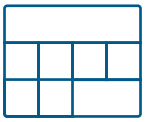
Dosing and Administration Guide

for REMICADE® and Infliximab

Remicade® INFLIXIMAB | Infliximab

INDICATIONS

DOSAGE BY INDICATION



DOSING CALCULATORS

RECONSTITUTION, DILUTION, AND ADMINISTRATION INSTRUCTIONS

INFUSION-RELATED REACTIONS

PATIENT ASSESSMENT

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Indications

Crohn's Disease

REMICADE® and Infliximab are indicated for:

- reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease (CD) who have had an inadequate response to conventional therapy.
- reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD.

Pediatric Crohn's Disease

REMICADE® and Infliximab are indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active CD who have had an inadequate response to conventional therapy.

Ulcerative Colitis

REMICADE® and Infliximab are indicated for reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response to conventional therapy.

Pediatric Ulcerative Colitis

REMICADE® and Infliximab are indicated for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active UC who have had an inadequate response to conventional therapy.

Rheumatoid Arthritis

REMICADE® or Infliximab, in combination with methotrexate, is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (RA).

Ankylosing Spondylitis

REMICADE® and Infliximab are indicated for reducing signs and symptoms in adult patients with active ankylosing spondylitis (AS).

Psoriatic Arthritis

REMICADE® and Infliximab are indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients with psoriatic arthritis (PsA).

Plaque Psoriasis

REMICADE® and Infliximab are indicated for treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis (Ps) who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. REMICADE® or Infliximab should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Recommended Dosing and Administration[1,2]

Remicade® INFLIXIMAB | Infliximab

Adults With Moderately to Severely Active Crohn's Disease

REMICADE® or Infliximab is administered by intravenous (IV) infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING*
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING†
5 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

*For adult patients who respond and then lose their response, consideration may be given to treatment with 10 mg/kg every 8 weeks.
†Patients who do not respond by Week 14 are unlikely to respond with continued dosing, and consideration should be given to discontinuing infliximab in these patients.

Moderately to Severely Active Pediatric Crohn's Disease (6 years of age and older)

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING
5 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Recommended Dosing and Administration[1,2] (cont)

Remicade® INFLIXIMAB | Infliximab

Adults With Moderately to Severely Active Ulcerative Colitis

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING
5 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

Moderately to Severely Active Pediatric Ulcerative Colitis (6 years of age and older)

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING
5 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

Adults With Moderately to Severely Active Rheumatoid Arthritis

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING
3 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING*
3 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

REMICADE® or Infliximab should be given in combination with methotrexate.

*For adult patients who have an incomplete response, consideration may be given to adjusting the dose up to 10 mg/kg or treating as often as every 4 weeks bearing in mind that risk of serious infections is increased at higher doses.

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Recommended Dosing and Administration[1,2] (cont)

Remicade® INFLIXIMAB | Infliximab

Adults With Active Ankylosing Spondylitis

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 6 weeks after 3 induction doses.

INDUCTION DOSING
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING
5 mg/kg IV given every 6 weeks thereafter as a maintenance regimen

Adults With Active Psoriatic Arthritis

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING
5 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

REMICADE® or Infliximab can be used with or without methotrexate in adult patients with active PsA.

Adults With Chronic Severe Plaque Psoriasis

REMICADE® or Infliximab is administered by IV infusion for at least 2 hours. Infusions occur every 8 weeks after 3 induction doses.

INDUCTION DOSING
5 mg/kg IV given at 0, 2, and 6 weeks as an induction regimen

FOLLOWED BY

MAINTENANCE DOSING
5 mg/kg IV given every 8 weeks thereafter as a maintenance regimen

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Dosing Calculator for **Adult Patients**

Remicade® INFLIXIMAB | Infliximab

		3 mg/kg[1-3] For patients with rheumatoid arthritis			4 mg/kg[1-3] For patients with rheumatoid arthritis		
Patient Weight (lb)	Patient Weight (kg)	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*
95	43	129	2	12.9	172	2	17.2
100	45	135	2	13.5	180	2	18.0
105	48	144	2	14.4	192	2	19.2
110	50	150	2	15.0	200	2	20.0
115	52	156	2	15.6	208	3	20.8
120	55	165	2	16.5	220	3	22.0
125	57	171	2	17.1	228	3	22.8
130	59	177	2	17.7	236	3	23.6
135	61	183	2	18.3	244	3	24.4
140	64	192	2	19.2	256	3	25.6
145	66	198	2	19.8	264	3	26.4
150	68	204	3	20.4	272	3	27.2
155	70	210	3	21.0	280	3	28.0
160	73	219	3	21.9	292	3	29.2
165	75	225	3	22.5	300	3	30.0
170	77	231	3	23.1	308	4	30.8
175	80	240	3	24.0	320	4	32.0
180	82	246	3	24.6	328	4	32.8
185	84	252	3	25.2	336	4	33.6
190	86	258	3	25.8	344	4	34.4
195	89	267	3	26.7	356	4	35.6
200	91	273	3	27.3	364	4	36.4
205	93	279	3	27.9	372	4	37.2
210	95	285	3	28.5	380	4	38.0
215	98	294	3	29.4	392	4	39.2
220	100	300	3	30.0	400	4	40.0
225	102	306	4	30.6	408	5	40.8
230	105	315	4	31.5	420	5	42.0
235	107	321	4	32.1	428	5	42.8
240	109	327	4	32.7	436	5	43.6
245	111	333	4	33.3	444	5	44.4
250	114	342	4	34.2	456	5	45.6
255	116	348	4	34.8	464	5	46.4
260	118	354	4	35.4	472	5	47.2
265	120	360	4	36.0	480	5	48.0
270	123	369	4	36.9	492	5	49.2
275	125	375	4	37.5	500	5	50.0
280	127	381	4	38.1	508	6	50.8
285	130	390	4	39.0	520	6	52.0
290	132	396	4	39.6	528	6	52.8
295	134	402	5	40.2	536	6	53.6
300	136	408	5	40.8	544	6	54.4

