Similar results were seen in an additional, 12-week study in 100 patients with moderate to severe psoriatic arthritis who had suboptimal response to DMARD therapy as manifested by ≥3 tender joints and ≥3 swollen joints at enrollment.

Radiographic Response

Radiographic changes were assessed in the PsA studies. Radiographs of hands, wrists, and feet were obtained at baseline and Week 24 during the double-blind period when patients were on HUMIRA or placebo and at Week 48 when all patients were on open-label HUMIRA. A modified Total Sharp Score (mTSS), which included distal interphalangeal joints (i.e., not identical to the TSS used for rheumatoid arthritis), was used by readers blinded to treatment group to assess the radiographs.

HUMIRA-treated patients demonstrated greater inhibition of radiographic progression compared to placebo-treated patients and this effect was maintained at 48 weeks (see Table 10).

Table 10. Change in Modified Total Sharp Score in Psoriatic Arthritis

	Placebo N=141	**HUMIRA N=133**	
	Week 24	Week 24	Week 48
Baseline mean	22.1	23.4	23.4
Mean Change ± SD	0.9 ± 3.1	-0.1 ± 1.7	-0.2 ± 4.9*
* <0.001 for the difference between HUMIRA, Week 48 and Placebo, Week 24 (primary analysis)			

Physical Function Response

In Study PsA-I, physical function and disability were assessed using the HAQ Disability Index (HAQ-DI) and the SF-36 Health Survey. Patients treated with 40 mg of HUMIRA every other week showed greater improvement from baseline in the HAQ-DI score (mean decreases of 47% and 49% at Weeks 12 and 24 respectively) in comparison to placebo (mean decreases of 1% and 3% at Weeks 12 and 24 respectively). At Weeks 12 and 24, patients treated with HUMIRA showed greater improvement from baseline in the SF-36 Physical Component Summary score compared to patients treated with placebo, and no worsening in the SF-36 Mental Component Summary score. Improvement in physical function based on the HAQ-DI was maintained for up to 84 weeks through the open-label portion of the study.

14.4 Ankylosing Spondylitis

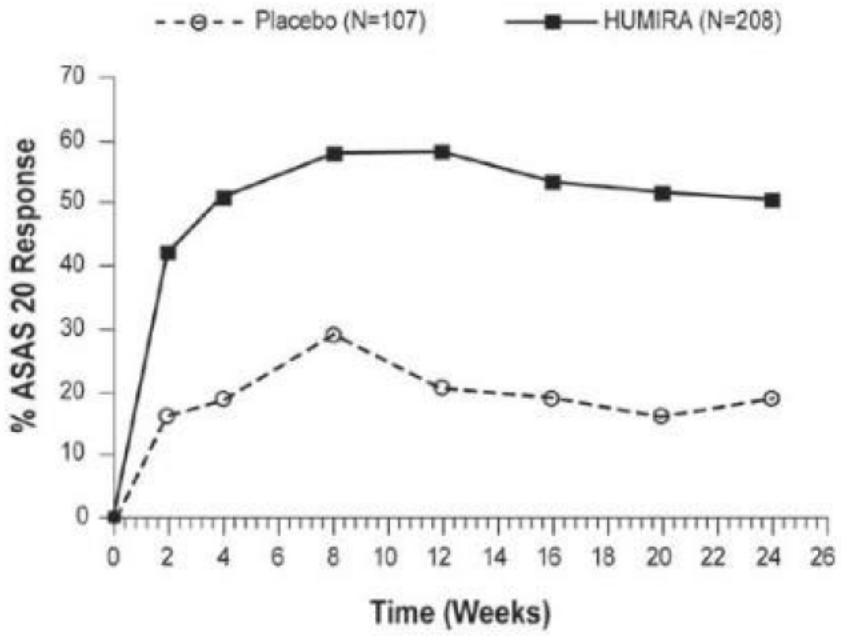
The safety and efficacy of HUMIRA 40 mg every other week was assessed in 315 adult patients in a randomized, 24 week double-blind, placebo-controlled study in patients with active ankylosing spondylitis (AS) who had an inadequate response to glucocorticoids, NSAIDs, analgesics, methotrexate or sulfasalazine. Active AS was defined as patients who fulfilled at least two of the following three criteria: (1) a Bath AS disease activity index (BASDAI) score ≥4 cm, (2) a visual analog score (VAS) for total back pain ≥ 40 mm, and (3) morning stiffness ≥ 1 hour. The blinded period was followed by an open-label period during which patients received HUMIRA 40 mg every other week subcutaneously for up to an additional 28 weeks.

Improvement in measures of disease activity was first observed at Week 2 and maintained through 24 weeks as shown in Figure 2 and Table 11.

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Responses of patients with total spinal ankylosis (n=11) were similar to those without total ankylosis.

Figure 2. ASAS 20 Response By Visit, Study AS-I



At 12 weeks, the ASAS 20/50/70 responses were achieved by 58%, 38%, and 23%, respectively, of patients receiving HUMIRA, compared to 21%, 10%, and 5% respectively, of patients receiving placebo ($p < 0.001$). Similar responses were seen at Week 24 and were sustained in patients receiving open-label HUMIRA for up to 52 weeks.

A greater proportion of patients treated with HUMIRA (22%) achieved a low level of disease activity at 24 weeks (defined as a value <20 [on a scale of 0 to 100 mm] in each of the four ASAS response parameters) compared to patients treated with placebo (6%).

Table 11. Components of Ankylosing Spondylitis Disease Activity

	Placebo N=107		HUMIRA N=208	
	Baseline mean	Week 24 mean	Baseline mean	Week 24 mean
ASAS 20 Response Criteria*				
Patient's Global Assessment of Disease Activity[a*]	65	60	63	38
Total back pain*	67	58	65	37
Inflammation[b*]	6.7	5.6	6.7	3.6
BASFI[c*]	56	51	52	34
BASDAI[d] score*	6.3	5.5	6.3	3.7
BASMI[e] score*	4.2	4.1	3.8	3.3
Tragus to wall (cm)	15.9	15.8	15.8	15.4

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Lumbar flexion (cm)	4.1	4.0	4.2	4.4
Cervical rotation (degrees)	42.2	42.1	48.4	51.6
Lumbar side flexion (cm)	8.9	9.0	9.7	11.7
Intermalleolar distance (cm)	92.9	94.0	93.5	100.8
CRP[f*]	2.2	2.0	1.8	0.6

[a] Percent of subjects with at least a 20% and 10-unit improvement measured on a Visual Analog Scale (VAS) with 0 = "none" and 100 = "severe"
[b] mean of questions 5 and 6 of BASDAI (defined in 'd')
[c] Bath Ankylosing Spondylitis Functional Index
[d] Bath Ankylosing Spondylitis Disease Activity Index
[e] Bath Ankylosing Spondylitis Metrology Index
[f] C-Reactive Protein (mg/dL)
* statistically significant for comparisons between HUMIRA and placebo at Week 24

A second randomized, multicenter, double-blind, placebo-controlled study of 82 patients with ankylosing spondylitis showed similar results.

Patients treated with HUMIRA achieved improvement from baseline in the Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) score (-3.6 *vs.* -1.1) and in the Short Form Health Survey (SF-36) Physical Component Summary (PCS) score (7.4 *vs.* 1.9) compared to placebo-treated patients at Week 24.

14.5 Adult Crohn's Disease

The safety and efficacy of multiple doses of HUMIRA were assessed in adult patients with moderately to severely active Crohn's disease, CD, (Crohn's Disease Activity Index (CDAI) ≥ 220 and ≤ 450) in randomized, double-blind, placebo-controlled studies. Concomitant stable doses of aminosalicylates, corticosteroids, and/or immunomodulatory agents were permitted, and 79% of patients continued to receive at least one of these medications.

Induction of clinical remission (defined as CDAI < 150) was evaluated in two studies. In Study CD-I, 299 TNF-blocker naïve patients were randomized to one of four treatment groups: the placebo group received placebo at Weeks 0 and 2, the 160/80 group received 160 mg HUMIRA at Week 0 and 80 mg at Week 2, the 80/40 group received 80 mg at Week 0 and 40 mg at Week 2, and the 40/20 group received 40 mg at Week 0 and 20 mg at Week 2. Clinical results were assessed at Week 4.

In the second induction study, Study CD-II, 325 patients who had lost response to, or were intolerant to, previous infliximab therapy were randomized to receive either 160 mg HUMIRA at Week 0 and 80 mg at Week 2, or placebo at Weeks 0 and 2. Clinical results were assessed at Week 4.

