					
V1.4.3.1.3/T4 – K1 (arterial blood pressure; blood-glucose levels, body weight)	Patients receiving LEF/CSA/TCL[c] should have their blood pressure assessed; patients on LEF should also have weight measured. Patients on TCL[c]/CSA should have blood glucose measured regularly.	BSR 2017	0/1	Less suitable	See also DGRh treatment monitoring sheets and SPCs [18-22]
T5: Folic acid supplementation					
V1.4.3.1.3/T5 – K1 (folic acid supplementation)	Patients treated with MTX should receive folic acid supplementation.	BSR 2017	1/1	Suitable	
T6: Eye assessment					
V1.4.3.1.3/T6 – K1 (eye monitoring)	Patients on HCQ treatment should be offered baseline eye assessment and annual check-ups, e.g. with OCT, if HCQ is administered for > 5 years.	BSR 2017	1/2	Suitable	
T7: Laboratory tests					
V1.4.3.1.3/T7 – K1 (laboratory tests)	RA patients on DMARD treatment should have regular assessment of blood count and of renal and liver function. The duration of the monitoring depends on the drug: APL, HCQ and MCN[c] do not require regular laboratory tests. SSZ does not need routine laboratory tests once patients are stable for 12 months.	ACR 2015, BSR 2017	0/14	Not assessable	Apremilast is not approved for RA treatment in Germany [23], MCN is approved for the treatment of infections [24]

(continued)

Table 10: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – conduct/monitoring and safety aspects (V1.4.3.1.3) (continued)

Name of the extraction table in Section A3.4.4.3.1.3	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T8: Tocilizumab					
V1.4.3.1.3/T8 – K1 (blood count)	A full blood count should be checked before the next TCZ infusion.	BSR 2013 TCZ	0/1	Less suitable	See also IQWiG benefit assessment A10-01 [17] for more information on tocilizumab as second-line treatment
V1.4.3.1.3/T8 – K2 (neutropenia)	Physicians and patients should be counselled regarding the risk of neutropenia under TCZ treatment and patients should be closely monitored in the first 6 months of treatment. Blood count should be checked if patients develop fever and appropriate treatment should be initiated if grade 3/4 neutropenia is identified.	BSR 2013 TCZ	0/2	Less suitable	For TCZ, see also treatment monitoring sheet [25]
V1.4.3.1.3/T8 – K3 (surgery)	In patients with RA undergoing elective surgery, a 4-week interruption of TCZ is advised prior to surgery and clinicians are advised to be highly vigilant for clinical signs of infection. Particular caution should be exercised in patients undergoing bowel surgery. TCZ treatment can be recommenced postoperatively if there is no evidence of infection or delayed wound healing.	BSR 2013 TCZ	0/4	Less suitable	

(continued)

Table 10: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – conduct/monitoring and safety aspects (V1.4.3.1.3) (continued)

Name of the extraction table in Section A3.4.4.3.1.3	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T8: Tocilizumab (continued)					
V1.4.3.1.3/T8 – K4 (hepatotoxicity)	Liver function tests should initially be performed in all patients receiving TCZ at 4-week intervals. Other hepatotoxic drugs should only be used cautiously in patients on TCZ, as is the case with MTX treatment.	BSR 2013 TCZ	0/2	Less suitable	See also treatment monitoring sheet [25]
V1.4.3.1.3/T8 – K5 (lipid levels)	All patients on TCZ should have a fasting lipid profile at regular intervals and in case of treatment switching. Further monitoring and, if necessary, treatment should be conducted in accordance with local guidelines.	BSR 2013 TCZ	0/2	Not assessable	See also treatment monitoring sheet

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has expired at the time point of sending the rapid report.
c: This drug is not approved in Germany for the treatment of RA.