*After reconstituting with 10 mL of Sterile Water for Injection, USP, the final concentration is 10 mg/mL.

Calculate the dose, total volume of reconstituted REMICADE® or Infliximab solution required, and the number of REMICADE® or Infliximab vials needed.[1,2]

Prior to reconstitution and use, vials of REMICADE® and Infliximab must be stored in a refrigerator at a temperature between 2 °C to 8 °C (36 °F to 46 °F).[1,2]

If needed, unopened REMICADE® and Infliximab vials may be stored at room temperature up to a maximum of 30 °C (86 °F) for a single period of up to 6 months but not exceeding the original expiration date. The new expiration date must be written in the space provided on the carton. Once removed from the refrigerator, REMICADE® and Infliximab cannot be returned to the refrigerator.[1,2]

The infusion of REMICADE® or Infliximab should begin within 3 hours of reconstitution and dilution.[1,2]

Prior to initiating REMICADE® or Infliximab, bring pediatric and adult patients up to date with all vaccinations. Live vaccines or therapeutic infectious agents should not be given with REMICADE® or Infliximab. At least a 6-month waiting period following birth is recommended before the administration of live vaccines to infants exposed *in utero* to infliximab.[1,2]

Dosing Calculator for **Adult Patients** (cont)

Remicade® INFLIXIMAB | Infliximab

		5 mg/kg[1-3]			6 mg/kg[1-3] For patients with rheumatoid arthritis		
Patient Weight (lb)	Patient Weight (kg)	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*
95	43	215	3	21.5	258	3	25.8
100	45	225	3	22.5	270	3	27.0
105	48	240	3	24.0	288	3	28.8
110	50	250	3	25.0	300	3	30.0
115	52	260	3	26.0	312	4	31.2
120	55	275	3	27.5	330	4	33.0
125	57	285	3	28.5	342	4	34.2
130	59	295	3	29.5	354	4	35.4
135	61	305	4	30.5	366	4	36.6
140	64	320	4	32.0	384	4	38.4
145	66	330	4	33.0	396	4	39.6
150	68	340	4	34.0	408	5	40.8
155	70	350	4	35.0	420	5	42.0
160	73	365	4	36.5	438	5	43.8
165	75	375	4	37.5	450	5	45.0
170	77	385	4	38.5	462	5	46.2
175	80	400	4	40.0	480	5	48.0
180	82	410	5	41.0	492	5	49.2
185	84	420	5	42.0	504	6	50.4
190	86	430	5	43.0	516	6	51.6
195	89	445	5	44.5	534	6	53.4
200	91	455	5	45.5	546	6	54.6
205	93	465	5	46.5	558	6	55.8
210	95	475	5	47.5	570	6	57.0
215	98	490	5	49.0	588	6	58.8
220	100	500	5	50.0	600	6	60.0
225	102	510	6	51.0	612	7	61.2
230	105	525	6	52.5	630	7	63.0
235	107	535	6	53.5	642	7	64.2
240	109	545	6	54.5	654	7	65.4
245	111	555	6	55.5	666	7	66.6
250	114	570	6	57.0	684	7	68.4
255	116	580	6	58.0	696	7	69.6
260	118	590	6	59.0	708	8	70.8
265	120	600	6	60.0	720	8	72.0
270	123	615	7	61.5	738	8	73.8
275	125	625	7	62.5	750	8	75.0
280	127	635	7	63.5	762	8	76.2
285	130	650	7	65.0	780	8	78.0
290	132	660	7	66.0	792	8	79.2
295	134	670	7	67.0	804	9	80.4
300	136	680	7	68.0	816	9	81.6

*After reconstituting with 10 mL of Sterile Water for Injection, USP, the final concentration is 10 mg/mL.

