

Appendix 1: Supplementary tables and reference list

Swiss Delphi study on iron deficiency

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Original article | doi:10.4414/smw.2019.20097

Cite this as: Swiss Med Wkly. 2019;149:w20097 (Appendix 1)

Supplementary Table S1

Minimal Proportion of Different Medical Institutions in the Sample							
Sample Sizes N = Full Sample n = Subsample	Internal Medicine (N = 20)	Cardiology (N = 20)	Nephrology (N = 20)	Gastroenterology (N = 20)	Gynecology (N = 20)	Oncology (N = 20)	Minimal Total
Public and / or University Hospitals	Minimal n = 10	Minimal n = 10	Minimal n = 10	Minimal n = 10	Minimal n = 10	Minimal n = 10	n = 60 (50%)
Private Hospitals	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	n = 25 (> 20%)
Medical (Group) Practices	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	Minimal n = 4 (20%)	n = 25 (> 20%)

Sample Composition Regarding Language Region												
Sample Sizes N = Full Sample n = Subsample	Internal Medicine (N = 20)		Cardiology (N = 20)		Nephrology (N = 20)		Gastroenterology (N = 20)		Gynecology (N = 20)		Oncology (N = 20)	
	German Speaking	French Speaking	German Speaking	French Speaking	German Speaking	French Speaking	German Speaking	French Speaking	German Speaking	French Speaking	German Speaking	French Speaking
Public and / or University Hospitals	n = 6-8	n = 4	n = 6-8	n = 4	n = 6-8	n = 4	n = 6-8	n = 4	n = 6-8	n = 4	n = 6-8	n = 4
Private Hospitals	n = 2-4	n = 2	n = 2-4	n = 2	n = 2-4	n = 2	n = 2-4	n = 2	n = 2-4	n = 2	n = 2-4	n = 2
Medical (Group) Practices	n = 3-5	n = 1	n = 3-5	n = 1	n = 3-5	n = 1	n = 3-5	n = 1	n = 3-5	n = 1	n = 3-5	n = 1
Total	n = 13	n = 7	n = 13	n = 7	n = 13	n = 7	n = 13	n = 7	n = 13	n = 7	n = 13	n = 7

Procedure for Panelists						
	Thematic Area					
	Cardiology	Nephrology	Gastroenterology	Gynaecology	Oncology	Internal Medicine
Questionnaire Part 1	General Part I	General Part I	General Part I	General Part I	General Part I	General Part I
Questionnaire Part 2	Cardiology Part	Nephrology Part	Gastroenterology Part	Gynaecology Part	Oncology Part	Internal Medicine Part
Questionnaire Part 2	General Part II	General Part II	General Part II	General Part II	General Part II	General Part II

Supplementary Table S2: Degree of agreement, critical agreement and disagreement regarding each statement.

A GENERAL PART I: DEFINITION AND CLINICAL RELEVANCE OF IRON DEFICIENCY	Top	Medium	Bottom	DK
	93 panelists			
Iron deficiency without anemia is characterized by normal hemoglobin (Hb) levels and abnormal values for one or several of the indicators of iron status (e.g., serum ferritin and transferrin saturation TSAT). [1-5]	98%	1%	1%	0%
Iron deficiency with anemia (subsequently referred to as iron deficiency anemia) is characterized by a defect in hemoglobin (Hb) synthesis which results in red blood cells that are usually microcytic (small mean corpuscular volume MCV) and contain a reduced amount of Hb (hypochromic).[6, 7]	100%	0%	0%	0%
Iron deficiency without anemia is a major public health problem.[8-15]	42%	20%	37%	1%
Iron deficiency (absolute and functional) without anemia is particularly frequent in women of childbearing age. [9-11]	94%	5%	0%	1%
Iron deficiency (absolute and functional) without anemia is frequent in:				
Children[14]	19%	18%	38%	25%
Adolescents[14]	40%	18%	26%	16%
Individuals with chronic diseases[16-19]	71%	16%	12%	1%
Iron deficiency without anemia has clinically relevant consequences in:				
Women of childbearing age (e.g., fatigue, reduction of birth weight, psychological health)[1, 2, 5, 20-25]	80%	10%	9%	2%
Children (e.g., fatigue, difficulties in concentration, muscle weakness)[14]	45%	14%	14%	27%
Adolescents (e.g., fatigue, difficulties in concentration, muscle weakness)[14]	58%	15%	12%	15%
Elderly (i.e., impairment of quality of life)[26]	65%	23%	12%	1%
Individuals with chronic diseases (i.e., impairment of quality of life)[16, 18, 19, 27]	70%	19%	9%	2%
Iron deficiency anemia is a widespread health problem.[28]	74%	16%	9%	1%
Iron deficiency anemia is particularly frequent in women of childbearing age and all other individuals with chronic blood loss.[8-11, 29]	99%	1%	0%	0%
Iron deficiency anemia is frequent in elderly.[26, 30, 31]	76%	17%	4%	2%
Iron deficiency anemia (absolute and functional) has clinically relevant consequences in:				
Women of childbearing age[28]	93%	7%	0%	1%
Children[28]	70%	9%	3%	18%
Elderly[26, 30, 31]	93%	4%	0%	3%
Individuals with chronic diseases[16, 19, 27]	93%	7%	0%	1%

GENERAL PART I: DIAGNOSIS OF IRON DEFICIENCY 1/4

Top	Medium	Bottom	DK
93 panelists			

A history of one or more of the following conditions (with increased probability of iron deficiency with or without anemia) indicates the need for iron status evaluation:

Chronic kidney disease (CKD)[32, 33]	95%	3%	2%	0%
Chronic heart failure (CHF)[34]	85%	8%	3%	4%
Malignant neoplasm (solid tumor or hematologic malignancy)[18, 27, 35-38]	88%	5%	4%	2%
Regular blood donation[39, 40]	73%	10%	15%	2%

A history of one or more of the following conditions (with increased probability of iron deficiency with or without anemia) may indicate the need for iron status evaluation:

Heavy uterine bleeding (e.g., hypermenorrhea, menorrhagia, metrorrhagia, and menometrorrhagia)[10, 41]	98%	2%	0%	0%
Pregnancy and postpartum[42]	89%	7%	2%	2%
Gastrointestinal diseases such as inflammatory bowel disease, chronic gastritis, gastric ulcer, duodenal ulcer, infection with H. pylori, coeliac disease, and tumors[19, 43]	99%	1%	0%	0%
Chronic autoimmune disease[44, 45]	81%	10%	4%	5%
Hemorrhage (traumatic, pathological [e.g., esophageal varices, hemorrhagic telangiectasia], or surgical)[46-48]	96%	1%	3%	0%

One or more of the following symptoms / syndromes are possibly associated with iron deficiency without anemia (and may indicate the need for iron status evaluation):

Fatigue[1, 2, 5, 20-25, 49]	96%	2%	1%	1%
Restless legs syndrome (RLS)[50]	67%	17%	9%	8%
Exercise intolerance[51, 52]	77%	12%	5%	5%
Cognitive problems[22, 49]	65%	18%	8%	10%
Alopecia[53]	81%	10%	4%	5%
Cold intolerance[54, 55]	52%	24%	12%	13%
Pica[56]	47%	18%	9%	26%
Infection(s)[57]	40%	26%	27%	8%

GENERAL PART I: DIAGNOSIS OF IRON DEFICIENCY 2/4

Top

Medium

Bottom

DK

93 panelists

In addition to the symptoms / syndromes listed in the previous statement 3, one or more of the following symptoms / syndromes, when considered in the broader clinical context, are possibly associated with iron deficiency anemia (indicating the need for iron status evaluation): General anemia symptoms:

Pale skin / mucosa[7, 55]	97%	1%	2%	0%
Fatigue[58]	98%	1%	1%	0%
Exercise intolerance[7, 55]	94%	3%	2%	1%
Dyspnea[7, 55]	91%	5%	3%	0%
Palpitations / Tachycardia[7, 55]	84%	9%	8%	0%
Headache[7, 55]	69%	19%	11%	1%
Symptoms specific to iron deficiency anemia:				
Koilonychia[55, 59]	75%	9%	4%	12%
Plummer-Vinson syndrome (PVS) (postcricoid membrane)	62%	10%	1%	27%
Non-specific symptoms that may indicate an iron deficiency anemia:				
Breaking nails[55]	80%	15%	3%	2%
Cheilosis[55, 60]	71%	11%	4%	14%
Atrophic glossitis[7, 55, 61, 62]	79%	10%	7%	5%
Statements with respect to the progression of iron deficiency anemia:				
Loss of tongue papillae is a good gauge of length or iron deficiency anemia.[62]	26%	22%	16%	37%
In severe cases of iron deficiency anemia:				
Atrophic glossitis is noted.[62]	68%	10%	9%	14%
Individuals might have dyspnoea at rest.[62]	81%	11%	8%	1%
Individuals might have angina pectoris.[62]	89%	7%	2%	2%
Individuals might have haemodynamic instability. [62]	66%	17%	12%	5%
In individuals presenting (i) one or more of the previously mentioned conditions and (ii) one or more of the above mentioned symptoms / syndromes, the following laboratory parameters should be measured in order to exclude or confirm the presence of iron deficiency with or without anemia:				
Ferritin combined with C-reactive protein (CRP) [1-3, 7, 49, 63]	88%	5%	5%	1%
Ferritin not necessarily combined with C-reactive protein (CRP)	22%	10%	68%	1%
Transferrin saturation (TSAT)[3, 7, 49]	75%	13%	11%	1%