Maintenance of clinical remission was evaluated in Study CD-III. In this study, 854 patients with active disease received open-label HUMIRA, 80 mg at week 0 and 40 mg at Week 2. Patients were then randomized at Week 4 to 40 mg HUMIRA every other week, 40 mg HUMIRA every week, or placebo. The total study duration was 56 weeks. Patients in clinical response (decrease in CDAI ≥70) at Week 4 were stratified and analyzed separately from those not in clinical response at Week 4.

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Induction of Clinical Remission

A greater percentage of the patients treated with 160/80 mg HUMIRA achieved induction of clinical remission versus placebo at Week 4 regardless of whether the patients were TNF blocker naïve (CD-I), or had lost response to or were intolerant to infliximab (CD-II) (see Table 12).

Table 12. Induction of Clinical Remission in Studies CD-I and CD-II (Percent of Patients)

	CD-I		CD-II	
	Placebo N=74	**HUMIRA 160/80 mg N=76**	**Placebo N=166**	**HUMIRA 160/80 mg N=159**
Week 4				
Clinical remission	12%	36%*	7%	21%*
Clinical response	34%	58%**	34%	52%**

Clinical remission is CDAI score < 150; clinical response is decrease in CDAI of at least 70 points.
* p<0.001 for HUMIRA *vs.* placebo pairwise comparison of proportions
** p<0.01 for HUMIRA *vs.* placebo pairwise comparison of proportions

Maintenance of Clinical Remission

In Study CD-III at Week 4, 58% (499/854) of patients were in clinical response and were assessed in the primary analysis. At Weeks 26 and 56, greater proportions of patients who were in clinical response at Week 4 achieved clinical remission in the HUMIRA 40 mg every other week maintenance group compared to patients in the placebo maintenance group (see Table 13). The group that received HUMIRA therapy every week did not demonstrate significantly higher remission rates compared to the group that received HUMIRA every other week.

Table 13. Maintenance of Clinical Remission in CD-III (Percent of Patients)

	Placebo	**40 mg HUMIRA every other week**
	N=170	**N=172**
Week 26		
Clinical remission	17%	40%*
Clinical response	28%	54%*
Week 56		
Clinical remission	12%	36%*
Clinical response	18%	43%*

Clinical remission is CDAI score < 150; clinical response is decrease in CDAI of at least 70 points.
*p<0.001 for HUMIRA vs. placebo pairwise comparisons of proportions

Of those in response at Week 4 who attained remission during the study, patients in the HUMIRA every other week group maintained remission for a longer time than patients in the placebo maintenance group. Among patients who were not in response by Week 12, therapy continued beyond 12 weeks did not result in significantly more responses.

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14.6 Pediatric Crohn's Disease

A randomized, double-blind, 52-week clinical study of 2 dose concentrations of HUMIRA (Study PCD-I) was conducted in 192 pediatric patients (6 to 17 years of age) with moderately to severely active Crohn's disease (defined as Pediatric Crohn's Disease Activity Index (PCDAI) score > 30). Enrolled patients had over the previous two year period an inadequate response to corticosteroids or an immunomodulator (i.e., azathioprine, 6-mercaptopurine, or methotrexate). Patients who had previously received a TNF blocker were allowed to enroll if they had previously had loss of response or intolerance to that TNF blocker.

Patients received open-label induction therapy at a dose based on their body weight (≥40 kg and <40 kg). Patients weighing ≥40 kg received 160 mg (at Week 0) and 80 mg (at Week 2). Patients weighing <40 kg received 80 mg (at Week 0) and 40 mg (at Week 2). At Week 4, patients within each body weight category (≥40 kg and <40 kg) were randomized 1:1 to one of two maintenance dose regimens (high dose and low dose). The high dose was 40 mg every other week for patients weighing ≥40 kg and 20 mg every other week for patients weighing <40 kg. The low dose was 20 mg every other week for patients weighing ≥40 kg and 10 mg every other week for patients weighing <40 kg.

Concomitant stable dosages of corticosteroids (prednisone dosage ≤40 mg/day or equivalent) and immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate) were permitted throughout the study.

At Week 12, patients who experienced a disease flare (increase in PCDAI of ≥ 15 from Week 4 and absolute PCDAI > 30) or who were non-responders (did not achieve a decrease in the PCDAI of ≥ 15 from baseline for 2 consecutive visits at least 2 weeks apart) were allowed to dose-escalate (i.e., switch from blinded every other week dosing to blinded every week dosing); patients who dose-escalated were considered treatment failures.

At baseline, 38% of patients were receiving corticosteroids, and 62% of patients were receiving an immunomodulator. Forty-four percent (44%) of patients had previously lost response or were intolerant to a TNF blocker. The median baseline PCDAI score was 40.

Of the 192 patients total, 188 patients completed the 4 week induction period, 152 patients completed 26 weeks of treatment, and 124 patients completed 52 weeks of treatment. Fifty-one percent (51%) (48/95) of patients in the low maintenance dose group dose-escalated, and 38% (35/93) of patients in the high maintenance dose group dose-escalated.

At Week 4, 28% (52/188) of patients were in clinical remission (defined as PCDAI ≤ 10).

The proportions of patients in clinical remission (defined as PCDAI ≤ 10) and clinical response (defined as reduction in PCDAI of at least 15 points from baseline) were assessed at Weeks 26 and 52.

At both Weeks 26 and 52, the proportion of patients in clinical remission and clinical response was numerically higher in the high dose group compared to the low dose group (Table 14). The recommended maintenance regimen is 20 mg every other week for patients weighing < 40 kg and 40 mg every other week for patients weighing ≥ 40 kg. Every week dosing is not the recommended maintenance dosing regimen *[see Dosage and Administration (2.3)]*.

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Table 14. Clinical Remission and Clinical Response in Study PCD-I

	Low Maintenance Dose[†] (20 or 10 mg every other week) N = 95	High Maintenance Dose[#] (40 or 20 mg every other week) N = 93
Week 26		
Clinical Remission[‡]	28%	39%
Clinical Response[§]	48%	59%
Week 52		
Clinical Remission[‡]	23%	33%
Clinical Response[§]	28%	42%

[†]The low maintenance dose was 20 mg every other week for patients weighing ≥ 40 kg and 10 mg every other week for patients weighing < 40 kg.
[#]The high maintenance dose was 40 mg every other week for patients weighing ≥ 40 kg and 20 mg every other week for patients weighing < 40 kg.
[‡]Clinical remission defined as PCDAI ≤ 10.
[§]Clinical response defined as reduction in PCDAI of at least 15 points from baseline.

14.7 Adult Ulcerative Colitis

The safety and efficacy of HUMIRA were assessed in adult patients with moderately to severely active ulcerative colitis (Mayo score 6 to 12 on a 12 point scale, with an endoscopy subscore of 2 to 3 on a scale of 0 to 3) despite concurrent or prior treatment with immunosuppressants such as corticosteroids, azathioprine, or 6-MP in two randomized, double-blind, placebo-controlled clinical studies (Studies UC-I and UC-II). Both studies enrolled TNF-blocker naïve patients, but Study UC-II also allowed entry of patients who lost response to or were intolerant to TNF-blockers. Forty percent (40%) of patients enrolled in Study UC-II had previously used another TNF-blocker.

Concomitant stable doses of aminosalicylates and immunosuppressants were permitted. In Studies UC-I and II, patients were receiving aminosalicylates (69%), corticosteroids (59%) and/or azathioprine or 6-MP (37%) at baseline. In both studies, 92% of patients received at least one of these medications.

Induction of clinical remission (defined as Mayo score ≤ 2 with no individual subscores > 1) at Week 8 was evaluated in both studies. Clinical remission at Week 52 and sustained clinical remission (defined as clinical remission at both Weeks 8 and 52) were evaluated in Study UC-II.

In Study UC-I, 390 TNF-blocker naïve patients were randomized to one of three treatment groups for the primary efficacy analysis. The placebo group received placebo at Weeks 0, 2, 4 and 6. The 160/80 group received 160 mg HUMIRA at Week 0 and 80 mg at Week 2, and the 80/40 group received 80 mg HUMIRA at Week 0 and 40 mg at Week 2. After Week 2, patients in both HUMIRA treatment groups received 40 mg every other week.

In Study UC-II, 518 patients were randomized to receive either HUMIRA 160 mg at Week 0, 80 mg at Week 2, and 40 mg every other week starting at Week 4 through Week 50, or placebo starting at Week 0 and every other week through Week 50. Corticosteroid taper was permitted starting at Week 8.