APL: apremilast, CSA: ciclosporin; DGRh: German Rheumatology Association; DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; HCQ: hydroxychloroquine; IQWiG: Institute for Quality and Efficiency in Health Care; K: key statement; LEF: leflunomide; MCN: minocycline; MTX: methotrexate; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; OCT: optical coherence tomography; RA: rheumatoid arthritis; SPC: Summary of Product Characteristics; SSZ: sulfasalazine; T: topic; TCL: tacrolimus; TCZ: tocilizumab; V: health care aspect

4.2.4.3.1.4 Comorbidities (V1.4.3.1.4)

Table 11: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – comorbidities (general treatment recommendations) (V1.4.3.1.4)

Name of the extraction table in Section A3.4.4.3.1.4	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: General treatment recommendations					
V1.4.3.1.4/T1 – K1 (general treatment recommendations)	In RA patients with concomitant liver, kidney or heart disease, this concomitant disease should be considered in the choice of DMARDs. Cardiovascular disease and prior malignancy are no contraindications to DMARD therapy.	BSR 2017	3/5	Suitable	See also contraindications of the individual drugs according to the SPC under comorbidities
T2: Vaccinations					
V1.4.3.1.4/T2 – K1 (vaccinations)	RA patients should be vaccinated against influenza and pneumococcus. Live attenuated vaccines are contraindicated, live vaccines should be used several weeks before initiating bDMARD therapy. High-risk groups should also receive vaccination for hepatitis B viruses and older patients should receive vaccination for herpes zoster.	ACR 2015, BSR 2017, BSR 2013 TCZ, CRA 2012 Safety[b]	3/25	Suitable	See also SPCs and vaccination recommendations
T3: Choice of drugs					
V1.4.3.1.4/T3 – K1 (choice of drugs)	RA patients with a history of skin cancer or solid malignancy or with current cancer disease can be treated with conventional DMARDs. Other drugs for the treatment of RA should only be used with caution, if at all.	ACR 2015, CRA 2012 Safety[b]	0/7	Less suitable	Suitable from a clinical point of view

(continued)

Table 11: Summary assessment on the health care aspect "therapeutic measures" – drug therapy – disease-modifying drugs – comorbidities (general treatment recommendations) (V1.4.3.1.4) (continued)

Name of the extraction table in Section A3.4.4.3.1.4	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T4: Treatment interruption					
V1.4.3.1.4/T4 – K1 (treatment interruption)	In patients with current cancer disease, DMARD treatment should be interrupted during chemotherapy or radiotherapy. Treatment decisions should be individualized, and should be made in conjunction with the oncologist and the patient.	CRA 2012 Safety[b]	0/1	Less suitable	Suitable from a clinical point of view
T5: Chronic heart failure					
V1.4.3.1.4/T5 – K1 (chronic heart failure)	RA patients with congestive heart failure whose symptoms have worsened under TNF inhibitor therapy should receive a combination of DMARDs or non-TNF biologics or tofacitinib. These drugs are preferable to other TNF inhibitors.	ACR 2015	0/2	Less suitable	Suitable from a clinical point of view, consider SPCs
T6: Malignant lymphoma					
V1.4.3.1.4/T6 – K1 (malignant lymphoma)	RA patients with a history of malignant lymphoma can be treated with HCQ, sulfasalazine, RTX or a combination of DMARDs. Treatment with TNFα antagonists is not recommended; other conventional or biological DMARDs, e.g. abatacept or TCZ, should be used with caution.	ACR 2015, CRA 2012 Safety[b]	1/3	Suitable	See also SPCs

(continued)

Table 11: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – comorbidities (general treatment recommendations) (V1.4.3.1.4) (continued)

Name of the extraction table in Section A3.4.4.3.1.4	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T7: Diverticulitis					
V1.4.3.1.4/T7 – K1 (diverticulitis)	In patients with a history of diverticulitis, TCZ must be used with extreme caution. Patients who are concomitantly on corticosteroids or NSAIDs, should be counselled regarding the risk of gastrointestinal perforation, the corresponding symptoms and the actions required in case of such symptoms.	BSR 2013 TCZ	0/1	Less suitable	Suitable from a clinical point of view (increased risk of intestinal perforation)
T8: Hepatitis					
V1.4.3.1.4/T8 – K1 (hepatitis)	In patients with impaired liver synthetic function, DMARD therapy should be used with extreme caution. Treatment-naive patients with chronic viral hepatitis infection should be considered for anti-viral treatment prior to DMARD initiation. Pretreated hepatitis patients receive the same therapy as other RA patients.	ACR 2015, BSR 2017	3/5	Suitable	
T9: Interstitial lung disease					
V1.4.3.1.4/T9 – K1 (interstitial lung disease)	An existing lung disease per se is not a contraindication to DMARD treatment. However, caution should be taken in patients with reduced lung function and DMARD treatment, which may induce (interstitial) lung disease.	BSR 2017	1/1	Suitable	

(continued)