GENERAL PART I: DIAGNOSIS OF IRON DEFICIENCY 3/4

Top	Medium	Bottom	DK
93 panelists			

In addition to these laboratory parameters, the following laboratory parameters could additionally be measured in order to exclude or confirm the presence of iron deficiency with or without anemia:

Hemoglobin (Hb)[1-3, 7, 49, 63]	97%	1%	2%	0%
Mean corpuscular volume (MCV)[3, 7, 49]	96%	1%	3%	0%
Mean corpuscular hemoglobin concentration (MCHC)[3, 7, 49, 63]	84%	5%	10%	1%

In individuals presenting potential symptoms of iron deficiency without anemia (e.g., fatigue, Restless legs syndrome RLS, exercise intolerance, cognitive problems, alopecia, cold intolerance, pica, and blue sclera), the presence of low ferritin (cf. statement below) is sufficient to confirm the diagnosis of iron deficiency without anemia.[1, 2, 5]	61%	12%	27%	0%
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To what extent do you agree/disagree with the following statements?

There is no generally accepted cut-off of ferritin to diagnose iron deficiency without anemia.[2, 3, 5, 12, 64, 65]	55%	14%	30%	1%
A value of ferritin 30 mcg/L can be considered as a cut-off to diagnose iron deficiency without anemia in the general population.[2, 3, 12]	72%	12%	15%	1%
With ferritin values of 30-50 mcg/L, TSAT should be measured to confirm the diagnosis of iron deficiency without anemia.[3, 20, 49]	68%	15%	14%	3%
With ferritin values of 30-50 mcg/L, a TSAT < 20% can confirm the diagnosis of iron deficiency without anemia.[3, 20, 49]	65%	18%	14%	3%
With ferritin values of 30-50 mcg/L, a TSAT < 20% can only confirm the diagnosis of iron deficiency without anemia if there is no inflammation and no metabolic disorder (e.g., diabetes).[66]	47%	16%	27%	10%

To what extent do you agree/disagree with the following statements?

In individuals showing hypochromic microcytic anemia (i.e., low Hb, low MCV, and low MCHC), the diagnosis of iron deficiency anemia may be considered.[3, 7]	100%	0%	0%	0%
In individuals showing hypochromic microcytic anemia (i.e., low Hb, low MCV, and low MCHC), the diagnosis of iron deficiency anemia can be definitely confirmed by low ferritin values.[3, 7]	83%	9%	8%	1%

GENERAL PART I: DIAGNOSIS OF IRON DEFICIENCY 4/4

Top	Medium	Bottom	DK
93 panelists			

To what extent do you agree/disagree with the following statements?

In individuals with chronic diseases, ferritin (being an acute phase protein) can be elevated. Therefore ferritin (without inflammatory markers) is not reliable as a marker of iron stores.[3]	87%	3%	10%	0%
In general, in individuals with recent infections, increased values of C-reactive protein can confirm the inflammatory state and consequently the lack of reliability of ferritin as marker of iron stores.[3]	94%	4%	1%	1%
In this situation (cf. previous statement), disease-specific guidelines have to be used in order to exclude or confirm the presence of iron deficiency with or without anemia.	75%	12%	8%	5%
If no disease-specific guidelines exist, low TSAT may indicate the need for iron therapy with equivocal ferritin levels.[19, 32, 34]	82%	5%	12%	1%
TSAT may misleadingly increase in the presence of inflammation as transferrin is a negative acute phase reactant.[67, 68]	54%	10%	14%	23%
If no disease-specific guidelines exist, measurement of additional parameters (such as serum transferrin receptor and ferritin index) may be necessary to optimally evaluate the need for iron therapy.[3]	66%	14%	5%	15%
If no disease-specific guidelines exist, a consultation with a physician experienced in the treatment of iron deficiency (e.g., a hematologist) is recommended to optimally evaluate the need for iron therapy.	74%	15%	10%	1%

To what extent do you agree/disagree with the following statements?

In individuals with liver diseases presenting increased levels of alanine aminotransferase (ALAT), ferritin can be elevated (and therefore, without inflammatory markers, is not reliable as a marker of iron stores).[3]	85%	2%	3%	10%
In this situation (cf. previous statement), ideally a consultation with a physician experienced in the treatment of iron deficiency (e.g., a hepatologist or a hematologist) would optimally evaluate the need for iron therapy.	73%	17%	9%	1%

GENERAL PART I: TREATMENT OF IRON DEFICIENCY 1/2	Top	Medium	Bottom	DK
	93 panelists			
Before initiation of iron therapy, the cause / causes of iron deficiency has / have to be elucidated.[1, 2, 5]	90%	4%	5%	0%
Iron therapy is usually indicated in all individuals with confirmed diagnosis of symptomatic iron deficiency without anemia.[1, 2, 5]	73%	10%	17%	0%
Oral iron therapy is usually the preferred therapy for individuals with confirmed diagnosis of symptomatic iron deficiency without anemia.[1, 2, 5]	63%	15%	20%	1%
Intravenous iron therapy is indicated in individuals with confirmed diagnosis of symptomatic iron deficiency without anemia if:				
Oral iron is not tolerated[69, 70]	96%	1%	3%	0%
Oral iron is not efficacious (i.e., the increase of ferritin and the improvement of symptoms are evaluated as insufficient by the treating physician)[69, 70]	95%	0%	5%	0%
Oral iron is not applicable because of risk of complications (e.g., in individuals with inflammatory bowel disease)[69, 70]	93%	4%	2%	1%
In cases of low adherence (i.e., an individual's behavior does not match agreed recommendations from the physician)[69-71]	66%	16%	18%	0%
A rapid replenishment of iron stores is desired (e.g., in the perioperative setting)[72]	90%	2%	7%	1%
Iron therapy is indicated in all individuals with confirmed diagnosis of:				
Symptomatic iron deficiency anemia[1, 62]	98%	1%	1%	0%
Asymptomatic iron deficiency anemia	70%	17%	13%	0%
With reference to the previous statements: No iron therapy is indicated in individuals with iron deficiency anemia in need of blood transfusion.	22%	15%	62%	1%
Oral iron therapy is usually the preferred therapy for individuals with confirmed diagnosis of:				
Symptomatic iron deficiency anemia[69, 70]	39%	18%	43%	0%
Asymptomatic iron deficiency anemia[69, 70]	67%	17%	16%	0%
Intravenous iron therapy is indicated in individuals with confirmed diagnosis of symptomatic iron deficiency anemia if:				
Oral iron is not tolerated.[69, 70]	99%	1%	0%	0%
Oral iron is not efficacious, that is, the therapeutic doses (recommended in the respective Summary of Product Characteristics SmPC) fail to produce an increase of Hb of (i) at least 0.1 g/dl/day or (ii) of at least 2-3 g/dl after 3 weeks (after exclusion of folate and B12 deficiency).[69, 70, 73-76]	87%	9%	3%	1%
Oral iron is not applicable because of risk of complications (e.g., in individuals with inflammatory bowel disease).[69, 70]	97%	1%	0%	2%
In cases of low adherence (i.e., an individual's behavior does not match agreed recommendations from the physician).[69-71]	74%	19%	7%	0%
A rapid increase in hemoglobin is needed (e.g., in late pregnancy, in presence of very low Hb values during pregnancy and postpartum, and in the perioperative setting).[42, 72]	95%	2%	1%	2%

GENERAL PART I: TREATMENT OF IRON DEFICIENCY 2/2

Top	Medium	Bottom	DK
93 panelists			

Intravenous iron therapy is indicated in individuals with confirmed diagnosis of asymptomatic iron deficiency anemia if:

Oral iron is not tolerated.[69, 70]	90%	5%	4%	0%
Oral iron is not efficacious, that is, the therapeutic doses (recommended in the respective Summary of Product Characteristics SmPC) fail to produce an increase of Hb of (i) at least 0.1 g/dl/day or (ii) of at least 2-3 g/dl after 3 weeks (after exclusion of folate and B12 deficiency).[69, 70, 73-76]	83%	13%	3%	1%
Oral iron is not applicable because of risk of complications (e.g., in individuals with inflammatory bowel disease).[69, 70]	91%	7%	2%	0%
In cases of low adherence (i.e., an individual's behavior does not match agreed recommendations from the physician).[69-71]	58%	25%	17%	0%
A rapid increase in hemoglobin is needed (e.g., in late pregnancy, in presence of very low Hb values during pregnancy and postpartum, and in the perioperative setting).[42, 72]	85%	9%	5%	1%

To what extent do you agree/disagree with the following statements?