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In both Studies UC-I and UC-II, a greater percentage of the patients treated with 160/80 mg of HUMIRA compared to patients treated with placebo achieved induction of clinical remission. In Study UC-II, a greater percentage of the patients treated with 160/80 mg of HUMIRA compared to patients treated with placebo achieved sustained clinical remission (clinical remission at both Weeks 8 and 52) (Table 15).

Table 15. Induction of Clinical Remission in Studies UC-I and UC-II and Sustained Clinical Remission in Study UC-II (Percent of Patients)

	Study UC-I			Study UC-II		
	Placebo N=130	HUMIRA 160/80 mg N=130	Treatment Difference (95% CI)	Placebo N=246	HUMIRA 160/80 mg N=248	Treatment Difference (95% CI)
Induction of Clinical Remission (Clinical Remission at Week 8)	9.2%	18.5%	9.3%* (0.9%, 17.6%)	9.3%	16.5%	7.2%* (1.2%, 12.9%)
Sustained Clinical Remission (Clinical Remission at both Weeks 8 and 52)	N/A	N/A	N/A	4.1%	8.5%	4.4%* (0.1%, 8.6%)
Clinical remission is defined as Mayo score ≤ 2 with no individual subscores > 1. CI=Confidence interval * $p<0.05$ for HUMIRA *vs.* placebo pairwise comparison of proportions						

In Study UC-I, there was no statistically significant difference in clinical remission observed between the HUMIRA 80/40 mg group and the placebo group at Week 8.

In Study UC-II, 17.3% (43/248) in the HUMIRA group were in clinical remission at Week 52 compared to 8.5% (21/246) in the placebo group (treatment difference: 8.8%; 95% confidence interval (CI): [2.8%, 14.5%]; $p<0.05$).

In the subgroup of patients in Study UC-II with prior TNF-blocker use, the treatment difference for induction of clinical remission appeared to be lower than that seen in the whole study population, and the treatment differences for sustained clinical remission and clinical remission at Week 52 appeared to be similar to those seen in the whole study population. The subgroup of patients with prior TNF-blocker use achieved induction of clinical remission at 9% (9/98) in the HUMIRA group versus 7% (7/101) in the placebo group, and sustained clinical remission at 5% (5/98) in the HUMIRA group versus 1% (1/101) in the placebo group. In the subgroup of patients with prior TNF-blocker use, 10% (10/98) were in clinical remission at Week 52 in the HUMIRA group versus 3% (3/101) in the placebo group.

14.8 Pediatric Ulcerative Colitis

The safety and efficacy of HUMIRA were assessed in a multicenter, randomized, double-blind trial (Study PUC-I, NCT02065557) in 93 pediatric patients 5 years to 17 years of age with moderately to severely active ulcerative colitis (Mayo score 6 to 12 with endoscopy subscore of

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2 to 3 points, confirmed by centrally read endoscopy) who had an inadequate response or intolerance to therapy with corticosteroids and/or an immunomodulator (i.e., azathioprine, 6-mercaptopurine, or methotrexate). Fifteen out of 93 patients (16%) in the study had prior experience with a TNF blocker. Patients who received corticosteroids at enrollment were allowed to taper their corticosteroid therapy after Week 4.

Seventy-seven patients were initially randomized 3:2 to receive double-blind treatment with one of two dosages of HUMIRA. Patients in both dosage groups received 2.4 mg/kg (maximum of 160 mg) at Week 0, 1.2 mg/kg (maximum of 80 mg) at Week 2, and 0.6 mg/kg (maximum of 40 mg) at Weeks 4 and 6. The higher dosage group also received an additional dosage of 2.4 mg/kg (maximum of 160 mg) at Week 1. Following an amendment to the study design, 16 additional patients were enrolled and received open-label treatment with HUMIRA at the higher dosage.

At Week 8, 62 patients who demonstrated clinical response per Partial Mayo Score (PMS; a subset of the Mayo score with no endoscopic component and defined as a decrease in PMS ≥ 2 points and $\geq 30\%$ from baseline) were randomized equally to receive double-blind treatment with HUMIRA 0.6 mg/kg (maximum of 40 mg) every other week (lower dosage group), or 0.6 mg/kg (maximum of 40 mg) every week (higher dosage group). Prior to an amendment to the study design, 12 additional patients who demonstrated clinical response per PMS were randomized to receive placebo.

There are no anticipated clinically relevant differences in efficacy between the studied higher dosage administered during the 52-week PUC-I trial and the recommended dosage of HUMIRA *[see Dosage and Administration (2.4), Clinical Pharmacology (12.2)]*.

Patients who met criteria for disease flare at or after Week 12 were randomized to receive a re-induction dose of 2.4 mg/kg (maximum of 160 mg) or a dose of 0.6 mg/kg (maximum of 40 mg) and then continued the dose to which they were randomized at Week 8.

The co-primary endpoints of the study were clinical remission per PMS (defined as PMS ≤ 2 and no individual subscore > 1) at Week 8, and clinical remission per the Mayo Score (defined as Mayo Score ≤ 2 and no individual subscore > 1) at Week 52 in patients who achieved clinical response per PMS at Week 8. Secondary endpoints included Mayo Score response (defined as a decrease in Mayo Score of ≥ 3 points and $\geq 30\%$ from baseline) at Week 52 in Week 8 PMS responders, endoscopic improvement (defined as a Mayo endoscopy subscore ≤ 1) at Week 52 in Week 8 PMS responders, and Mayo Score remission at Week 52 in Week 8 PMS remitters.

Week 8 Results

At Week 8, PMS remission was achieved by 60% [28/47; 95% confidence interval (CI): (44%, 74%)] of patients in the higher dosage group (not including the 16 patients receiving open-label higher dosage) and 43% [13/30; 95% CI: (25%, 63%)] of patients in the lower dosage group. Results from the higher dosage group are representative of the results expected with the recommended dosage *[see Dosage and Administration (2.4), Clinical Pharmacology (12.2)]*.

Week 52 Results

At Week 52, endpoints were assessed in the population of patients who received double-blind placebo, HUMIRA 0.6 mg/kg (maximum of 40 mg) every other week, or HUMIRA 0.6 mg/kg (maximum of 40 mg) every week between Week 8 and Week 52 (Table 16).

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Table 16. Clinical Remission, Clinical Response and Endoscopic Improvement at Week 52 in Pediatric Patients with Ulcerative Colitis (Study PUC-1)

	Placebo[a] n/N (%), 95% CI	HUMIRA Maximum of 40 mg (0.6 mg/kg) every other week[b] n/N (%), 95% CI	HUMIRA Maximum of 40 mg (0.6 mg/kg) every week[c] n/N (%), 95% CI
Clinical remission in Week 8 PMS responders	4/12 (33%) (10%, 65%)	9/31 (29%) (14%, 48%)	14/31 (45%) (27%, 64%)
Clinical response in Week 8 PMS responders	4/12 (33%) (10%, 65%)	19/31 (61%) (42%, 78%)	21/31 (68%) (49%, 83%)
Endoscopic improvement in Week 8 PMS responders	4/12 (33%) (10%, 65%)	12/31 (39%) (22%, 58%)	16/31 (52%) (33%, 70%)
Clinical remission in Week 8 PMS remitters	3/8 (38%) (9%, 76%)	9/21 (43%) (22%, 66%)	10/22 (45%) (24%, 68%)

CI=Confidence interval

[a] Twelve patients who demonstrated clinical response per PMS at Week 8 were randomized to receive placebo. There are limitations to the interpretability of the placebo data due to the small sample size.

[b] The every other week dosage studied during the 52-week PUC-I trial is a lower dosage than the recommended dosage of HUMIRA *[see Dosage and Administration (2.4)]*.

[c] There are no anticipated clinically relevant differences in efficacy between the studied higher dosage administered during the 52-week PUC-I trial and the recommended dosage of HUMIRA.

Note: Patients with missing values at Week 52 or who were randomized to receive re-induction or maintenance treatment due to disease flare were considered non-responders for Week 52 endpoints.

14.9 Plaque Psoriasis

The safety and efficacy of HUMIRA were assessed in randomized, double-blind, placebo-controlled studies in 1696 adult subjects with moderate to severe chronic plaque psoriasis (Ps) who were candidates for systemic therapy or phototherapy.