Calculate the dose, total volume of reconstituted REMICADE® or Infliximab solution required, and the number of REMICADE® or Infliximab vials needed.[1,2]

Prior to reconstitution and use, vials of REMICADE® and Infliximab must be stored in a refrigerator at a temperature between 2 °C to 8 °C (36 °F to 46 °F).[1,2]

If needed, unopened REMICADE® and Infliximab vials may be stored at room temperature up to a maximum of 30 °C (86 °F) for a single period of up to 6 months but not exceeding the original expiration date. The new expiration date must be written in the space provided on the carton. Once removed from the refrigerator, REMICADE® and Infliximab cannot be returned to the refrigerator.[1,2]

The infusion of REMICADE® or Infliximab should begin within 3 hours of reconstitution and dilution.[1,2]

Prior to initiating REMICADE® or Infliximab, bring pediatric and adult patients up to date with all vaccinations. Live vaccines or therapeutic infectious agents should not be given with REMICADE® or Infliximab. At least a 6-month waiting period following birth is recommended before the administration of live vaccines to infants exposed *in utero* to infliximab.[1,2]

Dosing Calculator for **Adult Patients** (cont)

Remicade® INFLIXIMAB | Infliximab

		7 mg/kg[1-3] For patients with rheumatoid arthritis			8 mg/kg[1-3] For patients with rheumatoid arthritis		
Patient Weight (lb)	Patient Weight (kg)	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*
95	43	301	4	30.1	344	4	34.4
100	45	315	4	31.5	360	4	36.0
105	48	336	4	33.6	384	4	38.4
110	50	350	4	35.0	400	4	40.0
115	52	364	4	36.4	416	5	41.6
120	55	385	4	38.5	440	5	44.0
125	57	399	4	39.9	456	5	45.6
130	59	413	5	41.3	472	5	47.2
135	61	427	5	42.7	488	5	48.8
140	64	448	5	44.8	512	6	51.2
145	66	462	5	46.2	528	6	52.8
150	68	476	5	47.6	544	6	54.4
155	70	490	5	49.0	560	6	56.0
160	73	511	6	51.1	584	6	58.4
165	75	525	6	52.5	600	6	60.0
170	77	539	6	53.9	616	7	61.6
175	80	560	6	56.0	640	7	64.0
180	82	574	6	57.4	656	7	65.6
185	84	588	6	58.8	672	7	67.2
190	86	602	7	60.2	688	7	68.8
195	89	623	7	62.3	712	8	71.2
200	91	637	7	63.7	728	8	72.8
205	93	651	7	65.1	744	8	74.4
210	95	665	7	66.5	760	8	76.0
215	98	686	7	68.6	784	8	78.4
220	100	700	7	70.0	800	8	80.0
225	102	714	8	71.4	816	9	81.6
230	105	735	8	73.5	840	9	84.0
235	107	749	8	74.9	856	9	85.6
240	109	763	8	76.3	872	9	87.2
245	111	777	8	77.7	888	9	88.8
250	114	798	8	79.8	912	10	91.2
255	116	812	9	81.2	928	10	92.8
260	118	826	9	82.6	944	10	94.4
265	120	840	9	84.0	960	10	96.0
270	123	861	9	86.1	984	10	98.4
275	125	875	9	87.5	1000	10	100.0
280	127	889	9	88.9	1016	11	101.6
285	130	910	10	91.0	1040	11	104.0
290	132	924	10	92.4	1056	11	105.6
295	134	938	10	93.8	1072	11	107.2
300	136	952	10	95.2	1088	11	108.8

*After reconstituting with 10 mL of Sterile Water for Injection, USP, the final concentration is 10 mg/mL.

Calculate the dose, total volume of reconstituted REMICADE® or Infliximab solution required, and the number of REMICADE® or Infliximab vials needed.[1,2]

Prior to reconstitution and use, vials of REMICADE® and Infliximab must be stored in a refrigerator at a temperature between 2 °C to 8 °C (36 °F to 46 °F).[1,2]

If needed, unopened REMICADE® and Infliximab vials may be stored at room temperature up to a maximum of 30 °C (86 °F) for a single period of up to 6 months but not exceeding the original expiration date. The new expiration date must be written in the space provided on the carton. Once removed from the refrigerator, REMICADE® and Infliximab cannot be returned to the refrigerator.[1,2]

The infusion of REMICADE® or Infliximab should begin within 3 hours of reconstitution and dilution.[1,2]

Prior to initiating REMICADE® or Infliximab, bring pediatric and adult patients up to date with all vaccinations. Live vaccines or therapeutic infectious agents should not be given with REMICADE® or Infliximab. At least a 6-month waiting period following birth is recommended before the administration of live vaccines to infants exposed *in utero* to infliximab.[1,2]

Dosing Calculator for **Adult Patients** (cont)