During the first weeks following the intravenous iron administration, a transient but marked increase of ferritin without correlation with the amount of iron in the iron stores occurs.[1, 2, 5, 77]	85%	4%	2%	9%
A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[1-3, 5, 77]	77%	9%	7%	8%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[2, 5, 77]	89%	3%	4%	3%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78-80]	47%	15%	17%	20%
Oral and intravenous iron therapy should be performed according to the Summary of Product Characteristics (SmPC) of the respective iron preparation. In addition, specific evidence-based guidelines on iron therapy in particular populations should if possible be taken into consideration.	98%	0%	2%	0%

In the Swiss healthcare system, there is a risk of overtreatment of:

Iron deficiency without anemia	69%	4%	25%	2%
Symptomatic iron deficiency anemia	4%	12%	81%	3%
Asymptomatic iron deficiency anemia	24%	24%	50%	3%

In the Swiss healthcare system, there is a risk of undertreatment of:

Iron deficiency without anemia	37%	16%	45%	2%
Symptomatic iron deficiency anemia	43%	18%	37%	2%
Asymptomatic iron deficiency anemia	40%	26%	31%	3%

B SPECIFIC PART - CARDIOLOGY: CLINICAL RELEVANCE OF IRON DEFICIENCY IN CHRONIC HEART FAILURE (CHF)

Top	Medium	Bottom	DK
13 panelists			

To what extent do you agree/disagree with the following statements?

Iron deficiency without anemia is a common problem in individuals with chronic heart failure (CHF).[16, 34, 81]	85%	8%	8%	0%
Iron deficiency without anemia is a clinically relevant problem in individuals with chronic heart failure (CHF).[16, 34, 81]	92%	8%	0%	0%
Iron deficiency without anemia is associated with increased mortality.[16, 81]	77%	15%	0%	8%
Iron deficiency anemia is a common and clinically relevant problem in individuals with chronic heart failure (CHF).[16, 34, 81]	85%	15%	0%	0%

SPECIFIC PART - CARDIOLOGY: DIAGNOSIS OF IRON DEFICIENCY IN CHRONIC HEART FAILURE (CHF)

Top	Medium	Bottom	DK
13 panelists			

In all individuals with chronic heart failure (CHF), the following laboratory parameters have to be routinely measured in order to exclude or confirm the presence of iron deficiency with or without anemia:

Hemoglobin[34]	100%	0%	0%	0%
Ferritin[34]	100%	0%	0%	0%
C-reactive protein (CRP)[34]	92%	8%	0%	0%
Transferrin saturation (TSAT)[34]	85%	15%	0%	0%

Iron deficiency without anemia in individuals with chronic heart failure (CHF) is defined as:

Ferritin < 100 mcg/L[34]	92%	0%	0%	8%
Ferritin of 100-300 mcg/L and TSAT < 20%[34]	92%	0%	0%	8%
Statements a and b also apply if there is a metabolic disorder (e.g., diabetes)	62%	0%	23%	15%

To what extent do you agree/disagree with the following statements?

The general practitioner (GP) should be responsible for the evaluation of the iron status / the diagnosis of iron deficiency without anemia in individuals with CHF.	62%	15%	23%	0%
The GP should inform the respective cardiologist if iron deficiency without anemia is diagnosed in an individual with CHF.	92%	8%	0%	0%

Iron deficiency anemia in individuals with CHF showing no relevant comorbidities (e.g., renal insufficiency) is defined as:

Low hemoglobin (i.e., Hb levels < 120g/L for women and < 130g/L for men) and ferritin < 100 mcg/L[34]	77%	8%	8%	8%
Low hemoglobin (i.e., Hb levels < 120g/L for women and < 130g/L for men), ferritin of 100-300 mcg/L, and TSAT < 20%[34]	77%	0%	15%	8%

To what extent do you agree/disagree with the following statements?

The GP should be responsible for the evaluation of the iron status / the diagnosis of iron deficiency anemia in individuals with CHF.	69%	15%	15%	0%
The GP should inform the respective cardiologist if iron deficiency anemia is diagnosed in an individual with CHF.	92%	8%	0%	0%

SPECIFIC PART - CARDIOLOGY: TREATMENT OF IRON DEFICIENCY IN CHRONIC HEART FAILURE

(CHF) 1/2

Top	Medium	Bottom	DK
13 panelists			

To what extent do you agree/disagree with the following statements?

Treatment of iron deficiency without anemia in a stable and symptomatic individual with CHF and with NYHA (New York Heart Association) class II-IV should be performed by a GP, who coordinates the treatment with a cardiologist.	69%	31%	0%	0%
Treatment of iron deficiency without anemia in decompensated individuals with CHF is at the discretion of the cardiologist.	85%	15%	0%	0%
Treatment of iron deficiency without anemia in individuals with CHF with NYHA class IV is at the discretion of the cardiologist.	77%	8%	15%	0%

To what extent do you agree/disagree with the following statements?

Treatment of iron deficiency anemia in a stable individual with CHF with NYHA class I-III should be performed by a GP, who coordinates the treatment with a cardiologist.	85%	15%	0%	0%
Treatment of iron deficiency anemia in decompensated individuals with CHF is at the discretion of the cardiologist.	77%	15%	8%	0%
Treatment of iron deficiency anemia in individuals with CHF with NYHA class IV is at the discretion of the cardiologist.	77%	15%	8%	0%

To what extent do you agree/disagree with the following statements?

Oral iron may be insufficiently effective in replenishing iron stores in CHF.[82, 83]	85%	8%	8%	0%
Oral iron may be ineffective in improvement of physical performance in CHF.[82]	77%	15%	8%	0%
Oral iron is not recommended in the current ESC (European Society of Cardiology) Guidelines 2016.[34]	77%	8%	15%	0%

Individuals with CHF can benefit from intravenous iron substitution of ferric carboxymaltose (Ferinject®), independently of Hb status, if:

Ferritin < 100 mcg/L[34, 84]	100%	0%	0%	0%
Ferritin of 100-300 mcg/L and TSAT < 20%[34, 84, 85]	92%	0%	0%	8%

In individuals with CHF, intravenous iron therapy with ferric carboxymaltose (Ferinject®) is considered as the preferred treatment, independently of Hb status, if:

Ferritin < 100 mcg/L[34, 84, 85]	92%	0%	8%	0%
Ferritin of 100-300 mcg/L and TSAT < 20%[34, 84, 85]	85%	0%	8%	8%

SPECIFIC PART - CARDIOLOGY: TREATMENT OF IRON DEFICIENCY IN CHRONIC HEART FAILURE

(CHF) 2/2

Top	Medium	Bottom	DK
13 panelists			

Treatment of iron deficiency in individuals with CHF should be performed using the treatment scheme used in the randomized placebo controlled study CONFIRM-HF that showed statistically significant improvement of symptoms, exercise tolerance, and quality of life in individuals with CHF following intravenous iron therapy:[84, 86]

Dosing of ferric carboxymaltose (Ferinject®) according to CONFIRM-HF:	100%	0%	0%	0%
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To what extent do you agree/disagree with the following statements?

A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[1-3, 5]	92%	0%	0%	8%
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A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[2, 5, 77]	92%	0%	0%	8%
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There is no evidence-based recommendation regarding the diagnostic and therapeutic approaches following the completion of the treatment schemes tested in the study CONFIRM-HF. Therefore, one of the following options can be considered according to the judgment of the treating physician (i.e., presumably the GP) following a consultation with the treating cardiologist:

Evaluation of ferritin, CRP, and TSAT once a year.[86]	100%	0%	0%	0%
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Consideration relevant comorbidities (e.g., diabetes).[34]	92%	8%	0%	0%
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Resumption of the already applied treatment scheme according to the study CONFIRM-HF if ferritin < 100 mcg/L, as long as adverse effects are absent.[86]	92%	8%	0%	0%
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Resumption of the already applied treatment scheme according to the study CONFIRM-HF if ferritin 100-300 mcg/L and TSAT < 20%, as long as adverse effects are absent.[86]	100%	0%	0%	0%
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If iron therapy is repeated more than one time, the following measures can be considered in order to avoid iron overload and / or toxicity:

No iron administration is permitted if TSAT > 50%. [87]	77%	23%	0%	0%
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Vigilance regarding the occurrence of signs or symptoms of iron overload or iron toxicity.[69]	100%	0%	0%	0%
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Vigilance regarding the occurrence of adverse reactions listed in the SmPC of ferric carboxymaltose (Ferinject®), especially the frequent ones.[69]	100%	0%	0%	0%
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Cessation and re-evaluation of iron therapy in case of suspicion of signs or symptoms of iron overload or iron toxicity.[69]	100%	0%	0%	0%
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Cessation and re-evaluation of iron therapy in case of clinically relevant adverse reactions.[69]	100%	0%	0%	0%
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SPECIFIC PART - NEPHROLOGY: CLINICAL RELEVANCE OF IRON DEFICIENCY IN CHRONIC KIDNEY DISEASE (CKD)

Top	Medium	Bottom	DK
16 panelists			

To what extent do you agree/disagree with the following statements?