Study Ps-I evaluated 1212 subjects with chronic Ps with ≥10% body surface area (BSA) involvement, Physician's Global Assessment (PGA) of at least moderate disease severity, and Psoriasis Area and Severity Index (PASI) ≥12 within three treatment periods. In period A, subjects received placebo or HUMIRA at an initial dose of 80 mg at Week 0 followed by a dose of 40 mg every other week starting at Week 1. After 16 weeks of therapy, subjects who achieved at least a PASI 75 response at Week 16, defined as a PASI score improvement of at least 75% relative to baseline, entered period B and received open-label 40 mg HUMIRA every other week.

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After 17 weeks of open label therapy, subjects who maintained at least a PASI 75 response at Week 33 and were originally randomized to active therapy in period A were re-randomized in period C to receive 40 mg HUMIRA every other week or placebo for an additional 19 weeks. Across all treatment groups the mean baseline PASI score was 19 and the baseline Physician's Global Assessment score ranged from "moderate" (53%) to "severe" (41%) to "very severe" (6%).

Study Ps-II evaluated 99 subjects randomized to HUMIRA and 48 subjects randomized to placebo with chronic plaque psoriasis with ≥10% BSA involvement and PASI ≥12. Subjects received placebo, or an initial dose of 80 mg HUMIRA at Week 0 followed by 40 mg every other week starting at Week 1 for 16 weeks. Across all treatment groups the mean baseline PASI score was 21 and the baseline PGA score ranged from "moderate" (41%) to "severe" (51%) to "very severe" (8%).

Studies Ps-I and II evaluated the proportion of subjects who achieved "clear" or "minimal" disease on the 6-point PGA scale and the proportion of subjects who achieved a reduction in PASI score of at least 75% (PASI 75) from baseline at Week 16 (see Table 17 and 18).

Additionally, Study Ps-I evaluated the proportion of subjects who maintained a PGA of "clear" or "minimal" disease or a PASI 75 response after Week 33 and on or before Week 52.

Table 17. Efficacy Results at 16 Weeks in Study Ps-I Number of Subjects (%)

	HUMIRA 40 mg every other week	Placebo
	N = 814	N = 398
PGA: *Clear* or *minimal**	506 (62%)	17 (4%)
PASI 75	578 (71%)	26 (7%)
* Clear = no plaque elevation, no scale, plus or minus hyperpigmentation or diffuse pink or red coloration Minimal = possible but difficult to ascertain whether there is slight elevation of plaque above normal skin, plus or minus surface dryness with some white coloration, plus or minus up to red coloration		

Table 18. Efficacy Results at 16 Weeks in Study Ps-II Number of Subjects (%)

	HUMIRA 40 mg every other week	Placebo
	N = 99	N = 48
PGA: *Clear* or *minimal**	70 (71%)	5 (10%)
PASI 75	77 (78%)	9 (19%)
* Clear = no plaque elevation, no scale, plus or minus hyperpigmentation or diffuse pink or red coloration Minimal = possible but difficult to ascertain whether there is slight elevation of plaque above normal skin, plus or minus surface dryness with some white coloration, plus or minus up to red coloration		

Additionally, in Study Ps-I, subjects on HUMIRA who maintained a PASI 75 were re-randomized to HUMIRA (N = 250) or placebo (N = 240) at Week 33. After 52 weeks of treatment with HUMIRA, more subjects on HUMIRA maintained efficacy when compared to

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subjects who were re-randomized to placebo based on maintenance of PGA of "clear" or "minimal" disease (68% *vs.* 28%) or a PASI 75 (79% *vs.* 43%).

A total of 347 stable responders participated in a withdrawal and retreatment evaluation in an open-label extension study. Median time to relapse (decline to PGA "moderate" or worse) was approximately 5 months. During the withdrawal period, no subject experienced transformation to either pustular or erythrodermic psoriasis. A total of 178 subjects who relapsed re-initiated treatment with 80 mg of HUMIRA, then 40 mg every other week beginning at week 1. At week 16, 69% (123/178) of subjects had a response of PGA "clear" or "minimal".

A randomized, double-blind study (Study Ps-III) compared the efficacy and safety of HUMIRA versus placebo in 217 adult subjects. Subjects in the study had to have chronic plaque psoriasis of at least moderate severity on the PGA scale, fingernail involvement of at least moderate severity on a 5-point Physician's Global Assessment of Fingernail Psoriasis (PGA-F) scale, a Modified Nail Psoriasis Severity Index (mNAPSI) score for the target-fingernail of ≥ 8, and either a BSA involvement of at least 10% or a BSA involvement of at least 5% with a total mNAPSI score for all fingernails of ≥ 20. Subjects received an initial dose of 80 mg HUMIRA followed by 40 mg every other week (starting one week after the initial dose) or placebo for 26 weeks followed by open-label HUMIRA treatment for an additional 26 weeks. This study evaluated the proportion of subjects who achieved "clear" or "minimal" assessment with at least a 2-grade improvement on the PGA-F scale and the proportion of subjects who achieved at least a 75% improvement from baseline in the mNAPSI score (mNAPSI 75) at Week 26.

At Week 26, a higher proportion of subjects in the HUMIRA group than in the placebo group achieved the PGA-F endpoint. Furthermore, a higher proportion of subjects in the HUMIRA group than in the placebo group achieved mNAPSI 75 at Week 26 (see Table 19).

Table 19. Efficacy Results at 26 Weeks

Endpoint	HUMIRA 40 mg every other week* N=109	Placebo N=108
PGA-F: ≥2-grade improvement and *clear* or *minimal*	49%	7%
mNAPSI 75	47%	3%

*Subjects received 80 mg of HUMIRA at Week 0, followed by 40 mg every other week starting at Week 1.

Nail pain was also evaluated and improvement in nail pain was observed in Study Ps-III.

14.10 Hidradenitis Suppurativa

Two randomized, double-blind, placebo-controlled studies (Studies HS-I and II) evaluated the safety and efficacy of HUMIRA in a total of 633 adult subjects with moderate to severe hidradenitis suppurativa (HS) with Hurley Stage II or III disease and with at least 3 abscesses or inflammatory nodules. In both studies, subjects received placebo or HUMIRA at an initial dose of 160 mg at Week 0, 80 mg at Week 2, and 40 mg every week starting at Week 4 and continued through Week 11. Subjects used topical antiseptic wash daily. Concomitant oral antibiotic use was allowed in Study HS-II.

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Both studies evaluated Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12. HiSCR was defined as at least a 50% reduction in total abscess and inflammatory nodule count with no increase in abscess count and no increase in draining fistula count relative to baseline (see Table 18). Reduction in HS-related skin pain was assessed using a Numeric Rating Scale in patients who entered the study with an initial baseline score of 3 or greater on a 11 point scale.

In both studies, a higher proportion of HUMIRA- than placebo-treated subjects achieved HiSCR (see Table 20).

Table 20. Efficacy Results at 12 Weeks in Subjects with Moderate to Severe Hidradenitis Suppurativa

	HS Study I		HS Study II*	
	Placebo	**Humira 40 mg Weekly**	**Placebo**	**Humira 40 mg Weekly**
Hidradenitis Suppurativa Clinical Response (HiSCR)	N = 154 40 (26%)	N = 153 64 (42%)	N=163 45 (28%)	N=163 96 (59%)
*19.3% of subjects in Study HS-II continued baseline oral antibiotic therapy during the study.				

In both studies, from Week 12 to Week 35 (Period B), subjects who had received HUMIRA were re-randomized to 1 of 3 treatment groups (HUMIRA 40 mg every week, HUMIRA 40 mg every other week, or placebo). Subjects who had been randomized to placebo were assigned to receive HUMIRA 40 mg every week (Study HS-I) or placebo (Study HS-II).

During Period B, flare of HS, defined as ≥25% increase from baseline in abscesses and inflammatory nodule counts and with a minimum of 2 additional lesions, was documented in 22 (22%) of the 100 subjects who were withdrawn from HUMIRA treatment following the primary efficacy timepoint in two studies.

14.11 Adult Uveitis

The safety and efficacy of HUMIRA were assessed in adult patients with non-infectious intermediate, posterior and panuveitis excluding patients with isolated anterior uveitis, in two randomized, double-masked, placebo-controlled studies (UV I and II). Patients received placebo or HUMIRA at an initial dose of 80 mg followed by 40 mg every other week starting one week after the initial dose. The primary efficacy endpoint in both studies was ´time to treatment failure´.

Treatment failure was a multi-component outcome defined as the development of new inflammatory chorioretinal and/or inflammatory retinal vascular lesions, an increase in anterior chamber (AC) cell grade or vitreous haze (VH) grade or a decrease in best corrected visual acuity (BCVA).