Table 11: Summary assessment on the health care aspect "therapeutic measures" – drug therapy – disease-modifying drugs – comorbidities (general treatment recommendations) (V1.4.3.1.4) (continued)

Name of the extraction table in Section A3.4.4.3.1.4	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T10: Mycobacterial infection					
V1.4.3.1.4/T10 – K1 (mycobacterial infection)	All RA patients should be screened for latent tuberculosis infection with various tests prior to starting treatment with TNFα antagonists, abatacept or TCZ. Physicians should consider to repeat screening in patients who tested negative; IGRA may be an option to identify false-positive results, e.g. after BCG vaccination. Biologics can be started 1 to 2 months after initiating prevention of reactivation of tuberculosis.	CRA 2012 Safety[b]	0/11	Less suitable	See also SPCs on individual drugs, e.g. [26]
T11: After serious infection					
V1.4.3.1.4/T11 – K1 (after serious infection)	In patients with a history of one or several serious infections, csDMARD combinations or abatacept are preferred to TNFα antagonists.	ACR 2015	0/2	Less suitable	Suitable from a clinical point of view, see also [27]

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has not expired at the time point of sending the rapid report.

BCG: bacille Calmette-Guérin; bDMARD: biologic disease-modifying antirheumatic drug; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; HCQ: hydroxychloroquine; IQWiG: Institute for Quality and Efficiency in Health Care; IGRA: interferon-gamma release assay; K: key statement; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; NSAID: nonsteroidal anti-inflammatory drug; RA: rheumatoid arthritis; RTX: rituximab; T: topic; TCZ: tocilizumab; TNF: tumour necrosis factor; V: health care aspect

4.2.4.3.1.5 Further disease constellations (V1.4.3.1.5)

Table 12: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – further disease constellations – perioperative DMARD management (V1.4.3.1.5)

Name of the extraction table in Section A3.4.4.3.1.5	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)		IQWiG designation[a]/ notes
T1: Perioperative DMARD management					
V1.4.3.1.5/T1 – K1 (perioperative phase)	DMARD therapy should not routinely be stopped before surgery, although individualized decisions should be made for high-risk procedures.	BSR 2017	0/1	Less suitable	
V1.4.3.1.5/T1 – K2 (basic medication)	Treatment with non-biologic DMARDs (e.g. methotrexate) can be continued for RA patients despite an upcoming elective orthopaedic surgery.	ACR 2017, CRA 2012 Safety[b]	1/2	Suitable	
V1.4.3.1.5/T1 – K3 (bDMARD therapy)	Treatment with bDMARDs should be interrupted prior to surgical procedures. The timing should be based on the individual patient, the pharmacokinetic properties of the agent and the nature of the surgery. bDMARD treatment can be recommenced postoperatively if there is no evidence of infection or delayed wound healing and once all sutures, staples and drains are out.	ACR 2017, CRA 2012 Safety[b]	0/3	Less suitable	Suitable from a clinical point of view
V1.4.3.1.5/T1 – K4 (tofacitinib)	In patients receiving a knee or hip replacement, tofacitinib should be withheld for at least 7 days prior to surgery.	ACR 2017	0/1	Less suitable	

(continued)

Table 12: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – further disease constellations – perioperative DMARD management (V1.4.3.1.5) (continued)

Name of the extraction table in Section A3.4.4.3.1.5	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)		IQWiG designation[a]/ notes
T1: Perioperative DMARD management					
V1.4.3.1.5/T1 – K5 (glucocorticoids)	In adult patients receiving a knee or hip replacement, the daily dose of glucocorticoids should be continued instead of increased.	ACR 2017	0/1	Less suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has not expired at the time point of sending the rapid report.

bDMARD: biologic disease-modifying antirheumatic drug; DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; T: topic; V: health care aspect

4.2.4.3.1.6 Pregnancy and lactation (V1.4.3.1.6)

Table 13: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – disease-modifying drugs – pregnancy and lactation (V1.4.3.1.6)