One of the most common complications of chronic kidney disease (CKD) is anemia.[88]	100%	0%	0%	0%
The consequences of anemia in individuals with CKD range from fatigue, associated with cognitive and even depressive disorders, to increased cardiovascular morbidity and mortality.[88]	100%	0%	0%	0%
At advanced stages, anemia may be a risk factor for the progression of chronic renal insufficiency.[88]	50%	6%	44%	0%
The frequency of anemia increases as kidney failure progresses.[88]	100%	0%	0%	0%
The severity of anemia increases as kidney failure progresses.[88]	100%	0%	0%	0%

To what extent do you agree/disagree with the following statements?

Iron deficiency anemia is a common and clinically relevant problem in individuals with CKD.[32]	94%	6%	0%	0%
The most commonly encountered reversible cause of chronic anemia or worsening anemia in individuals with CKD, other than anemia related directly to CKD, is iron deficiency anemia.[33]	88%	6%	6%	0%

To what extent do you agree/disagree with the following statements?

Iron deficiency can be a clinically relevant problem in individuals with CKD receiving erythropoiesis-stimulating agents (ESA).[32]	100%	0%	0%	0%
Iron deficiency is a main cause of unresponsiveness of individuals with CKD to ESA.[32]	100%	0%	0%	0%

C SPECIFIC PART - NEPHROLOGY: DIAGNOSIS OF IRON DEFICIENCY IN CHRONIC KIDNEY DISEASE (CKD)

Top	Medium	Bottom	DK
16 panelists			

In all individuals with CKD, the following parameters should be routinely measured:

Hemoglobin (Hb)[32]	100%	0%	0%	0%
Ferritin[32]	100%	0%	0%	0%
Transferrin saturation (TSAT)[32]	88%	6%	6%	0%

The diagnosis of anemia can be made in individuals with CKD when:

Hb concentrations are < 13.5 g/dL in adult males[32]	81%	0%	19%	0%
Hb concentrations are < 13.2 g/dL in adult males > 70 years[32]	75%	6%	19%	0%
Hb concentrations are < 12.0 g/dL in adult females of all ages[32]	88%	0%	13%	0%

With reference to statement 2 above: Further evaluation should be undertaken in individuals with CKD when:

Hb concentrations are < 11 g/dL in adult males[32]	100%	0%	0%	0%
Hb concentrations are < 11 g/dL in adult males > 70 years[32]	100%	0%	0%	0%
Hb concentrations are < 11 g/dL in adult females of all ages[32]	94%	6%	0%	0%

Iron deficiency can be considered if TSAT < 25% and serum ferritin < 200 mcg/L.[32]

69%	13%	19%	0%
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SPECIFIC PART - NEPHROLOGY: TREATMENT OF IRON DEFICIENCY IN CHRONIC KIDNEY DISEASE (CKD) 1/2	Top	Medium	Bottom	DK
	16 panelists			
The diagnosis of iron deficiency in individuals with CKD should be coordinated with the nephrologist.[88]	81%	19%	0%	0%
To what extent do you agree/disagree with the following statements?				
Treatment of iron deficiency in predialysis should be performed by a GP, who coordinates the treatment with a nephrologist.	81%	13%	6%	0%
Treatment of iron deficiency in dialysis should be performed by a nephrologist.	100%	0%	0%	0%
The treatment of iron deficiency in individuals with CKD is basically focusing on treatment of renal anemia, which also includes the potential need for ESA in advanced CKD.	94%	0%	6%	0%
There is no generally accepted consensus on treatment of iron deficiency without anemia in nephrology.	81%	6%	13%	0%
For adult individuals with CKD (usually ≥ stage 3b) with anemia not on iron or ESA therapy, a trial with iron therapy (either intravenous or, when tolerated, orally as a first-step in predialysis) is suggested if there is:				
An iron deficiency (TSAT < 25% and / or serum ferritin < 200 mcg/L).[32]	88%	0%	13%	0%
An (i) increase in Hb concentration without starting ESA treatment is desired and (ii) TSAT is < 25% and / or ferritin is < 200 mcg/L.[32]	94%	0%	6%	0%
Following iron treatment:				
The limit of TSAT of 45% should not be exceeded.[87]	81%	0%	13%	6%
The limit of serum ferritin of 500 mcg/L should not be exceeded.[32]	56%	13%	31%	0%
The choice of oral or intravenous iron in individuals with CKD depends on:				
Individual physician preference[89]	44%	25%	31%	0%
The facilities that are available[89]	38%	13%	50%	0%
The market approval (and specified indications) of an iron therapy[69, 70]	69%	0%	25%	6%

SPECIFIC PART - NEPHROLOGY: TREATMENT OF IRON DEFICIENCY IN CHRONIC KIDNEY DISEASE

(CKD) 2/2

Top	Medium	Bottom	DK
16 panelists			

Relevant considerations regarding oral or intravenous iron therapy in individuals with CKD:

Oral iron is simple and cheap to administer and does not require hospital visits.[89]	94%	0%	6%	0%
Oral iron is poorly absorbed in advanced CKD.[89]	100%	0%	0%	0%
Oral iron is associated with unpleasant gastrointestinal side effects.[89]	94%	6%	0%	0%
Intravenous iron requires specialist clinic services.[89]	63%	0%	38%	0%
Intravenous iron guarantees iron bioavailability and avoids problems of variable absorption of iron from the gastrointestinal tract.[89]	100%	0%	0%	0%
Intravenous iron is associated with hypersensitivity reactions, albeit very rarely.[89]	100%	0%	0%	0%
The efficacy of intravenous iron in improving Hb, ferritin, and TSAT in individuals with CKD is well established and superior to oral iron.[89]	88%	6%	0%	6%
The long-term safety of administering intravenous iron has not been established and there are theoretical concerns that individuals may be exposed to increased oxidative stress and exacerbation of infections.[89]	75%	13%	13%	0%
Intravenous iron can be considered as the preferred choice in anemic individuals with CKD (Hb < 11 g/dL in adult males and females) with iron deficiency (AID) (TSAT < 25% and serum ferritin < 200 mcg/L).[89]	88%	6%	6%	0%
A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[1-3, 5]	88%	0%	6%	6%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[2, 5, 77]	88%	0%	13%	0%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78-80]	69%	19%	6%	6%

D SPECIFIC PART - GASTROENTEROLOGY: CLINICAL RELEVANCE OF IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE (IBD)

Top	Medium	Bottom	DK
14 panelists			

Anemia is the most common systemic complication of inflammatory bowel disease (IBD).[19, 90, 91]	93%	7%	0%	0%
The impact of anemia on the quality of life of individuals with IBD is substantial. It affects various aspects of quality of life, such as:				
Physical functions[19, 92]	86%	7%	0%	7%
Emotional Functions[19, 92]	93%	0%	7%	0%
Cognitive functions[19, 92]	71%	21%	7%	0%
The ability to work[19, 92]	86%	7%	7%	0%
Hospitalization[19, 92]	64%	7%	29%	0%
Healthcare costs[19, 92]	79%	0%	21%	0%
IBD-associated anemia can be multifactorial, that is, a combination of (i) blood loss, (ii) chronic iron deficiency, and (iii) anemia of chronic disease (ACD).[19]	100%	0%	0%	0%

SPECIFIC PART - GASTROENTEROLOGY: DIAGNOSIS OF IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE (IBD)

	Top	Medium	Bottom	DK
	14 panelists			
The currently used WHO definition of anemia (Hb < 13 g/dL in adult males and < 12.0 g/dL in non-pregnant adult females) applies also to individuals with IBD.[19]	86%	14%	0%	0%
All individuals with IBD should be assessed for the presence of anemia.[19]	100%	0%	0%	0%
Diagnostic criteria for iron deficiency depend on the level of inflammation.[19]	86%	14%	0%	0%
In individuals without clinical, endoscopic, or biochemical evidence of active disease (i.e., no presence of inflammation), serum ferritin < 30 mcg/L is an appropriate criterion for iron deficiency.[19]	93%	7%	0%	0%
In the presence of inflammation, a serum ferritin up to 100 mcg/L may still be consistent with iron deficiency.[19]	100%	0%	0%	0%
With ferritin values of 30-50 mcg/L, a TSAT < 20% can confirm the diagnosis of iron deficiency.[3, 19, 20, 49]	79%	21%	0%	0%

SPECIFIC PART - GASTROENTEROLOGY: TREATMENT OF IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE (IBD) 1/2

Top	Medium	Bottom	DK
14 panelists			

Treatment of iron deficiency anemia in IBD is performed by the treating gastroenterologist.	50%	43%	7%	0%
Treatment of iron deficiency anemia in IBD is performed by the general practitioner (GP), who coordinates the treatment with the gastroenterologist.	50%	29%	21%	0%
Iron supplementation can be considered in individuals with IBD when iron deficiency without anemia is present.[93, 94]	86%	7%	7%	0%
Iron supplementation is indicated in all individuals with IBD when iron deficiency anemia is present.[19]	79%	0%	21%	0%
The goal of iron supplementation is to normalize hemoglobin levels and iron stores.[19]	79%	14%	7%	0%
The goal of early iron treatment is to maintain Hb and serum ferritin levels within the normal range.[19]	79%	14%	7%	0%
The estimation of iron need is usually based on baseline Hb and body weight.[19]	79%	14%	7%	0%
The estimation of iron need based on baseline Hb and body weight is more effective for the treatment of iron deficiency anemia in individuals with IBD than individualized dosing based on the traditional Ganzoni's formula (i.e., the approved formula to calculate total iron dose according to the SmPCs of the intravenous iron preparations approved in Switzerland).[19, 69, 70]	64%	14%	14%	7%
Please indicate your level of agreement with the following table summarizing the estimation of iron need (total iron dose in form of ferric carboxymaltose (Ferinject®)).[19]	71%	14%	14%	0%
Oral iron may be used in individuals with IBD and mild anemia under the following circumstances:				
Disease is clinically inactive[19]	50%	7%	43%	0%
No previous intolerance to oral iron[19]	50%	7%	43%	0%
No more than 100 mg elemental iron per day is taken[19]	36%	29%	36%	0%
Intravenous iron should be considered as the preferred treatment in individuals with IBD under the following circumstances:				
Clinically active IBD[19]	93%	7%	0%	0%
Previous intolerance to oral iron[19]	100%	0%	0%	0%
Hb < 10 g/dL[19]	93%	7%	0%	0%
Individuals who need erythropoiesis-stimulating agents (ESA)[19]	79%	14%	7%	0%
A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[2, 5, 77]	86%	7%	7%	0%