Remicade® INFLIXIMAB | Infliximab

		9 mg/kg[1-3] For patients with rheumatoid arthritis			10 mg/kg[1-3] For patients with rheumatoid arthritis or Crohn's disease		
Patient Weight (lb)	Patient Weight (kg)	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*
95	43	387	4	38.7	430	5	43.0
100	45	405	5	40.5	450	5	45.0
105	48	432	5	43.2	480	5	48.0
110	50	450	5	45.0	500	5	50.0
115	52	468	5	46.8	520	6	52.0
120	55	495	5	49.5	550	6	55.0
125	57	513	6	51.3	570	6	57.0
130	59	531	6	53.1	590	6	59.0
135	61	549	6	54.9	610	7	61.0
140	64	576	6	57.6	640	7	64.0
145	66	594	6	59.4	660	7	66.0
150	68	612	7	61.2	680	7	68.0
155	70	630	7	63.0	700	7	70.0
160	73	657	7	65.7	730	8	73.0
165	75	675	7	67.5	750	8	75.0
170	77	693	7	69.3	770	8	77.0
175	80	720	8	72.0	800	8	80.0
180	82	738	8	73.8	820	9	82.0
185	84	756	8	75.6	840	9	84.0
190	86	774	8	77.4	860	9	86.0
195	89	801	9	80.1	890	9	89.0
200	91	819	9	81.9	910	10	91.0
205	93	837	9	83.7	930	10	93.0
210	95	855	9	85.5	950	10	95.0
215	98	882	9	88.2	980	10	98.0
220	100	900	9	90.0	1000	10	100.0
225	102	918	10	91.8	1020	11	102.0
230	105	945	10	94.5	1050	11	105.0
235	107	963	10	96.3	1070	11	107.0
240	109	981	10	98.1	1090	11	109.0
245	111	999	10	99.9	1110	12	111.0
250	114	1026	11	102.6	1140	12	114.0
255	116	1044	11	104.4	1160	12	116.0
260	118	1062	11	106.2	1180	12	118.0
265	120	1080	11	108.0	1200	12	120.0
270	123	1107	12	110.7	1230	13	123.0
275	125	1125	12	112.5	1250	13	125.0
280	127	1143	12	114.3	1270	13	127.0
285	130	1170	12	117.0	1300	13	130.0
290	132	1188	12	118.8	1320	14	132.0
295	134	1206	13	120.6	1340	14	134.0
300	136	1224	13	122.4	1360	14	136.0

*After reconstituting with 10 mL of Sterile Water for Injection, USP, the final concentration is 10 mg/mL.

Calculate the dose, total volume of reconstituted REMICADE® or Infliximab solution required, and the number of REMICADE® or Infliximab vials needed.[1,2]

Prior to reconstitution and use, vials of REMICADE® and Infliximab must be stored in a refrigerator at a temperature between 2 °C to 8 °C (36 °F to 46 °F).[1,2]

If needed, unopened REMICADE® and Infliximab vials may be stored at room temperature up to a maximum of 30 °C (86 °F) for a single period of up to 6 months but not exceeding the original expiration date. The new expiration date must be written in the space provided on the carton. Once removed from the refrigerator, REMICADE® and Infliximab cannot be returned to the refrigerator.[1,2]

The infusion of REMICADE® or Infliximab should begin within 3 hours of reconstitution and dilution.[1,2]

Prior to initiating REMICADE® or Infliximab, bring pediatric and adult patients up to date with all vaccinations. Live vaccines or therapeutic infectious agents should not be given with REMICADE® or Infliximab. At least a 6-month waiting period following birth is recommended before the administration of live vaccines to infants exposed *in utero* to infliximab.[1,2]

Dosing Calculator for **Pediatric Patients**

Remicade® INFLIXIMAB | Infliximab

		5 mg/kg[1-3] For pediatric patients with ulcerative colitis or Crohn's disease		
Patient Weight (lb)	Patient Weight (kg)	Total Dose of REMICADE® or Infliximab (mg)	Number of REMICADE® or Infliximab Vials Required	Volume of Reconstituted REMICADE® or Infliximab to Be Withdrawn (mL)*
45	20	100	1	10.0
50	23	115	2	11.5
55	25	125	2	12.5
60	27	135	2	13.5
65	30	150	2	15.0
70	32	160	2	16.0
75	34	170	2	17.0
80	36	180	2	18.0
85	39	195	2	19.5
90	41	205	3	20.5
95	43	215	3	21.5
100	45	225	3	22.5
105	48	240	3	24.0
110	50	250	3	25.0
115	52	260	3	26.0
120	55	275	3	27.5
125	57	285	3	28.5
130	59	295	3	29.5
135	61	305	4	30.5
140	64	320	4	32.0
145	66	330	4	33.0
150	68	340	4	34.0
155	70	350	4	35.0
160	73	365	4	36.5
165	75	375	4	37.5
170	77	385	4	38.5
175	80	400	4	40.0
180	82	410	5	41.0
185	84	420	5	42.0
190	86	430	5	43.0
195	89	445	5	44.5
200	91	455	5	45.5

*After reconstituting with 10 mL of Sterile Water for Injection, USP, the final concentration is 10 mg/mL.

Calculate the dose, total volume of reconstituted REMICADE® or Infliximab solution required, and the number of REMICADE® or Infliximab vials needed.[1,2]

Prior to reconstitution and use, vials of REMICADE® and Infliximab must be stored in a refrigerator at a temperature between 2 °C to 8 °C (36 °F to 46 °F).[1,2]

If needed, unopened REMICADE® and Infliximab vials may be stored at room temperature up to a maximum of 30 °C (86 °F) for a single period of up to 6 months but not exceeding the original expiration date. The new expiration date must be written in the space provided on the carton. Once removed from the refrigerator, REMICADE® and Infliximab cannot be returned to the refrigerator.[1,2]

The infusion of REMICADE® or Infliximab should begin within 3 hours of reconstitution and dilution.[1,2]

Prior to initiating REMICADE® or Infliximab, bring pediatric and adult patients up to date with all vaccinations. Live vaccines or therapeutic infectious agents should not be given with REMICADE® or Infliximab. At least a 6-month waiting period following birth is recommended before the administration of live vaccines to infants exposed *in utero* to infliximab.[1,2]

Reconstitution, Dilution, and Administration Instructions[1,2]

Remicade® INFLIXIMAB | Infliximab

REMICADE® and Infliximab are intended for use under the guidance and supervision of a healthcare provider. The supplied lyophilized powder must be reconstituted and diluted prior to administration. The infusion solution, either REMICADE® or Infliximab, should be prepared and administered by a trained medical professional using aseptic technique by the following procedure:

Calculate the dose, total volume of reconstituted solution required, and the number of vials needed. More than 1 vial may be needed for a full dose.