Study UV I evaluated 217 patients with active uveitis while being treated with corticosteroids (oral prednisone at a dose of 10 to 60 mg/day). All patients received a standardized dose of prednisone 60 mg/day at study entry followed by a mandatory taper schedule, with complete corticosteroid discontinuation by Week 15.

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Study UV II evaluated 226 patients with inactive uveitis while being treated with corticosteroids (oral prednisone 10 to 35 mg/day) at baseline to control their disease. Patients subsequently underwent a mandatory taper schedule, with complete corticosteroid discontinuation by Week 19.

Clinical Response

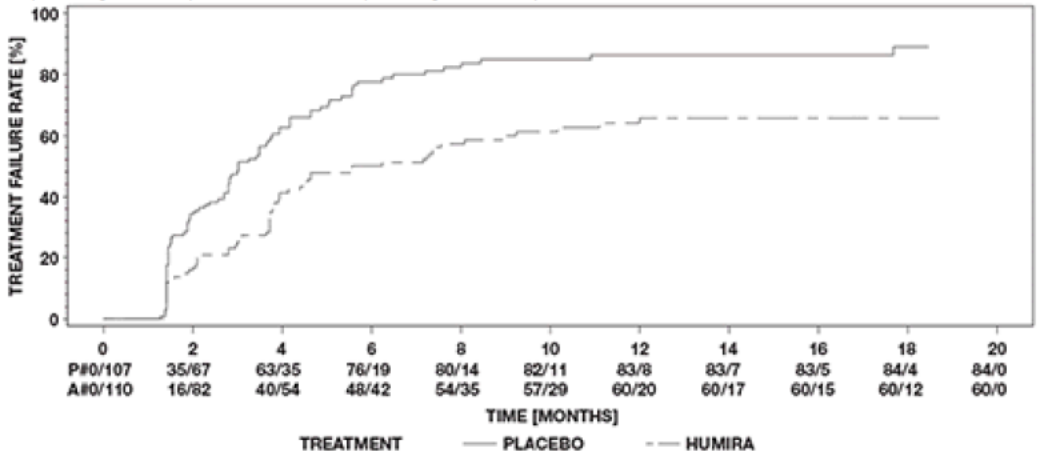
Results from both studies demonstrated statistically significant reduction of the risk of treatment failure in patients treated with HUMIRA versus patients receiving placebo. In both studies, all components of the primary endpoint contributed cumulatively to the overall difference between HUMIRA and placebo groups (Table 21).

Table 21. Time to Treatment Failure in Studies UV I and UV II

	UV I			UV II		
	Placebo (N = 107)	HUMIRA (N = 110)	HR [95% CI][a]	Placebo (N = 111)	HUMIRA (N = 115)	HR [95% CI][a]
Failure[b] n (%)	84 (78.5)	60 (54.5)	0.50 [0.36, 0.70]	61 (55.0)	45 (39.1)	0.57 [0.39, 0.84]
Median Time to Failure (Months) [95% CI]	3.0 [2.7, 3.7]	5.6 [3.9, 9.2]	N/A	8.3 [4.8, 12.0]	NE[c]	N/A

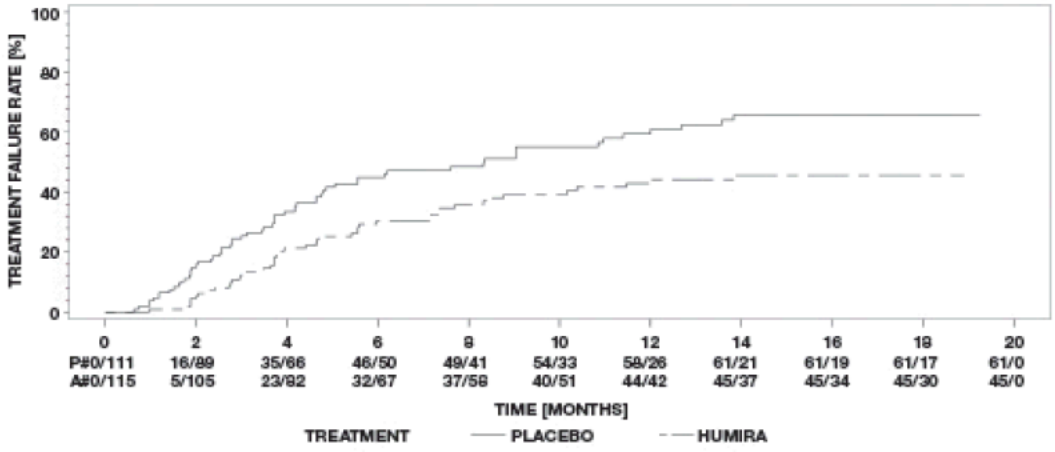
[a] HR of HUMIRA versus placebo from proportional hazards regression with treatment as factor.
[b] Treatment failure at or after Week 6 in Study UV I, or at or after Week 2 in Study UV II, was counted as event. Subjects who discontinued the study were censored at the time of dropping out.
[c] NE = not estimable. Fewer than half of at-risk subjects had an event.

Figure 3: Kaplan-Meier Curves Summarizing Time to Treatment Failure on or after Week 6 (Study UV I) or Week 2 (Study UV II)



Study UV I

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Study UV II

Note: P# = Placebo (Number of Events/Number at Risk); A# = HUMIRA (Number of Events/Number at Risk).

14.12 Pediatric Uveitis

The safety and efficacy of HUMIRA were assessed in a randomized, double-masked, placebo-controlled study of 90 pediatric patients from 2 to < 18 years of age with active JIA-associated non-infectious uveitis (PUV-I). Patients received either placebo or 20 mg adalimumab (if < 30 kg) or 40 mg adalimumab (if ≥ 30 kg) every other week in combination with a dose of methotrexate. Concomitant dosages of corticosteroids were permitted at study entry followed by a mandatory reduction in topical corticosteroids within 3 months.

The primary endpoint was 'time to treatment failure'. The criteria determining treatment failure were worsening or sustained non-improvement in ocular inflammation, or worsening of ocular co-morbidities.

Clinical Response

HUMIRA significantly decreased the risk of treatment failure by 75% relative to placebo (HR = 0.25 [95% CI: 0.12, 0.49]) (Table 22).

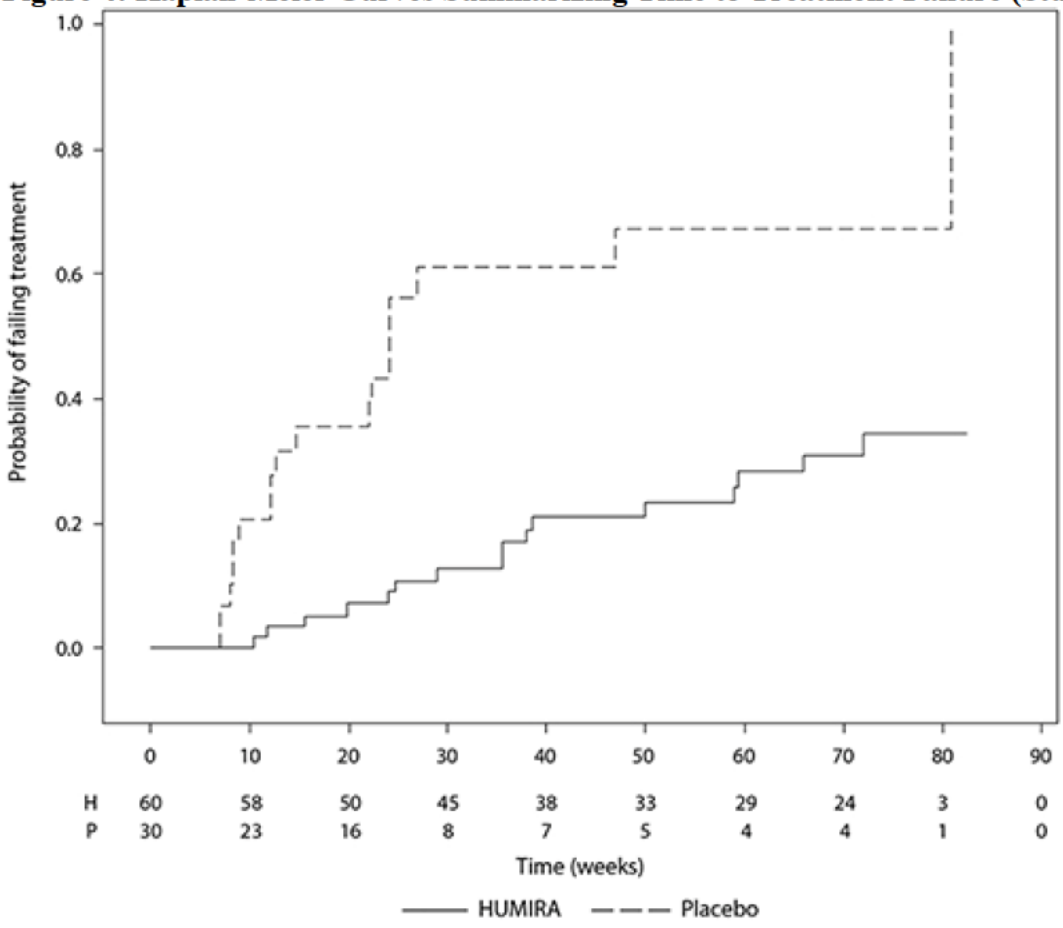
Table 22. Analysis Results of Time to Treatment Failure (Study PUV-I)