SPECIFIC PART - GASTROENTEROLOGY: TREATMENT OF IRON DEFICIENCY IN INFLAMMATORY BOWEL DISEASE (IBD) 2/2

Top	Medium	Bottom	DK
14 panelists			

A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[2, 5, 77]	100%	0%	0%	0%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78-80]	43%	36%	14%	7%
Individuals with IBD should be monitored for recurrent iron deficiency every 3 months for at least a year after correction, and between 6 and 12 months thereafter.[19]	79%	21%	0%	0%
IBD-associated iron deficiency and anemia recur frequently and fast, even after treatment with intravenous iron.[19]	71%	14%	14%	0%
Excluding HFE mutations (i.e., mutations of the HFE protein) and other iron loading mutations.[95]	21%	14%	57%	7%
No iron administration is permitted if TSAT > 50%.[87]	50%	29%	14%	7%
Hematological consultation once a year or every second year.	21%	36%	43%	0%
Vigilance regarding the occurrence of signs or symptoms of iron overload or iron toxicity.[69]	64%	36%	0%	0%
Vigilance regarding the occurrence of adverse reactions listed in the SmPC of the respective iron preparation (especially the frequent ones).[69]	79%	21%	0%	0%
Cessation and re-evaluation of iron therapy in case of suspicion of signs or symptoms of iron overload or iron toxicity.[69]	93%	7%	0%	0%
Cessation and re-evaluation of iron therapy in case of clinically relevant adverse reactions.[69]	93%	7%	0%	0%

E SPECIFIC PART - GYNECOLOGY: IRON STATUS AND IRON DEFICIENCY IN WOMEN IN
 CHILDBEARING AGE (EXCLUDING PREGNANCY AND POSTPARTUM) 1/2

Top	Medium	Bottom	DK
13 panelists			

Iron deficiency without anemia is particularly frequent and has clinically relevant consequences in women of childbearing age.[8-11, 29]	92%	8%	0%	0%
Iron deficiency anemia is particularly frequent and has clinically relevant consequences in women of childbearing age.[8-11, 29]	85%	8%	8%	0%
Iron-deficient women in childbearing age show:				
Poorer cognition[22]	39%	39%	15%	8%
Poorer mental health[22]	54%	23%	15%	8%
Increased fatigue[22, 52]	92%	8%	0%	0%
Following oral or intravenous iron therapy / supplementation, iron-deficient women in childbearing age show improvement in:				
Iron parameters[22, 52]	100%	0%	0%	0%
Cognition / cognitive function[22, 52]	77%	15%	0%	8%
Fatigue[22, 52]	92%	0%	0%	8%
Mental quality of life[22, 52]	85%	8%	0%	8%
Physical performance[22, 52]	92%	8%	0%	0%
Iron deficiency without anemia is diagnosed in presence of low ferritin levels.[1-3, 12]	85%	8%	8%	0%
A value of ferritin < 30 mcg/L can be considered as a cut-off to diagnose iron deficiency without anemia in the general population.[2, 3, 5, 12, 64, 96]	77%	8%	15%	0%
With ferritin values of 30-50 mcg/L, TSAT should be measured to confirm the diagnosis of iron deficiency without anemia.[3, 20, 49]	46%	15%	31%	8%
With ferritin values between 30 and 50 mcg/L, a TSAT < 20% can confirm the diagnosis of iron deficiency without anemia.[3, 20, 49]	69%	0%	23%	8%
Iron deficiency anemia is defined as Hb < 11 g/dL and ferritin levels < 30 mcg/L.[2, 3, 5, 12, 64, 96]	77%	15%	8%	0%
Iron therapy in non-pregnant women of childbearing age is performed by the general practitioner (GP).	31%	62%	8%	0%
Iron therapy is in non-pregnant women of childbearing age indicated in all symptomatic individuals with confirmed diagnosis of iron deficiency without anemia.[2, 5, 20, 24, 25, 49]	77%	8%	15%	0%
Oral iron therapy in non-pregnant women of childbearing age is the preferred therapy for individuals with confirmed diagnosis of symptomatic iron deficiency without anemia.[1, 2, 20, 24, 25, 49]	92%	8%	0%	0%

SPECIFIC PART - GYNECOLOGY: IRON STATUS AND IRON DEFICIENCY IN WOMEN IN CHILDBEARING AGE (EXCLUDING PREGNANCY AND POSTPARTUM) 2/2

Top	Medium	Bottom	DK
13 panelists			

Intravenous iron therapy in non-pregnant women of childbearing age is indicated in individuals with confirmed diagnosis of symptomatic iron deficiency without anemia if:				
Oral iron is not tolerated.[69, 70]	100%	0%	0%	0%
Oral iron is not efficacious (i.e., the increase of ferritin and the improvement of symptoms are evaluated as insufficient by the treating physician).[69, 70]	85%	8%	8%	0%
Oral iron is not applicable because of risk of complications (e.g., in individuals with inflammatory bowel disease IBD).[69, 70]	100%	0%	0%	0%
In cases of low adherence (i.e., an individual's behavior does not match agreed recommendations from the physician).[69-71]	62%	8%	31%	0%
Ferritin ≤ 30 mcg/L.	39%	15%	46%	0%
Iron therapy in non-pregnant women of childbearing age is indicated in all individuals with confirmed diagnosis of iron deficiency anemia.[2, 5]	85%	0%	15%	0%
Oral iron therapy in non-pregnant women of childbearing age is the preferred therapy for individuals with confirmed diagnosis of iron deficiency anemia.[1, 2, 5]	69%	15%	15%	0%
Intravenous iron therapy is indicated in individuals with confirmed diagnosis of iron deficiency anemia if:				
Oral iron is not tolerated.[69]	100%	0%	0%	0%
Oral iron may not be efficacious, that is, the therapeutic doses (recommended in the respective Summary of Product Characteristics SmPC) fail to produce an increase of Hb of (i) at least 0.1 g/dl/day or (ii) of at least 2-3 g/dl after 3 weeks (after exclusion of folate and B12 deficiency).[73-76]	92%	8%	0%	0%
Oral iron is not applicable because of risk of complications (e.g., in individuals with inflammatory bowel disease IBD).[69, 70]	100%	0%	0%	0%
In cases of low adherence (i.e., an individual's behavior does not match agreed recommendations from the physician).[69, 70]	77%	15%	8%	0%
A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[2, 3, 5, 77]	77%	8%	8%	8%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[2, 5, 77]	92%	0%	0%	8%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78, 79]	31%	8%	31%	31%
Oral and intravenous iron therapy should be performed according to the SmPC of the respective iron preparation.	100%	0%	0%	0%
Oral and intravenous iron therapy should be performed according to the Summary of Product Characteristics (SmPC) of the respective iron preparation that also includes, if existent, specific evidence-based guidelines on iron therapy in particular populations.	100%	0%	0%	0%

SPECIFIC PART - GYNECOLOGY: IRON DEFICIENCY IN WOMEN IN CHILDBEARING AGE DURING PREGNANCY AND POSTPARTUM 1/5	Top	Medium	Bottom	DK
	13 panelists			
Anemia is one of the most common problems in obstetrics.[42]	69%	15%	15%	0%
Anemia is a major risk factor in maternal morbidity.[42]	69%	23%	8%	0%
Anemia is a major risk factor in fetal morbidity.[42]	62%	23%	15%	0%
The maternal risks of anemia include:				
Increased risk of foreign blood transfusion in case of a greater blood loss[42]	85%	15%	0%	0%
Cardiovascular load[42]	92%	0%	8%	0%
Anemia symptoms (i.e., fatigue, reduced physical and mental performance, headache, orthostatic dizziness, exhaustion, etc.)[42]	100%	0%	0%	0%
Increased duration of hospitalization[42]	85%	8%	8%	0%
Reduced milk production after birth[42]	69%	31%	0%	0%
Reduced maternal iron storage during the postpartum period and later[42]	77%	23%	0%	0%
The fetal risks of anemia include:				
Increased preterm birth rate[42]	77%	15%	0%	8%
Intrauterine growth retardation[42]	77%	23%	0%	0%
Disturbance of placenta development[42]	54%	15%	15%	15%
Decreased neonatal iron stores in case of iron deficiency anemia of the mother[42]	62%	15%	8%	15%
Iron deficiency is a frequent cause of anemia during pregnancy.[42]	100%	0%	0%	0%
Iron deficiency can affect more than one third of pregnant women during the first half of pregnancy.[42]	62%	15%	8%	15%
Anemia is defined as:				
Hb < 11 g/dL in the first trimester[42]	92%	8%	0%	0%
Hb < 10.5 g/dL in the second trimester[42]	85%	15%	0%	0%
Hb < 11 g/dL in the last trimester[42]	85%	8%	8%	0%
At ferritin < 30 mcg/L, there is a 90% probability of empty iron stores[42]	77%	0%	8%	15%
Iron deficiency without anemia is diagnosed if ferritin < 30 mcg/L.[42]	85%	0%	15%	0%