Reconstitute each 100-mg vial with 10 mL of Sterile Water for Injection, USP, to obtain a concentration of 10 mg/mL, using a syringe equipped with a 21-gauge or smaller needle as follows:

- Remove the flip-top from the vial and wipe the top with an alcohol swab
- Insert the syringe needle into the vial through the center of the rubber stopper and direct the stream of Sterile Water for Injection, USP, to the glass wall of the vial. Gently swirl the solution by rotating the vial to dissolve the lyophilized powder, which has a cake-like appearance. Avoid prolonged or vigorous agitation. DO NOT SHAKE. Foaming of the solution on reconstitution is not unusual
- Allow the reconstituted solution to stand for 5 minutes. Visually inspect the reconstituted solution for particulate matter and discoloration. The reconstituted solution should be colorless to light yellow and opalescent, and the solution may develop a few translucent particles as infliximab is a protein. Do not use if the lyophilized powder has not fully dissolved or if opaque particles, discoloration, or other foreign particles are present. Do not store unused reconstituted solutions

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Reconstitution, Dilution, and Administration Instructions[1,2] (cont)

Dilute the total volume of the reconstituted solution to 250 mL* with sterile 0.9% Sodium Chloride Injection, USP (do not dilute with any other diluent) as follows:

- Withdraw a volume from the 0.9% Sodium Chloride Injection, USP, 250-mL bottle or bag equal to the total volume of reconstituted solution required for a dose. Slowly add the total volume of reconstituted solution from the vial(s) to the 250-mL infusion bottle or bag
- Discard any unused portion of the reconstituted solution remaining in the vial(s)
- Gently invert the bag to mix the solution. The resulting infusion concentration should range between 0.4 mg/mL (minimum recommended concentration) and 4 mg/mL (maximum recommended concentration) of infliximab

*For volumes greater than 250 mL, either use a larger infusion bag (eg, 500 mL) or multiple 250-mL infusion bags to ensure that the concentration of the infusion solution does not exceed 4 mg/mL.

The infusion should begin within 3 hours of reconstitution and dilution. The infusion must be administered intravenously for at least 2 hours with an infusion set with an in-line, sterile, nonpyrogenic, low-protein–binding filter (pore size 1.2 µm or less).

Given that the vials do not contain antibacterial preservatives, discard any unused portion of the infusion solution (do not store for reuse).

No physical biochemical compatibility studies have been conducted to evaluate the coadministration of the solution with other agents. Concomitant infusion in the same IV line with other agents should not be done.

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Reconstitution, Dilution, and Administration Instructions[1,2] (cont)

INFUSION REACTIONS

An infusion reaction was defined in clinical trials as any adverse event occurring during an infusion or within 1 hour after an infusion. In all the clinical studies, approximately 20% of REMICADE® or Infliximab-treated patients experienced an infusion reaction compared with 10% of placebo-treated patients. Of REMICADE® or Infliximab-treated patients who had an infusion reaction during the induction period, 27% experienced an infusion reaction during the maintenance period. Of patients who did not have an infusion reaction during the induction period, 9% experienced an infusion reaction during the maintenance period.

Among all REMICADE® or Infliximab infusions, 3% were accompanied by nonspecific symptoms such as fever or chills, 1% were accompanied by cardiopulmonary reactions (primarily chest pain, hypotension, hypertension or dyspnea), and <1% were accompanied by pruritus, urticaria, or the combined symptoms of pruritus/urticaria and cardiopulmonary reactions. Serious infusion reactions occurred in <1% of patients and included anaphylaxis, convulsions, erythematous rash and hypotension. Approximately 3% of patients discontinued REMICADE® or Infliximab because of infusion reactions, and all patients recovered with treatment and/or discontinuation of the infusion. REMICADE® or Infliximab infusions beyond the initial infusion were not associated with a higher incidence of reactions. The infusion reaction rates remained stable in Ps through 1 year in Ps Study I. In psoriasis Study II, the rates were variable over time and somewhat higher following the final infusion than after the initial infusion. Across the 3 Ps studies, the percent of total infusions resulting in infusion reactions (ie, an adverse event occurring within 1 hour) was 7% in the 3 mg/kg group, 4% in the 5 mg/kg group, and 1% in the placebo group.

Patients who became positive for antibodies to infliximab were more likely (approximately two to three-fold) to have an infusion reaction than were those who were negative. Use of concomitant immunosuppressant agents appeared to reduce the frequency of both antibodies to infliximab and infusion reactions.