Name of the extraction table in Section A3.4.4.3.1.6	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Pregnancy planning					
V1.4.3.1.6/T1 – K1 (pregnancy planning)	Family planning should be addressed in RA patients and RA treatment should be adjusted before a pregnancy. The risks for the mother and for the child should be weighed against each other. TCZ should be stopped at least 3 months prior to planned conception.	BSR 2013 TCZ, EULAR 2016	0/3	Not assessable	Suitable from a clinical point of view
T2: Contraindicated drugs					
V1.4.3.1.6/T2 – K1 (contraindicated drugs)	Conventional DMARDs that are teratogenic should be withdrawn before pregnancy; conventional and biological DMARDs with insufficient evidence concerning their safe use in pregnancy should be avoided if possible.	EULAR 2016	0/3	Not assessable	Suitable from a clinical point of view
T3: Permitted drugs					
V1.4.3.1.6/T3 – K1 (permitted drugs)	DMARDs with proven safety are an option for RA patients to maintain remission during pregnancy. In the first and second trimester, nonselective COX inhibitors and prednisone can be considered to control symptoms. In severe, refractory disease, methylprednisolone, possibly immunoglobulins or even second or third trimester use of cyclophosphamide should be considered.	EULAR 2016	0/4	Not assessable	First section suitable from a clinical point of view Second section less suitable from a clinical point of view

(continued)

Table 13: Summary assessment on the health care aspect "therapeutic measures" – drug therapy – disease-modifying drugs – pregnancy and lactation (V1.4.3.1.6) (continued)

Name of the extraction table in Section A3.4.4.3.1.6	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T4: Drugs during lactation					
V1.4.3.1.6/T4 – K1 (lactation)	Treatment with conventional DMARDs and anti-inflammatory drugs should be continued during lactation provided the child does not have conditions that contraindicate it. Lactation should not be discouraged. The following drugs are an option: hydoxychloroquine, chloroquine, sulfasalazine, azathioprine, ciclosporin, tacrolimus, colchicine, prednisone, immunoglobulin, nonselective COX inhibitors, celecoxib. Low transfer to breast milk has been shown for infliximab, adalimumab, etanercept and certolizumab. TNFi are considered safe. In contrast, MTX, mycophenolate mofetil, cyclophosphamide, leflunomide, tofacitinib and cyclooxygenase II inhibitors other than celecoxib, as well as RTX, anakinra, belimumab, ustekinumab, tocilizumab and abatacept should be avoided.	BSR 2013 TCZ, EULAR 2016	0/5	Less suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).

COX: cyclooxygenase; DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; MTX: methotrexate; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; RTX: rituximab; T: topic; TCZ: tocilizumab; TNFi: tumour necrosis factor inhibitor; V: health care aspect

4.2.4.3.2 Symptomatic and anti-inflammatory therapy (V1.4.3.2)

Table 14: Summary assessment on the health care aspect “therapeutic measures” – drug therapy – symptomatic and anti-inflammatory therapy – glucocorticoids and nonsteroidal anti-inflammatory drugs” (V1.4.3.2)

Name of the extraction table in Section A3.4.4.3.2	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Glucocorticoids					
V1.4.3.2/T1 – K1 (glucocorticoids)	Patients with persisting moderate or high disease activity despite treatment with DMARD or DMARD/TNFi or non-TNF biologics or with inflammation flare-ups under the treatments mentioned should receive short-term low-dose glucocorticoids. Glucocorticoid treatment should be administered at the lowest possible dose and for the shortest possible duration; the therapeutic indication has to be checked regularly in case of longer administration.	ACR 2015, BSR 2017, DGRh 2012[b], EULAR 2017, EULAR 2016 CV	1/9	Suitable	
T2: Nonsteroidal anti-inflammatory drugs					
V1.4.3.2/T2 – K1 (nonsteroidal anti-inflammatory drugs)	Use of NSAIDs in RA should be with caution, especially for patients with cardiovascular risk factors or cardiovascular disease.	EULAR 2016 CV	0/1	Less suitable	Suitable from a clinical point of view

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has expired at the time point of sending the rapid report.

DMARD: disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement;
NSAID: nonsteroidal anti-inflammatory drug; RA: rheumatoid arthritis; T: topic; TNF: tumour necrosis factor; TNFi: tumour necrosis factor inhibitor; V: health care aspect

4.2.5 Health care aspect “monitoring” (V1.5)

Table 15: Summary assessment on the health care aspect “monitoring” (V1.5)