SPECIFIC PART - GYNECOLOGY: IRON DEFICIENCY IN WOMEN IN CHILDBEARING AGE DURING PREGNANCY AND POSTPARTUM 2/5

Top	Medium	Bottom	DK
13 panelists			

Iron deficiency anemia can be considered as proven if (i) Hb is under the cut-off (of the respective trimester) and (ii) ferritin < 30 mcg/L. [42]	92%	8%	0%	0%
Iron deficiency anemia is proven if (i) Hb is under the cut-off (of the respective trimester) and (ii) ferritin < 15 mcg/L.[42]	77%	8%	15%	0%
Treatment of iron deficiency in pregnancy should be performed by the treating gynecologist.[42]	77%	8%	15%	0%
Treatment of iron deficiency in pregnancy can be performed by the general practitioner (GP), who coordinates the treatment with the treating gynecologist.	100%	0%	0%	0%
In the first trimester:				
Iron deficiency without anemia (ferritin < 30 mcg/L and Hb normal) should be treated with oral iron therapy at (160-200 mg/day).[42]	100%	0%	0%	0%
Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0 - 10.5 g/dL) should be treated with oral iron therapy at (160-200 mg/day).[42]	85%	0%	15%	0%
Intravenous iron therapy is contraindicated.	39%	0%	62%	0%
In the second trimester, intravenous iron therapy indicated in the following cases:				
Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0-10.5 g / dL) and missing response to oral iron (Hb increase by less than 1 g/dL within 14 days)[42]	92%	0%	8%	0%
Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0-10.5 g / dL) and lack of adherence to oral iron (i.e., an individual's behavior does not match agreed recommendations from the physician)[42]	85%	8%	8%	0%
Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0-10.5 g / dL) and intolerance to oral iron (gastrointestinal side effects)[42]	92%	8%	0%	0%
Severe or advanced anemia (ferritin < 30 mcg/L and <Hb 9.0 g/dL)[42]	100%	0%	0%	0%
In the second trimester, desire for rapid intravenous iron therapy is indicated in the following cases:				
Advanced gestational age[42]	54%	15%	31%	0%
Witness of Jehovah[42]	54%	8%	39%	0%

SPECIFIC PART - GYNECOLOGY: IRON DEFICIENCY IN WOMEN IN CHILDBEARING AGE DURING PREGNANCY AND POSTPARTUM 3/5

Top	Medium	Bottom	DK
13 panelists			

In the third trimester, intravenous iron therapy is indicated in the following cases:

Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0-10.5 g / dL) and missing response to oral iron (Hb increase by less than 1 g/dL within 14 days)[42]	77%	15%	8%	0%
Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0-10.5 g / dL) and lack of adherence to oral iron (i.e., an individual's behavior does not match agreed recommendations from the physician)[42]	85%	8%	8%	0%
Mild iron deficiency anemia (ferritin < 30 mcg/L and Hb 9.0-10.5 g / dL) and intolerance to oral iron (gastrointestinal side effects)[42]	100%	0%	0%	0%
Severe or advanced anemia (ferritin < 30 mcg/L and <Hb 9.0 g/dL)[42]	100%	0%	0%	0%

In the third trimester, desire for rapid intravenous iron therapy may be considered in the following cases:

Advanced gestational age[42]	85%	8%	8%	0%
Witness of Jehovah [42]	77%	0%	23%	0%
Increased risk for postpartum hemorrhage (PPH)[42]	62%	8%	31%	0%

The following treatment with ferric carboxymaltose (Ferinject®) is indicated:[69]

Total dose [mg] = body weight* [kg] × (target Hb** - Hb) [g/dL] × 2.4 + storage iron*** [mg] *To calculate the amount of iron needed, the body weight before the beginning of pregnancy should be used **Target Hb = 15 g/dL, ***storage iron = 500 mg	46%	15%	23%	15%
The total dose is administered in individual doses of max. 1000 mg (not exceeding 20 mg/kg) once per week[69]	85%	0%	15%	0%
The goal of intravenous iron therapy during pregnancy is to achieve an Hb > 10.5 g/dL.[42]	77%	15%	8%	0%
A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[2, 3, 5, 77]	77%	8%	15%	0%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[2, 5, 77]	92%	0%	0%	8%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78-80]	39%	8%	31%	23%
Postpartum anemia is defined as Hb < 12 g/dL (and is clinically significant if Hb < 10 g/dL).[42]	85%	15%	0%	0%
Postpartum anemia is a combination of bleeding anemia and pre-existing iron deficiency without anemia.[42]	54%	23%	23%	0%

SPECIFIC PART - GYNECOLOGY: IRON DEFICIENCY IN WOMEN IN CHILDBEARING AGE DURING PREGNANCY AND POSTPARTUM 4/5	Top	Medium	Bottom	DK
	13 panelists			
The decision about Hb control in postpartum will depend on:				
The blood loss[42]	77%	0%	23%	0%
The clinical condition of the pregnant woman (i.e., anemia symptoms)[42]	77%	8%	15%	0%
The prepartal Hb[42]	62%	8%	31%	0%
The nadir of the Hb in postpartum is reached after approximately 48 hours after delivery.[42]				
	77%	8%	8%	8%
Please indicate the level of agreement with the following statements regarding the evaluation of iron stores using ferritin in postpartum:				
Serum ferritin value is expected to be falsely elevated within the first 6 weeks after delivery.[42]	62%	8%	15%	15%
The ferritin can be measured before delivery or starting at a time point of about 6 weeks after delivery.[42]	77%	0%	8%	15%
The determination of ferritin (in addition to Hb) in postpartum makes no sense within the first 6 weeks after delivery.[42]	85%	15%	0%	0%
In the case of combined pre- and postpartum anemia, the iron stores can be considered as empty.[42]	69%	15%	15%	0%
The determination of ferritin is unnecessary in the case of combined pre- and postpartum anemia.[42]	54%	15%	31%	0%
Stationary treatment of iron deficiency in postpartum is performed by the respective obstetrician.[42]				
	92%	8%	0%	0%
Ambulatory treatment of iron deficiency is performed by the treating gynecologist.				
	92%	8%	0%	0%
Ambulatory treatment of iron deficiency is performed by the GP, who coordinates the treatment with the gynecologist.				
	77%	8%	15%	0%
In case of Hb 9.5-12 g/dL, an oral iron therapy (iron-II salts or iron-III-polymaltose) using daily doses of 80 - 200 mg is indicated.[42]				
	85%	8%	8%	0%
An intravenous iron therapy is a good alternative to an oral therapy in case of:				
Poor (gastrointestinal) tolerability of oral iron therapy[42]	85%	8%	8%	0%
Hb of 7.0 - 9.5 g/dL[42]	85%	0%	15%	0%
The following treatment with ferric carboxymaltose (Ferinject®) is indicated:[69]				
Total dose [mg] = body weight* [kg] × (target Hb** - Hb) [g/dL] × 2.4 + storage iron [mg] *To calculate the amount of iron needed, the body weight before the beginning of pregnancy should be used **Target Hb = 15 g/dL, storage iron = 500 mg	54%	8%	15%	23%
The total dose is administered in individual doses of max. 1000 mg (not exceeding 20 mg/kg) once per week[69]				
	85%	8%	0%	8%
The goal of intravenous iron therapy postpartum is to achieve an Hb > 11 g/dL.				
	62%	15%	15%	8%

SPECIFIC PART - GYNECOLOGY: IRON DEFICIENCY IN WOMEN IN CHILDBEARING AGE DURING PREGNANCY AND POSTPARTUM 5/5

Top	Medium	Bottom	DK
13 panelists			

A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[2, 3, 5, 77]	85%	0%	15%	0%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[1, 2, 5, 77]	92%	0%	0%	8%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78-80]	46%	0%	31%	23%