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

INFUSION REACTIONS

Infusion Reactions Following Re-administration

In a clinical trial of patients with moderate to severe Ps designed to assess the efficacy of long-term maintenance therapy versus re-treatment with an induction regimen of REMICADE® or Infliximab following disease flare, 4% (8/219) of patients in the re-treatment induction therapy arm experienced serious infusion reactions versus <1% (1/222) in the maintenance therapy arm. Patients enrolled in this trial did not receive any concomitant immunosuppressant therapy. In this study, the majority of serious infusion reactions occurred during the second infusion at Week 2. Symptoms included, but were not limited to, dyspnea, urticaria, facial edema, and hypotension. In all cases, REMICADE® or Infliximab treatment was discontinued and/or other treatment instituted with complete resolution of signs and symptoms.

Delayed Reactions/Reactions Following Re-administration

In Ps studies, approximately 1% of REMICADE® or Infliximab-treated patients experienced a possible delayed hypersensitivity reaction, generally reported as serum sickness or a combination of arthralgia and/or myalgia with fever and/or rash. These reactions generally occurred within 2 weeks after repeat infusion.

Cardiovascular and Cerebrovascular Reactions During and After Infusion

Serious cerebrovascular accidents, myocardial ischemia/infarction (some fatal), hypotension, hypertension, and arrhythmias have been reported during and within 24 hours of initiation of REMICADE® or Infliximab infusion. Cases of transient visual loss have been reported during or within 2 hours of infusion of REMICADE® or Infliximab. Monitor patients during infusion and if serious reaction occurs, discontinue infusion. Further management of reactions should be dictated by signs and symptoms.

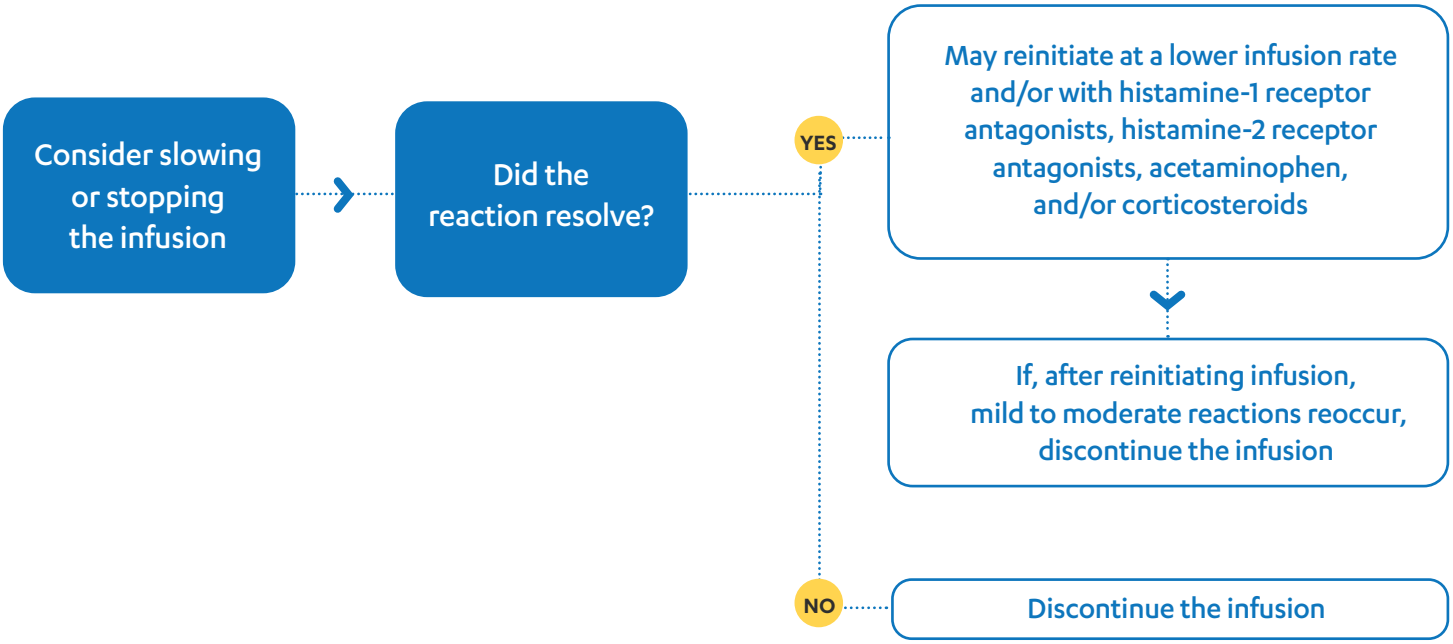
SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Administration Instructions Regarding Infusion Reactions

Prior to treatment, ensure appropriate personnel and medication are available to treat reactions (eg, hypersensitivity, other reactions) that occur during infusion and shortly after infusion. Prior to infusion with REMICADE® or Infliximab, patients may be premedicated with histamine-1 receptor antagonists, histamine-2 receptor antagonists, acetaminophen, and/or corticosteroids.

In the event of a mild to moderate reaction during infusion[1,2]



Discontinue the infusion if severe hypersensitivity reactions occur during the infusion. Discontinue the infusion if mild to moderate reactions reoccur.