	Placebo (N=30)	**HUMIRA (N=60)**	**HR (95% CI)[a]**
Failure (n[%])	18 (60%)	16 (26.7%)	0.25 (0.12, 0.49)
Median Time to Failure (Weeks) (95% CI)[b]	24.1 (12.4, 81.0)	NE[c]	

[a] HR of adalimumab versus placebo from proportional hazards regression with treatment as factor.
[b] Estimated based on Kaplan-Meier curve.
[c] NE = not estimable. Fewer than half of at-risk subjects had an event.

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Figure 4: Kaplan-Meier Curves Summarizing Time to Treatment Failure (Study PUV-I)



Study PUV-I
Note: P = Placebo (Number at Risk); H = HUMIRA (Number at Risk).

15 REFERENCES

1. National Cancer Institute. Surveillance, Epidemiology, and End Results Database (SEER) Program. SEER Incidence Crude Rates, 17 Registries, 2000-2007.

16 HOW SUPPLIED/STORAGE AND HANDLING

HUMIRA® (adalimumab) is supplied as a preservative-free, sterile, clear and colorless solution for subcutaneous administration. The following packaging configurations are available.

- **HUMIRA Pen Carton - 40 mg/0.8 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 40 mg/0.8 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-4339-02.
- **HUMIRA Pen Carton - 40 mg/0.4 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose

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tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 40 mg/0.4 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0554-02.

- **HUMIRA Pen Carton – 80 mg/0.8 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 80 mg/0.8 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0124-02.
- **HUMIRA Pen 40 mg/0.8 mL - Starter Package for Crohn's Disease, Ulcerative Colitis or Hidradenitis Suppurativa**
  HUMIRA is supplied in a carton containing 6 alcohol preps and 6 dose trays (Starter Package for Crohn's Disease, Ulcerative Colitis or Hidradenitis Suppurativa). Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 40 mg/0.8 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-4339-06.
- **HUMIRA Pen 40 mg/0.4 mL - Starter Package for Crohn's Disease, Ulcerative Colitis or Hidradenitis Suppurativa**
  HUMIRA is supplied in a carton containing 6 alcohol preps and 6 dose trays (Starter Package for Crohn's Disease, Ulcerative Colitis or Hidradenitis Suppurativa). Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 40 mg/0.4 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0554-06.
- **HUMIRA Pen 80 mg/0.8 mL - Starter Package for Crohn's Disease, Ulcerative Colitis or Hidradenitis Suppurativa**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 3 dose trays (Starter Package for Crohn's Disease, Ulcerative Colitis or Hidradenitis Suppurativa). Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 80 mg/0.8 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0124-03.
- **HUMIRA Pen 40 mg/0.8 mL - Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter Package**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 4 dose trays (Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter Package). Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 40 mg/0.8 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-4339-07.
- **HUMIRA Pen 40 mg/0.4 mL - Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter Package**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 4 dose trays (Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter Package). Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 40 mg/0.4 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0554-04.

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- **HUMIRA Pen 80 mg/0.8 mL and 40 mg/0.4 mL - Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter Package**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 3 dose trays (Psoriasis, Uveitis or Adolescent Hidradenitis Suppurativa Starter Package). One dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 80 mg/0.8 mL of HUMIRA. The other two dose trays each consist of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 40 mg/0.4 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-1539-03.
- **HUMIRA Pen 80 mg/0.8 mL – Starter Package for Pediatric Ulcerative Colitis (4 count)**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 4 dose trays (Starter Package for Pediatric Ulcerative Colitis). Each dose tray consists of a single-dose pen, containing a 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 80 mg/0.8 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0124-04.
- **Prefilled Syringe Carton - 40 mg/0.8 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 40 mg/0.8 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-3799-02.
- **Prefilled Syringe Carton - 40 mg/0.4 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 40 mg/0.4 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0243-02.
- **Prefilled Syringe Carton - 20 mg/0.4 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 20 mg/0.4 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-9374-02.
- **Prefilled Syringe Carton - 20 mg/0.2 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 20 mg/0.2 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0616-02.
- **Prefilled Syringe Carton - 10 mg/0.2 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 10 mg/0.2 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-6347-02.
- **Prefilled Syringe Carton - 10 mg/0.1 mL**
  HUMIRA is supplied in a carton containing two alcohol preps and two dose trays. Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed thin wall, ½ inch

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needle, providing 10 mg/0.1 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0817-02.

- **HUMIRA Prefilled Syringe 40 mg/0.8 mL - Pediatric Crohn's Disease Starter Package (6 count)**
  HUMIRA is supplied in a carton containing 6 alcohol preps and 6 dose trays (Pediatric Starter Package). Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 40 mg/0.8 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-3799-06.
- **HUMIRA Prefilled Syringe 80 mg/0.8 mL - Pediatric Crohn's Disease Starter Package (3 count)**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 3 dose trays (Pediatric Starter Package). Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 80 mg/0.8 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-2540-03.
- **HUMIRA Prefilled Syringe 40 mg/0.8 mL - Pediatric Crohn's Disease Starter Package (3 count)**
  HUMIRA is supplied in a carton containing 4 alcohol preps and 3 dose trays (Pediatric Starter Package). Each dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed ½ inch needle, providing 40 mg/0.8 mL of HUMIRA. The needle cover may contain natural rubber latex. The NDC number is 0074-3799-03.
- **HUMIRA Prefilled Syringe 80 mg/0.8 mL and 40 mg/0.4 mL - Pediatric Crohn's Disease Starter Package (2 count)**
  HUMIRA is supplied in a carton containing 2 alcohol preps and 2 dose trays (Pediatric Starter Package). One dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 80 mg/0.8 mL of HUMIRA. The other dose tray consists of a single-dose, 1 mL prefilled glass syringe with a fixed thin wall, ½ inch needle, providing 40 mg/0.4 mL of HUMIRA. The black needle cover is not made with natural rubber latex. The NDC number is 0074-0067-02.
- **Single-Dose Institutional Use Vial Carton - 40 mg/0.8 mL**
  HUMIRA is supplied for institutional use only in a carton containing a single-dose, glass vial, providing 40 mg/0.8 mL of HUMIRA. The vial stopper is not made with natural rubber latex. The NDC number is 0074-3797-01.

Storage and Stability

Do not use beyond the expiration date on the container. HUMIRA must be refrigerated at 36°F to 46°F (2°C to 8°C). DO NOT FREEZE. Do not use if frozen even if it has been thawed.

Store in original carton until time of administration to protect from light.

If needed, for example when traveling, HUMIRA may be stored at room temperature up to a maximum of 77°F (25°C) for a period of up to 14 days, with protection from light. HUMIRA should be discarded if not used within the 14-day period. Record the date when HUMIRA is first removed from the refrigerator in the spaces provided on the carton and dose tray.

Do not store HUMIRA in extreme heat or cold.

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17 PATIENT COUNSELING INFORMATION

Advise the patient or caregiver to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Infections

Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct patients of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis, invasive fungal infections, and reactivation of hepatitis B virus infections *[see Warnings and Precautions (5.1, 5.2, 5.4)]*.

Malignancies

Counsel patients about the risk of malignancies while receiving HUMIRA *[see Warnings and Precautions (5.2)]*

Hypersensitivity Reactions

Advise patients to seek immediate medical attention if they experience any symptoms of severe hypersensitivity reactions. Advise latex-sensitive patients that the needle cap of the HUMIRA 40 mg/0.8 mL Pen and 40 mg/0.8 mL, 20 mg/0.4 mL and 10 mg/0.2 mL prefilled syringe may contain natural rubber latex *[see Warnings and Precautions (5.3), How Supplied/Storage and Handling (16)]*.