F SPECIFIC PART - ONCOLOGY: CLINICAL RELEVANCE OF IRON DEFICIENCY IN INDIVIDUALS WITH CANCER

	Top	Medium	Bottom	DK
	19 panelists			
There is a very high prevalence of iron deficiency (functional and absolute) in individuals with cancer[18, 27]	68%	26%	5%	0%
Anemia is frequent in the situation of absolute iron deficiency (AID).[27, 36]	79%	16%	5%	0%
Anemia is associated with a poor performance status and higher mortality in individuals with cancer.[27, 37]	79%	16%	5%	0%
A causal relationship between anemia and mortality has not been established.[27]	32%	21%	37%	11%
A causal relationship between anemia and quality of life has been established.[27, 35, 38]	90%	11%	0%	0%
In individuals with cancer, there is a association between Hb levels and:				
Physical fitness[27]	95%	5%	0%	0%
Quality of life[27, 35, 38]	90%	11%	0%	0%
In individuals with cancer, the following erythropoietin-associated disorders may contribute do development of anemia:				
Blunt endogenous erythropoietin production in the kidney[97]	74%	5%	16%	5%
Reduced sensitivity to erythropoietin[97]	79%	0%	5%	16%

SPECIFIC PART - ONCOLOGY: DIAGNOSIS OF IRON DEFICIENCY IN INDIVIDUALS WITH CANCER

Top	Medium	Bottom	DK
19 panelists			

In individuals with cancer, markers of iron metabolism can be influenced by the tumor independent of the iron stores.[98-103]	100%	0%	0%	0%
In individuals with cancer, measurement of baseline ferritin and TSAT can be taken into consideration.[27]	74%	5%	16%	5%
In individuals with cancer:				
Ferritin may be elevated and is therefore not reliable as a marker of iron stores.[98, 104]	95%	0%	5%	0%
The elevation of ferritin is associated with the tumor load (and the resulting inflammatory stage).[98, 104]	68%	26%	0%	5%
In individuals with cancer, absolute iron deficiency (AID) is defined by a TSAT < 50% and a serum ferritin level < 100 mcg/L.[27]	32%	16%	47%	5%
In individuals with cancer, functional iron deficiency (FID) is defined by a TSAT < 50% and a serum ferritin level > 100 but < 500 mcg/L.[27]	37%	16%	42%	5%
Optionally, the following parameters can be determined in individuals with cancer:				
Percentage of hypochromic red cells (%HYPO)[27]	68%	11%	5%	16%
Hb content of reticulocytes (CHr)[27]	58%	11%	11%	21%
Soluble transferrin receptor (sTfR)[27]	84%	5%	5%	5%
Ferritin index (sTfR/log ferritin)[27]	68%	11%	5%	16%

SPECIFIC PART - ONCOLOGY: TREATMENT OF IRON DEFICIENCY IN INDIVIDUALS WITH CANCER 1/3

	Top	Medium	Bottom	DK
	19 panelists			
Treatment of iron deficiency in individuals with oncologic diseases can be performed by all treating physicians (e.g., general practitioner, oncologist, and surgeon).	68%	11%	21%	0%
Treatment of iron deficiency in individuals with oncologic diseases should be coordinated with all treating physicians (but especially with the oncologist).	84%	11%	5%	0%
Oral iron is a valuable option for non-cancer individuals with absolute iron deficiency (AID) (i) without inflammation, (ii) with only few symptoms, and (iii) without an urgent need for anemia correction.[27]	74%	5%	21%	0%
Oral iron is a valuable option for individuals with cancer in complete or very good remission with absolute iron deficiency (AID) (i) without inflammation, (ii) with only few symptoms, and (iii) without an urgent need for anemia correction.[27]	63%	11%	26%	0%
In individuals with active cancer who are symptomatic due to functional iron deficiency (FID) (e.g., pallor, cold skin, weakness and fatigue, reduced physical fitness, brittle nails, angular cheilosis, impairment of cognitive functions, headaches, insomnia, restless legs syndrome, depression), treatment with intravenous iron is indicated (as correction is done faster).[27]	90%	5%	5%	0%
Functional iron deficiency (FID) should be corrected by intravenous iron if:				
Individuals are symptomatic because of iron deficiency and / or of anemia.[27]	68%	5%	26%	0%
Individuals are scheduled for erythropoiesis-stimulating therapy.[27]	90%	0%	5%	5%
In individuals with cancer scheduled for erythropoiesis-stimulating agents (ESA) therapy and who are symptomatic due to anemia and / or iron deficiency (TSAT < 50%), concomitant treatment with intravenous iron is indicated.[27]	84%	0%	11%	5%
Patients with anemia may be treated with red blood cell transfusion (1ml erythrocytes = 1mg iron), erythropoietin (with or without iron), and / or with iron administration only. [27, 35]	63%	11%	26%	0%
Intravenous iron therapy can be started in individuals (not scheduled for blood transfusion) with absolute iron deficiency (AID) independent of the actual Hb level.[27]	42%	26%	32%	0%
Starting intravenous iron therapy in individuals with absolute iron deficiency (AID) independent of the actual Hb level is particularly important in individuals with cancer scheduled for surgery with a bleeding risk, where iron deficiency should be corrected whenever possible before the planned intervention.[27]	68%	11%	21%	0%
In individuals with high ferritin levels (> 500 but < 800 mcg/L), iron supplementation should be based on individual decisions.[27]	58%	26%	16%	0%
Intravenous iron supplementation should be withheld in those with ferritin levels > 800 mcg/L.[27]	74%	26%	0%	0%

SPECIFIC PART - ONCOLOGY: TREATMENT OF IRON DEFICIENCY IN INDIVIDUALS WITH CANCER 2/3

Top	Medium	Bottom	DK
19 panelists			

In individuals with cancer of higher age:

The risk for clinical sequelae of iron deficiency may be increased.[27]	90%	5%	0%	5%
The risk for symptoms (e.g., weakness, fatigue, and impaired physical fitness and wellbeing) due to absolute iron deficiency (AID), functional iron deficiency (FID), and anemia may be increased.[27]	95%	0%	0%	5%
Iron deficiency should be corrected in all individuals symptomatic of iron deficiency.[27]	74%	11%	16%	0%
Iron therapy in symptomatic individuals with proven iron deficiency should be initiated without delay / as soon as possible (provided the reason for iron deficiency is known).[27]	84%	11%	5%	0%

In individuals with cancer with coexistent comorbidities:

The risk for clinical sequelae / secondary diseases is increased.[27]	90%	5%	0%	5%
The risk for symptoms due to absolute iron deficiency (AID), functional iron deficiency (FID), and anemia is increased.[27]	90%	5%	0%	5%
Iron deficiency should be corrected in all individuals symptomatic of iron deficiency.[27]	84%	11%	5%	0%
Iron therapy should be initiated without delay / as soon as possible (provided the reason for iron deficiency is known).[27]	74%	21%	5%	0%

If iron deficiency and anemia do not impair the individual's quality of life and do not cause any untoward symptoms, therapy of functional iron deficiency (FID) can be withheld, provided the individual is monitored carefully in order to start therapy if symptoms or anemia occur.[27]	74%	11%	16%	0%
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Statements regarding ferric carboxymaltose (Ferinject®):

Ferric carboxymaltose (Ferinject®) binds iron tightly to its carbohydrate shell.[27]	63%	0%	0%	37%
Ferric carboxymaltose (Ferinject®) is not associated with relevant release of free iron and production of potentially toxic free oxygen species, because iron is tightly bound to its carbohydrate shell.[27]	42%	11%	5%	42%
Ferric carboxymaltose (Ferinject®), due to binding iron tightly to its carbohydrate shell, results in potentially toxic free oxygen species.[27]	21%	11%	26%	42%
Ferric carboxymaltose (Ferinject®) allows the administration of high doses within one infusion.[27]	95%	5%	0%	0%
The administration of high doses within one infusion enhances individual comfort.[27]	95%	5%	0%	0%
The administration of high doses within one infusion reduces multiple visits in the clinic[27]	95%	5%	0%	0%
Usually, a loading dose with 1000 mg (not exceeding 20 mg/kg) of ferric carboxymaltose (Ferinject®) will result in adequate iron supply.[27]	68%	16%	16%	0%
If lower doses (than 1000 mg), such as 200 mg per infusion, are used, repeated administration (not exceeding a total dose of 20 mg/kg per month) is indicated according to the clinical course (control of anemia, symptom control).[27]	79%	5%	16%	0%
Ferritin levels will increase as well, but treatment should be discontinued if ferritin increases > 800 mcg/L.[27]	63%	16%	16%	5%

SPECIFIC PART - ONCOLOGY: TREATMENT OF IRON DEFICIENCY IN INDIVIDUALS WITH CANCER 3/3

Top	Medium	Bottom	DK
19 panelists			

Long-term treatment with intravenous iron should be avoided in individuals with cancer (as safety data for prolonged use in cancer are not available as yet).[27]	47%	11%	37%	5%
A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated.[1-3, 5, 77]	84%	5%	11%	0%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration.[1, 2, 5, 77]	95%	0%	5%	0%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration.[78-80]	37%	32%	11%	21%
Necessary target values of iron therapy if the required methodology, for which the below mentioned parameters are validated, is available:				
TSAT should rise > 20-50%[27]	79%	16%	5%	0%
Ferritin should rise clearly > 100 mcg/L[27]	58%	26%	16%	0%
With reference to the previous statement: Optional target values of iron therapy if the required methodology, for which the below mentioned parameters are validated, is available:				
Reduction of the percentage of hypochromic erythrocytes (%HYPO) to < 5 %[27]	47%	11%	5%	37%
Increase in Hb of reticulocytes (CHr) to > 28 pg[27]	63%	5%	0%	32%
Normalization of levels of soluble transferrin receptor (levels vary depending on the local laboratory)[27]	74%	0%	11%	16%
Normalization of the ferritin index (sTfR/log ferritin)[27]	68%	11%	0%	21%