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Pre-Infusion Patient Assessment and Counseling

Remicade® INFLIXIMAB | Infliximab

Patients should be given the Medication Guide for REMICADE® and Infliximab, and provided the opportunity to read it and discuss their questions with you prior to each treatment session. The Medication Guide for REMICADE® and Infliximab may be viewed online at www.remicade.com and www.infliximab.com, at the end of this document, or you may call 1-800-JANSSEN for additional copies.

Things to consider before infusion:

- Serious infections
- Malignancies
- Hepatitis B reactivation
- Hepatotoxicity
- Heart failure
- Hematologic events
- Hypersensitivity
- Cardiovascular and cerebrovascular reactions during and after infusion
- Neurologic events
- Concurrent administration with other biologics
- Autoimmunity
- Vaccinations and use of live vaccines/therapeutic infectious agents
- Adverse reactions

Switching between biological DMARDs

Care should be taken when switching from one biologic to another, since overlapping biological activity may further increase the risk of infection.

DMARDs=disease-modifying anti-rheumatic drugs.

References: 1. REMICADE® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** Infliximab [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **3.** Data on file. Janssen Biotech, Inc.

SELECTED IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with REMICADE® and Infliximab. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. REMICADE® and Infliximab are contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to REMICADE® and Infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome. Please see related and other Important Safety Information on pages 17-20 for REMICADE® and Infliximab.

Important Safety Information

SERIOUS INFECTIONS

Patients treated with either REMICADE® or Infliximab are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Discontinue either REMICADE® or Infliximab if a patient develops a serious infection or sepsis.

Reported infections include:

- **Active tuberculosis (TB), including reactivation of latent TB. Patients frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before and during treatment with either REMICADE® or Infliximab.[1,2] Treatment for latent infection should be initiated prior to treatment with either REMICADE® or Infliximab.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, pneumocystosis, and cryptococcosis. Patients may present with disseminated, rather than localized, disease. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella, Listeria, and Salmonella.**

The risks and benefits of treatment with either REMICADE® or Infliximab should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Closely monitor patients for the development of signs and symptoms of infection during and after treatment with either REMICADE® or Infliximab, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy, who are on treatment for latent TB, or who were previously treated for TB infection.

Risk of infection may be higher in patients greater than 65 years of age, pediatric patients, patients with co-morbid conditions and/or patients taking concomitant immunosuppressant therapy. In clinical trials, other serious infections observed in patients treated with either REMICADE® or Infliximab included pneumonia, cellulitis, abscess, and skin ulceration.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including either REMICADE® or Infliximab. Approximately half of these cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of malignancies, including rare malignancies that are usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. The malignancies occurred after a median of 30 months after the first dose of therapy. Most of the patients were receiving concomitant immunosuppressants.

Important Safety Information (cont)

MALIGNANCIES (cont)

Postmarketing cases of hepatosplenic T-cell lymphoma, a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including either REMICADE® or Infliximab. These cases have had a very aggressive disease course and have been fatal. The majority of reported REMICADE® and Infliximab cases have occurred in patients with Crohn's disease or ulcerative colitis and most were in adolescent and young adult males. Almost all of these patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with either REMICADE® or Infliximab at or prior to diagnosis. Carefully assess the risks and benefits of treatment with either REMICADE® or Infliximab, especially in these patient types.

In clinical trials of all TNF blockers, more cases of lymphoma were observed compared with controls and the expected rate in the general population. However, patients with Crohn's disease, rheumatoid arthritis, or plaque psoriasis may be at higher risk for developing lymphoma. In clinical trials of some TNF blockers, including either REMICADE® or Infliximab, more cases of other malignancies were observed compared with controls. The rate of these malignancies among patients treated with either REMICADE® or Infliximab was similar to that expected in the general population whereas the rate in control patients was lower than expected. Cases of acute and chronic leukemia have been reported with postmarketing TNF-blocker use. As the potential role of TNF blockers in the development of malignancies is not known, caution should be exercised when considering treatment of patients with a current or a past history of malignancy or other risk factors such as chronic obstructive pulmonary disease (COPD).

Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-blocker therapies, including either REMICADE® or Infliximab. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.

A population-based retrospective cohort study found a 2- to 3-fold increase in the incidence of invasive cervical cancer in women with rheumatoid arthritis treated with either REMICADE® or Infliximab compared to biologics-naïve patients or the general population, particularly those over 60 years of age. A causal relationship between either REMICADE® or Infliximab and cervical cancer cannot be excluded. Periodic screening should continue in women treated with either REMICADE® or Infliximab.

CONTRAINDICATIONS

The use of either REMICADE® or Infliximab at doses >5 mg/kg is contraindicated in patients with moderate or severe heart failure. REMICADE® and Infliximab are contraindicated in patients with a previous severe hypersensitivity reaction to infliximab or any of the inactive ingredients of REMICADE® and Infliximab or any murine proteins (severe hypersensitivity reactions have included anaphylaxis, hypotension, and serum sickness).

HEPATITIS B REACTIVATION

TNF blockers, including REMICADE® and Infliximab, have been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases were fatal. Patients should be tested for HBV infection before initiating either REMICADE® or Infliximab. For patients who test positive, consult

Important Safety Information (cont)

HEPATITIS B REACTIVATION (cont)

a physician with expertise in the treatment of hepatitis B. Exercise caution when prescribing either REMICADE® or Infliximab for patients identified as carriers of HBV and monitor closely for active HBV infection during and following termination of therapy with either REMICADE® or Infliximab. Discontinue either REMICADE® or Infliximab in patients who develop HBV reactivation and initiate antiviral therapy with appropriate supportive treatment. Exercise caution when considering resumption of either REMICADE® or Infliximab and monitor patients closely.