Other Medical Conditions

Advise patients to report any signs of new or worsening medical conditions such as congestive heart failure, neurological disease, autoimmune disorders, or cytopenias. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever *[see Warnings and Precautions (5.5, 5.6, 5.8, 5.9)]*.

Instructions on Injection Technique

Inform patients that the first injection is to be performed under the supervision of a qualified health care professional. If a patient or caregiver is to administer HUMIRA, instruct them in injection techniques and assess their ability to inject subcutaneously to ensure the proper administration of HUMIRA *[see Instructions for Use]*.

For patients who will use the HUMIRA Pen, tell them that they:

- Will hear a **loud 'click'** when the plum-colored activator button is pressed. The loud click means the **start** of the injection.
- Must keep holding the HUMIRA Pen against their squeezed, raised skin until all of the medicine is injected. This can take up to 15 seconds.
- Will know that the injection has finished when the yellow marker fully appears in the window view and stops moving.

Instruct patients to dispose of their used needles and syringes or used Pen in a FDA-cleared sharps disposal container immediately after use. **Instruct patients not to dispose of loose needles and syringes or Pen in their household trash.** Instruct patients that if they do not have a FDA-cleared sharps disposal container, they may use a household container that is made of a heavy-duty plastic, can be closed with a tight-fitting and puncture-resistant lid without sharps being able to come out, upright and stable during use, leak-resistant, and properly labeled to warn of hazardous waste inside the container.

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Instruct patients that when their sharps disposal container is almost full, they will need to follow their community guidelines for the correct way to dispose of their sharps disposal container. Instruct patients that there may be state or local laws regarding disposal of used needles and syringes. Refer patients to the FDA's website at http://www.fda.gov/safesharpsdisposal for more information about safe sharps disposal, and for specific information about sharps disposal in the state that they live in.

Instruct patients not to dispose of their used sharps disposal container in their household trash unless their community guidelines permit this. Instruct patients not to recycle their used sharps disposal container.

AbbVie Inc.

North Chicago, IL 60064, U.S.A.

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MEDICATION GUIDE
HUMIRA® (Hu-MARE-ah)
(adalimumab)
injection, for subcutaneous use

Read the Medication Guide that comes with HUMIRA before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment.

What is the most important information I should know about HUMIRA?

HUMIRA is a medicine that affects your immune system. HUMIRA can lower the ability of your immune system to fight infections. **Serious infections have happened in people taking HUMIRA. These serious infections include tuberculosis (TB) and infections caused by viruses, fungi or bacteria that have spread throughout the body. Some people have died from these infections.**

- Your doctor should test you for TB before starting HUMIRA.
- Your doctor should check you closely for signs and symptoms of TB during treatment with HUMIRA.

You should not start taking HUMIRA if you have any kind of infection unless your doctor says it is okay.

Before starting HUMIRA, tell your doctor if you:

- think you have an infection or have symptoms of an infection such as:
  - fever, sweats, or chills
  - muscle aches
  - cough
  - shortness of breath
  - blood in phlegm
  - warm, red, or painful skin or sores on your body
  - diarrhea or stomach pain
  - burning when you urinate or urinate more often than normal
  - feel very tired
  - weight loss
- are being treated for an infection.
- get a lot of infections or have infections that keep coming back.
- have diabetes.
- have TB, or have been in close contact with someone with TB.
- were born in, lived in, or traveled to countries where there is more risk for getting TB. Ask your doctor if you are not sure.
- live or have lived in certain parts of the country (such as the Ohio and Mississippi River valleys) where there is an increased risk for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, or blastomycosis). These infections may happen or become more severe if you use HUMIRA. Ask your doctor if you do not know if you have lived in an area where these infections are common.
- have or have had hepatitis B.
- use the medicine ORENCIA (abatacept), KINERET (anakinra), RITUXAN (rituximab), IMURAN (azathioprine), or PURINETHOL (6–mercaptopurine, 6-MP).
- are scheduled to have major surgery.

After starting HUMIRA, call your doctor right away if you have an infection, or any sign of an infection.

HUMIRA can make you more likely to get infections or make any infection that you may have worse.

Cancer

- For children and adults taking Tumor Necrosis Factor (TNF)-blockers, including HUMIRA, the chances of getting cancer may increase.

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- There have been cases of unusual cancers in children, teenagers, and young adults using TNF-blockers.
- People with rheumatoid arthritis (RA), especially more serious RA, may have a higher chance for getting a kind of cancer called lymphoma.
- If you use TNF blockers including HUMIRA your chance of getting two types of skin cancer may increase (basal cell cancer and squamous cell cancer of the skin). These types of cancer are generally not life-threatening if treated. Tell your doctor if you have a bump or open sore that does not heal.
- Some people receiving TNF blockers including HUMIRA developed a rare type of cancer called hepatosplenic T-cell lymphoma. This type of cancer often results in death. Most of these people were male teenagers or young men. Also, most people were being treated for Crohn's disease or ulcerative colitis with another medicine called IMURAN (azathioprine) or PURINETHOL (6-mercaptopurine, 6–MP).

What is HUMIRA?

HUMIRA is a medicine called a Tumor Necrosis Factor (TNF) blocker. HUMIRA is used:

- To reduce the signs and symptoms of:
  - **moderate to severe RA in adults.** HUMIRA can be used alone, with methotrexate, or with certain other medicines.
  - **moderate to severe polyarticular juvenile idiopathic arthritis (JIA) in children** 2 years and older. HUMIRA can be used alone or with methotrexate.
  - **psoriatic arthritis (PsA) in adults.** HUMIRA can be used alone or with certain other medicines.
  - **ankylosing spondylitis (AS) in adults.**
  - **moderate to severe hidradenitis suppurativa (HS) in people 12 years and older.**
- **To treat moderate to severe Crohn's disease (CD) in adults and children 6 years of age and older**.
- **To treat moderate to severe ulcerative colitis (UC) in adults and children 5 years of age and older**. It is not known if HUMIRA is effective in people who stopped responding to or could not tolerate TNF-blocker medicines.
- **To treat moderate to severe chronic (lasting a long time) plaque psoriasis (Ps) in adults** who have the condition in many areas of their body and who may benefit from taking injections or pills (systemic therapy) or phototherapy (treatment using ultraviolet light alone or with pills).
- **To treat non-infectious intermediate, posterior, and panuveitis in adults and children 2 years of age and older.**

What should I tell my doctor before taking HUMIRA?

HUMIRA may not be right for you. Before starting HUMIRA, tell your doctor about all of your medical conditions, including if you:

- have an infection. See **"What is the most important information I should know about HUMIRA?"**
- have or have had cancer.
- have any numbness or tingling or have a disease that affects your nervous system such as multiple sclerosis or Guillain-Barré syndrome.
- have or had heart failure.
- have recently received or are scheduled to receive a vaccine. You may receive vaccines, except for live vaccines while using HUMIRA. Children should be brought up to date with all vaccines before starting HUMIRA.
- are allergic to rubber or latex. Tell your doctor if you have any allergies to rubber or latex.

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- The needle cover for the HUMIRA Pen 40 mg/0.8 mL, HUMIRA 40 mg/0.8 mL prefilled syringe, HUMIRA 20 mg/0.4 mL prefilled syringe, and HUMIRA 10 mg/0.2 mL prefilled syringe may contain natural rubber or latex.
- The black needle cover for the HUMIRA Pen 80 mg/0.8 mL, HUMIRA 80 mg/0.8 mL prefilled syringe, HUMIRA Pen 40 mg/0.4 mL, HUMIRA 40 mg/0.4 mL prefilled syringe, HUMIRA 20 mg/0.2 mL prefilled syringe, HUMIRA 10 mg/0.1 mL prefilled syringe and the vial stopper on the HUMIRA institutional use vial are not made with natural rubber or latex.

- are allergic to HUMIRA or to any of its ingredients. See the end of this Medication Guide for a list of ingredients in HUMIRA.
- are pregnant or plan to become pregnant, breastfeeding or plan to breastfeed. You and your doctor should decide if you should take HUMIRA while you are pregnant or breastfeeding.
- have a baby and you were using HUMIRA during your pregnancy. Tell your baby's doctor before your baby receives any vaccines.

Tell your doctor about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Especially tell your doctor if you use:

- ORENCIA (abatacept), KINERET (anakinra), REMICADE (infliximab), ENBREL (etanercept), CIMZIA (certolizumab pegol) or SIMPONI (golimumab), because you should not use HUMIRA while you are also using one of these medicines.
- RITUXAN (rituximab). Your doctor may not want to give you HUMIRA if you have received RITUXAN (rituximab) recently.
- IMURAN (azathioprine) or PURINETHOL (6–mercaptopurine, 6-MP).