Name of the extraction table in Section A3.4.5	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Disease activity					
V1.5/T1 – K1 (disease activity)	If a patient is in persistent remission after having tapered glucocorticoids, one can consider tapering bDMARDs, especially if this treatment is combined with csDMARDs. If a patient is in persistent remission, tapering the csDMARDs could also be considered. Remission is defined as the absence of signs and symptoms of significant inflammatory disease activity. Disease activity should be measured and documented regularly with validated instruments; treatment should be based on disease activity to keep the cardiovascular risk low, among other things.	EULAR 2017, EULAR 2015	2/6	Suitable	
T2: Structural changes					
V1.5/T2 – K1 (structural changes)	Since ultrasound and MRI are superior to clinical examination in detecting joint inflammation, they can be useful in monitoring disease activity. The periodic evaluation of joint damage by imaging techniques should be considered; MRI and ultrasound can be used to monitor disease progression.	EULAR 2013 Imaging	0/5	Not assessable	Suitable from a clinical point of view

(continued)

Table 15: Summary assessment on the health care aspect “monitoring” (V1.5) (continued)

Name of the extraction table in Section A3.4.5	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T2: Structural changes (continued)					
V1.5/T2 – K1 (structural changes) (continued)	Imaging can also be used to assess response to treatment. Monitoring of functional instability of the cervical spine by radiograph should be performed in RA patients with suspicion of cervical involvement. When the radiograph is positive or neurological symptoms and signs are present, MRI should be performed.	EULAR 2013 Imaging	0/5	Not assessable	Suitable from a clinical point of view
T3: Follow-up					
V1.5/T3 – K1 (follow-up)	Therapy should be adjusted until reaching the treatment goal and should then be sustained; the frequencies of follow-up examinations should be adjusted in accordance with the level of disease activity.	EULAR 2017, EULAR 2015	1/3	Suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).

bDMARD: biologic disease-modifying antirheumatic drug; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; MRI: magnetic resonance imaging; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; T: topic; V: health care aspect

4.2.6 Health care aspect “rehabilitation”

No key statement was formulated on this health care aspect because the guidelines included do not address this health care aspect.

4.2.7 Health care aspect "cooperation of health care sectors" (V1.6)

Table 16: Summary assessment on the health care aspect "cooperation of health care sectors" (V1.6)

Name of the extraction table in Section A3.4.6	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
T1: Coordination of health care					
V1.6/T1 – K1 (coordination of health care)	Rheumatologist should lead the best possible care for RA patients. The prescriber has responsibility for ensuring patients are adhering to monitoring guidance. In the collaboration with further health care sectors, responsibilities of each party should be laid down in writing. If the specified laboratory parameters change, treatment should be interrupted and the treating rheumatologist should be contacted.	BSR 2017, DGRh 2012[b]	3/6	Suitable	
T2: Referral to a specialist					
V1.6/T2 – K1 (referral to a specialist)	The treating rheumatologist should lead the medical care for RA patients. This also applies to the management of the cardiovascular risk.	EULAR 2017, EULAR 2016 CV	0/2	Not assessable	Suitable from a clinical point of view
T3: Multidisciplinary care					
V1.6/T3 – K1 (multidisciplinary care)	Treatment decisions should be based on agreement between the treating physicians and the patient. The same applies to care during pregnancy and lactation.	BSR 2017, EULAR 2016	1/2	Suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).
b: The validity of the guideline has expired at the time point of sending the rapid report.
DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; RA: rheumatoid arthritis; T: topic; V: health care aspect

4.2.8 Health care aspect “patient training” (V1.7)

Table 17: Summary assessment on the health care aspect “patient training” (V1.7)

Name of the extraction table in Section A3.4.7	Key statement	Underlying recommendations of the following guideline(s)	High GoR (n/N)	Suitability for a DMP methodological assessment	IQWiG designation[a]/ notes
V1.7/T1 – K1 (patient education, trainings)	The training of RA patients should be interactive and comprehensive and should form an integral part of the treatment. It should be conducted by qualified staff, be patient-centred and be evaluated for its effectiveness.	BSR 2017, EULAR 2015, EULAR 2014	6/14	Suitable	

a: Key statements that, due to the described methodological approach, are less suitable for a DMP, but refer to a well-tried care of patients and may therefore be considered in the production of a DMP, are specifically marked (IQWiG designation).

DMP: disease management programme; GoR: grade of recommendation; K: key statement; IQWiG: Institute for Quality and Efficiency in Health Care; n: number of recommendations with high GoR; N: total number of recommendations for this key statement; T: topic; V: health care aspect

5 Classification of the work result

Rapid report V17-01 is an update of the final report V14-02 [12]. The number of included guidelines and the extracted recommendations is small compared with the final report V14-02. The rapid report should be considered together with the final report V14-02 as a basis for a DMP “rheumatoid arthritis”.