HEPATOTOXICITY

Severe hepatic reactions, including acute liver failure, jaundice, hepatitis, and cholestasis have been reported in patients receiving either REMICADE® or Infliximab postmarketing. Some cases were fatal or required liver transplant. Aminotransferase elevations were not noted prior to discovery of liver injury in many cases. Patients with symptoms or signs of liver dysfunction should be evaluated for evidence of liver injury. If jaundice and/or marked liver enzyme elevations (eg, ≥5 times the upper limit of normal) develop, either REMICADE® or Infliximab should be discontinued, and a thorough investigation of the abnormality should be undertaken.

HEART FAILURE

In a randomized, placebo-controlled study in patients with moderate or severe heart failure (NYHA Functional Class III/IV), higher mortality rates and a higher risk of hospitalization were observed at Week 28 at a dose of 10 mg/kg and higher rates of cardiovascular events were observed at both 5 mg/kg and 10 mg/kg. There have been postmarketing reports of new onset and worsening heart failure, with and without identifiable precipitating factors. Patients with moderate or severe heart failure taking either REMICADE® or Infliximab (≤5 mg/kg) or patients with mild heart failure should be closely monitored and treatment should be discontinued if new or worsening symptoms appear.

HEMATOLOGIC EVENTS

Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia (some fatal) have been reported. The causal relationship to REMICADE® and Infliximab therapy remains unclear. Exercise caution in patients who have ongoing or a history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs and symptoms of blood dyscrasias or infection. Consider discontinuation of either REMICADE® or Infliximab in patients who develop significant hematologic abnormalities.

HYPERSENSITIVITY

REMICADE® and Infliximab have been associated with hypersensitivity reactions that differ in their time of onset. Anaphylaxis, acute urticaria, dyspnea, and hypotension have occurred in association with infusions of either REMICADE® or Infliximab. Medications for the treatment of hypersensitivity reactions should be available.

CARDIOVASCULAR AND CEREBROVASCULAR REACTIONS DURING AND AFTER INFUSION

Serious cerebrovascular accidents, myocardial ischemia/infarction (some fatal), hypotension,

Important Safety Information (cont)

CARDIOVASCULAR AND CEREBROVASCULAR REACTIONS DURING AND AFTER INFUSION (cont)

hypertension, and arrhythmias have been reported during and within 24 hours of initiation of either REMICADE® or Infliximab infusions. Cases of transient visual loss have been reported during or within 2 hours of either REMICADE® or Infliximab infusions. Monitor patients during infusion and if a serious reaction occurs, discontinue infusion. Manage reactions according to signs and symptoms.

NEUROLOGIC EVENTS

TNF blockers, including REMICADE® and Infliximab, have been associated with CNS manifestation of systemic vasculitis, seizure, and new onset or exacerbation of CNS demyelinating disorders, including multiple sclerosis and optic neuritis, and peripheral demyelinating disorders, including Guillain-Barré syndrome. Exercise caution when considering either REMICADE® or Infliximab in patients with these disorders and consider discontinuation if these disorders develop.

CONCURRENT ADMINISTRATION WITH OTHER BIOLOGICS

Concurrent use of either REMICADE® or Infliximab with anakinra, abatacept, tocilizumab, or other biologics used to treat the same conditions as REMICADE® and Infliximab is not recommended because of the possibility of an increased risk of infection. Care should be taken when switching from one biologic to another, since overlapping biological activity may further increase the risk of infection.

AUTOIMMUNITY

Treatment with either REMICADE® or Infliximab may result in the formation of autoantibodies and in the development of a lupus-like syndrome. Discontinue treatment if symptoms of a lupus-like syndrome develop.

VACCINATIONS AND USE OF LIVE VACCINES/THERAPEUTIC INFECTIOUS AGENTS

Prior to initiating either REMICADE® or Infliximab, update vaccinations in accordance with current vaccination guidelines. Live vaccines or therapeutic infectious agents should not be given with either REMICADE® or Infliximab due to the possibility of clinical infections, including disseminated infections.

At least a 6-month waiting period following birth is recommended before the administration of any live vaccine to infants exposed *in utero* to either REMICADE® or Infliximab.

ADVERSE REACTIONS

In clinical trials, the most common adverse reactions occurring in >10% of REMICADE®- and Infliximab-treated patients included infections (eg, upper respiratory, sinusitis, and pharyngitis), infusion-related reactions, headache, and abdominal pain.

cp-253861

For more information, please see the full Prescribing Information, including Boxed Warning and Medication Guide for REMICADE® and full Prescribing Information, including Boxed Warning and Medication Guide for Infliximab. Provide the Medication Guides to your patients and encourage discussion.

References: 1. American Thoracic Society, Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. *Am J Respir Crit Care Med*. 2000;161:S221-S247. **2.** See latest Centers for Disease Control guidelines and recommendations for tuberculosis testing in immunocompromised patients.