G SPECIFIC PART - INTERNAL MEDICINE: CLINICAL RELEVANCE OF IRON DEFICIENCY IN ELDERLY INDIVIDUALS	Top	Medium	Bottom	DK
	18 panelists			
Iron deficiency is relatively common among the elderly population.[26, 30, 31]	78%	22%	0%	0%
Iron deficiency among the elderly population contributes substantially to a high prevalence of anemia observed in the last decades of life.[26]	78%	17%	0%	6%
Anemia in geriatric individuals is primarily due to:				
Anemia of inflammation (also called anemia of chronic disease ACD).[26, 30, 31]	67%	28%	6%	0%
Iron deficiency.[26, 30, 31]	50%	33%	17%	0%
Mixed etiology involving a combination of chronic disease and iron deficiency, with absolute iron deficiency (AID) playing a comparatively minor role.[26, 30, 31]	83%	11%	0%	6%
In the elderly population, anemia has important implications on:				
Quality of life[26, 30, 31]	94%	6%	0%	0%
Survival[26, 30, 31]	72%	22%	6%	0%
In elderly subjects, iron deficiency is often multifactorial (i.e., due to multiple concurring causes, including inadequate dietary intake or absorption, occult bleeding, or medications).[26]	100%	0%	0%	0%
Iron deficiency anemia is frequent in elderly individuals.[105]	67%	33%	0%	0%

SPECIFIC PART - INTERNAL MEDICINE: DIAGNOSIS OF IRON DEFICIENCY IN ELDERLY INDIVIDUALS

	Top	Medium	Bottom	DK
	18			
The statements in the General Part I – Diagnosis of Iron Deficiency also apply to elderly individuals.	83%	11%	0%	6%

SPECIFIC PART - INTERNAL MEDICINE: TREATMENT OF IRON DEFICIENCY IN ELDERLY INDIVIDUALS	Top	Medium	Bottom	DK
	18 panelists			
The statements in the General Part I – Treatment of Iron Deficiency also apply to elderly individuals.	89%	6%	0%	6%
Treatment of iron deficiency is problematic in elderly.[26]	39%	11%	44%	6%
Treatment of iron deficiency is problematic in elderly because:				
Response to oral iron is often slow.[26]	72%	6%	17%	6%
A substantial fraction of elderly is refractory to treatment.[26]	50%	17%	33%	0%
A substantial fraction of individuals requires cumbersome intravenous administration.[26]	44%	11%	44%	0%
In anemic geriatric individuals, the intravenous therapy with ferric carboxymaltose (Ferinject®):				
Can be well-tolerated.[80]	100%	0%	0%	0%
Is efficacious, that is, the therapeutic doses (recommended in the respective Summary of Product Characteristics SmPC) produce an increase of Hb of (i) at least 0.1 g/dl/day or (ii) of at least 2-3 g/dl after 3 weeks.[73-76]	72%	11%	6%	11%
In elderly individuals (≥ 65 years old) with restless legs syndrome (RLS) and iron deficiency (defined as baseline ferritin < 50 mcg/L or TSAT < 16 %), the administration of ferric carboxymaltose (Ferinject®) is associated with a significant improvement of RLS symptoms.[106]	83%	0%	11%	6%

H GENERAL PART II: DEFINITION AND CLINICAL RELEVANCE OF IRON DEFICIENCY 1/2

Top	Medium	Bottom	DK
93 panelists			

In (i) individuals not suffering from chronic diseases or (ii) individuals suffering from chronic disease(s) and normal CRP, oral iron is the preferred therapeutic option in presence of anemia (i.e., Hb < 13 g/dL in adult males and Hb < 12 g/dL in adult females) and / or symptoms of iron deficiency if:

Ferritin < 30 mcg/L [1-3, 44, 69, 70, 107, 108]	62%	16%	20%	1%
Ferritin 30 - 50 mcg/L and TSAT < 20% [44, 107, 108]	69%	18%	11%	2%

In individuals not suffering from chronic diseases or individuals suffering from chronic disease(s) and not presenting signs of inflammation (normal CRP), intravenous iron can be considered as a therapeutic option in presence of anemia (i.e., Hb < 13 g/dL in adult males and < 12 g/dL in adult females) and / or symptoms of iron deficiency if ferritin < 30 mcg/L, provided that:

Oral iron is not tolerated. [1-3, 44, 69, 70, 107, 108]	96%	3%	0%	1%
Oral iron may not be efficacious, that is, the therapeutic doses (recommended in the respective Summary of Product Characteristics SmPC) fail to produce an increase of Hb of (i) at least 0.1 g/dl/day or (ii) of at least 2-3 g/dl after 3 weeks (in individuals with anemia after exclusion of folate and B12 deficiency)). [1-3, 44, 69, 70, 107, 108] [73-76]	91%	5%	2%	1%
Oral iron is not applicable because of risk of complications. [1-3, 44, 69, 70, 107, 108] [73-76]	93%	4%	2%	1%
A rapid increase in Hb is needed (e.g., presence of very low hemoglobin values during pregnancy and postpartum, in the perioperative setting). [1-3, 44, 69, 70, 107, 108] [42, 72-76]	94%	2%	3%	1%

In (i) individuals not suffering from chronic diseases or (ii) individuals suffering from chronic disease(s) and not presenting signs of inflammation (normal CRP), intravenous iron can be considered as a therapeutic option in presence of anemia (i.e., Hb < 13 g/dL in adult males and < 12 g/dL in adult females) and / or symptoms of iron deficiency if ferritin 30 - 50 mcg/L and TSAT < 20%, provided that:

Oral iron is not tolerated. [1-3, 44, 69, 70, 107, 108] [73-76]	90%	5%	3%	1%
Oral iron may not be efficacious, that is, the therapeutic doses (recommended in the respective Summary of Product Characteristics SmPC) fail to produce an increase of Hb of (i) at least 0.1 g/dl/day or (ii) of at least 2-3 g/dl after 3 weeks (in individuals with anemia after exclusion of folate and B12 deficiency)). [1-3, 44, 69, 70, 107, 108] [73-76]	84%	9%	7%	1%
Oral iron is not applicable because of risk of complications. [1-3, 44, 69, 70, 107, 108] [73-76]	88%	5%	5%	1%
A rapid increase in Hb is needed (e.g., presence of very low hemoglobin values during pregnancy and postpartum, in the perioperative setting). [1-3, 44, 69, 70, 107, 108] [42, 72-76]	86%	8%	5%	1%

H GENERAL PART II: DEFINITION AND CLINICAL RELEVANCE OF IRON DEFICIENCY 2/2

Top	Medium	Bottom	DK
93 panelists			

In individuals with signs of chronic inflammation, intravenous iron is considered as the preferred therapeutic option (when compared to the oral substitution) if ferritin < 100 mcg/L and TSAT < 20%, provided that:

The presence of anemia is confirmed (i.e., Hb < 13 g/dL in adult males and < 12 g/dL in adult females).[44, 107, 108]	60%	15%	17%	8%
A maintenance treatment in order to avoid re-occurrence of anemia is desired.[19, 33, 34, 84, 85, 109-112]	48%	19%	27%	5%
A maintenance treatment in order to avoid re-occurrence of iron deficiency is desired. [19, 33, 34, 84, 85, 109-112]	40%	24%	31%	5%
A therapy is needed because of symptoms.[27]	73%	11%	10%	7%

In individuals with signs of chronic inflammation, oral iron may not be sufficient as a therapeutic option if ferritin < 100 mcg/L and TSAT < 20%, provided that:

The presence of anemia is confirmed (i.e., Hb < 13 g/dL in adult males and < 12 g/dL in adult females). [44, 107, 108]	68%	8%	17%	8%
A maintenance treatment in order to avoid re-occurrence of anemia is desired. [19, 33, 34, 84, 85, 109-112]	56%	13%	24%	8%
A maintenance treatment in order to avoid re-occurrence of iron deficiency is desired[19, 33, 34, 84, 85, 109-112]	53%	14%	26%	8%
There are any symptoms in the presence of which the administration is indicated.[27]	74%	7%	12%	8%

In individuals suffering from chronic disease(s), treatment of iron deficiency can be performed using higher ferritin-cut-offs according to the respective disease-specific guideline.

A control of ferritin can be performed 4 weeks following the intravenous iron administration, but the measured value can be falsely elevated. [2, 3, 5, 77]	83%	7%	7%	4%
A control of ferritin is ideally performed 8-12 weeks following the intravenous iron administration. [1, 2, 5, 77]	94%	1%	2%	3%
A control of TSAT seems reasonable at least 2-4 weeks following the intravenous iron administration. [78-80]	56%	16%	13%	15%

Oral and intravenous iron therapy should be performed according to the SmPC of the respective iron preparation.

91%	7%	1%	1%
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