Comparison between the final report V14-02 and the rapid report V17-01

The recommendations for the health care aspect “diagnostics” in the final report V14-02 refer to the physical examination and the measurement of general and specific inflammatory parameters in the blood. In rapid report V17-01, this is supplemented with recommendations on the measurement of blood pressure and on imaging techniques for the confirmation of diagnosis and the determination of disease activity.

The recommendations for the “treatment goals” in both reports are largely consistent. In the final report V14-02, a treat-to-target therapy is named for the planning of the individual treatment strategy, and remission and/or minimization of disease activity are named as treatment goals. Rapid report V17-01 addresses the shared treatment decision of physician and patient as well as the demand to consider the protection of the unborn child in the choice of drugs for pregnant patients.

Rapid report V17-01 adds recommendations on prudent treatment decisions in view of high treatment costs to the health care aspect “therapeutic measures – general aspects”.

Recommendations on the prognostically relevant cardiovascular risk management were included in both reports.

In contrast to V14-02, the rapid report does not contain any recommendations on physiotherapy or occupational therapy, podiatry, orthoses, and surgical interventions for the health care aspect “non-drug therapy and general measures”. For this health care aspect, rapid report V17-01 contains recommendations on regular exercise and on a hand exercise programme. In contrast to the final report V14-02, the rapid report does not address autoimmune disorders other than RA and opportunistic infections. The final report V14-02 additionally contains recommendations on psychological care, particularly in cases of inadequate coping with the disease. These topics are not addressed in the guidelines included in rapid report V17-01.

In the final report V14-02 and in rapid report V17-01, recommendations on disease-modifying antirheumatic drugs and on symptomatic and anti-inflammatory therapy could be identified for the health care aspect “drug therapy”.

The final report V14-02 additionally contains recommendations on dietary supplements. Rapid report V17-01 does not contain any recommendations on this topic.

Rapid report V17-01 contains further recommendations on pregnancy and lactation.

The recommendations on the monitoring of disease activity in the final report V14-02 refer to the measurement instrument to be used and the time intervals. Both reports contain recommendations on disease activity including structural changes and follow-up examinations. Both the final report and the rapid report contain only few recommendations on monitoring of the eyes. The importance of these assessments for patients with rheumatoid arthritis was emphasized in the oral hearing on the preliminary report V14-02 [12].

No recommendations were identified for the health care aspect “rehabilitation” for rapid report V17-01, as had already been the case for the final report V14-02.

In the final report V14-02, recommendations were identified for the health care aspect “cooperation of health care sectors”. Except for nursing management, all topics are also addressed in rapid report V17-01.

The recommendations for the health care aspect “patient training” in the final report V14-02 and in rapid report V17-01 are consistent except for 2 new recommendations from the British Society for Rheumatology (BSR) 2017 guideline. The recommendations refer to the content and design of training.

6 Conclusion

13 evidence-based guidelines were included in rapid report V17-01. (Particularly) suitable key statements could be generated from these for the following health care aspects:

- diagnostics
- treatment goals
- therapeutic measures
  - non-drug therapy and general measures
  - drug therapy
    - disease-modifying drugs
    - symptomatic and anti-inflammatory therapy
- monitoring
- cooperation of health care sectors
- patient training

Due to the prognostic relevance, cardiovascular risk management, for which the European League Against Rheumatism (EULAR) publishes a separate guideline, was included in the list of health care aspects in both reports (V14-02 and V17-01).

Only few recommendations were identified for the health care aspect “non-drug therapy and general measures” and no recommendations were identified for the health care aspect “rehabilitation”. This had already been the case in the final report V14-02. In contrast to the final report V14-02, the rapid report V17-01 does not contain recommendations on the topics of occupational therapy, physiotherapy, orthoses, surgical interventions and nursing management of rheumatoid arthritis. In addition, no recommendations were identified on podiatry, other autoimmune disorders, opportunistic infections and psychological care in the guidelines included in the rapid report.

The rapid report focuses on drug therapy, which plays a key role in the guidelines included. The guidelines of rapid report V17-01 only contain few recommendations on the topic of analgesics, however.

References for English extract

Please see full rapid report for full reference list.

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The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/health-care/v17-01-update-of-the-guideline-synopsis-for-the-dmp-rheumatoid-arthritis-rapid-report.7848.html.