Keep a list of your medicines with you to show your doctor and pharmacist each time you get a new medicine.

How should I take HUMIRA?

- HUMIRA is given by an injection under the skin. Your doctor will tell you how often to take an injection of HUMIRA. This is based on your condition to be treated. **Do not inject HUMIRA more often than you were prescribed.**
- See the **Instructions for Use** inside the carton for complete instructions for the right way to prepare and inject HUMIRA.
- Make sure you have been shown how to inject HUMIRA before you do it yourself. You can call your doctor or 1-800-4HUMIRA (1-800-448-6472) if you have any questions about giving yourself an injection. Someone you know can also help you with your injection after they have been shown how to prepare and inject HUMIRA.
- **Do not** try to inject HUMIRA yourself until you have been shown the right way to give the injections. If your doctor decides that you or a caregiver may be able to give your injections of HUMIRA at home, you should receive training on the right way to prepare and inject HUMIRA.
- Do not miss any doses of HUMIRA unless your doctor says it is okay. If you forget to take HUMIRA, inject a dose as soon as you remember. Then, take your next dose at your regular scheduled time. This will put you back on schedule. In case you are not sure when to inject HUMIRA, call your doctor or pharmacist.
- If you take more HUMIRA than you were told to take, call your doctor.

What are the possible side effects of HUMIRA?

HUMIRA can cause serious side effects, including:

See "What is the most important information I should know about HUMIRA?"

- **Serious Infections.**
  Your doctor will examine you for TB and perform a test to see if you have TB. If your doctor

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feels that you are at risk for TB, you may be treated with medicine for TB before you begin treatment with HUMIRA and during treatment with HUMIRA. Even if your TB test is negative your doctor should carefully monitor you for TB infections while you are taking HUMIRA. People who had a negative TB skin test before receiving HUMIRA have developed active TB. Tell your doctor if you have any of the following symptoms while taking or after taking HUMIRA:

- cough that does not go away
- low grade fever
- weight loss
- loss of body fat and muscle (wasting)

- **Hepatitis B infection in people who carry the virus in their blood.**
If you are a carrier of the hepatitis B virus (a virus that affects the liver), the virus can become active while you use HUMIRA. Your doctor should do blood tests before you start treatment, while you are using HUMIRA, and for several months after you stop treatment with HUMIRA. Tell your doctor if you have any of the following symptoms of a possible hepatitis B infection:
  - muscle aches
  - feel very tired
  - dark urine
  - skin or eyes look yellow
  - little or no appetite
  - vomiting
  - clay-colored bowel movements
  - fever
  - chills
  - stomach discomfort
  - skin rash
- **Allergic reactions.** Allergic reactions can happen in people who use HUMIRA. Call your doctor or get medical help right away if you have any of these symptoms of a serious allergic reaction:
  - hives
  - trouble breathing
  - swelling of your face, eyes, lips or mouth
- **Nervous system problems.** Signs and symptoms of a nervous system problem include: numbness or tingling, problems with your vision, weakness in your arms or legs, and dizziness.
- **Blood problems.** Your body may not make enough of the blood cells that help fight infections or help to stop bleeding. Symptoms include a fever that does not go away, bruising or bleeding very easily, or looking very pale.
- **New heart failure or worsening of heart failure you already have. Call your doctor right away** if you get new worsening symptoms of heart failure while taking HUMIRA, including:
  - shortness of breath
  - sudden weight gain
  - swelling of your ankles or feet
- **Immune reactions including a lupus-like syndrome.** Symptoms include chest discomfort or pain that does not go away, shortness of breath, joint pain, or a rash on your cheeks or arms that gets worse in the sun. Symptoms may improve when you stop HUMIRA.
- **Liver problems.** Liver problems can happen in people who use TNF-blocker medicines. These problems can lead to liver failure and death. Call your doctor right away if you have any of these symptoms:
  - feel very tired
  - poor appetite or vomiting
  - skin or eyes look yellow
  - pain on the right side of your stomach (abdomen)
- **Psoriasis.** Some people using HUMIRA had new psoriasis or worsening of psoriasis they already had. Tell your doctor if you develop red scaly patches or raised bumps that are filled with pus. Your doctor may decide to stop your treatment with HUMIRA.

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Call your doctor or get medical care right away if you develop any of the above symptoms. Your treatment with HUMIRA may be stopped.

The most common side effects of HUMIRA include:

- injection site reactions: redness, rash, swelling, itching, or bruising. These symptoms usually will go away within a few days. Call your doctor right away if you have pain, redness or swelling around the injection site that does not go away within a few days or gets worse.
- upper respiratory infections (including sinus infections).
- headaches.
- rash.

These are not all the possible side effects with HUMIRA. Tell your doctor if you have any side effect that bothers you or that does not go away. Ask your doctor or pharmacist for more information.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store HUMIRA?

- Store HUMIRA in the refrigerator at 36ºF to 46ºF (2ºC to 8ºC). Store HUMIRA in the original carton until use to protect it from light.
- **Do not freeze HUMIRA.** Do not use HUMIRA if frozen, even if it has been thawed.
- Refrigerated HUMIRA may be used until the expiration date printed on the HUMIRA carton, dose tray, Pen or prefilled syringe. Do not use HUMIRA after the expiration date.
- If needed, for example when you are traveling, you may also store HUMIRA at room temperature up to 77°F (25°C) for up to 14 days. Store HUMIRA in the original carton until use to protect it from light.
- Throw away HUMIRA if it has been kept at room temperature and not been used within 14 days.
- Record the date you first remove HUMIRA from the refrigerator in the spaces provided on the carton and dose tray.
- Do not store HUMIRA in extreme heat or cold.
- Do not use a Pen or prefilled syringe if the liquid is cloudy, discolored, or has flakes or particles in it.
- Do not drop or crush HUMIRA. The prefilled syringe is glass.

Keep HUMIRA, injection supplies, and all other medicines out of the reach of children.

General information about the safe and effective use of HUMIRA.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use HUMIRA for a condition for which it was not prescribed. Do not give HUMIRA to other people, even if they have the same condition. It may harm them.
This Medication Guide summarizes the most important information about HUMIRA. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about HUMIRA that is written for health professionals.

What are the ingredients in HUMIRA?
Active ingredient: adalimumab

HUMIRA Pen 40 mg/0.8 mL, HUMIRA 40 mg/0.8 mL prefilled syringe, HUMIRA 20 mg/0.4 mL prefilled syringe, HUMIRA 10 mg/0.2 mL prefilled syringe, and HUMIRA 40 mg/0.8 mL institutional use vial:

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Inactive ingredients: citric acid monohydrate, dibasic sodium phosphate dihydrate, mannitol, monobasic sodium phosphate dihydrate, polysorbate 80, sodium chloride, sodium citrate and Water for Injection. Sodium hydroxide is added as necessary to adjust pH.

HUMIRA Pen 80 mg/0.8 mL, HUMIRA 80 mg/0.8 mL prefilled syringe, HUMIRA Pen 40 mg/0.4 mL, HUMIRA 40 mg/0.4 mL prefilled syringe, HUMIRA 20 mg/0.2 mL prefilled syringe and HUMIRA 10 mg/0.1 mL prefilled syringe:

Inactive ingredients: mannitol, polysorbate 80, and Water for Injection.

Manufactured by: AbbVie Inc., North Chicago, IL 60064, U.S.A.
For more information go to www.HUMIRA.com or you can enroll in a patient support program by calling 1-800-4HUMIRA (1-800-448-6472).
US License Number 1889

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 02/2021
20066566

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INSTRUCTIONS FOR USE

HUMIRA® (Hu-MARE-ah)

(adalimumab)

40 MG/0.8 ML

SINGLE-DOSE PEN

Do not try to inject HUMIRA yourself until you have been shown the right way to give the injections and have read and understand this Instructions for Use. If your doctor decides that you or a caregiver may be able to give your injections of HUMIRA at home, you should receive training on the right way to prepare and inject HUMIRA. It is important that you read, understand, and follow these instructions so that you inject HUMIRA the right way. It is also important to talk to your doctor to be sure you understand your HUMIRA dosing instructions. To help you remember when to inject HUMIRA, you can mark your calendar ahead of time. Call your healthcare provider if you or your caregiver have any questions about the right way to inject HUMIRA.

IMPORTANT:

- Do not use HUMIRA if frozen, even if it has been thawed.
- The HUMIRA Pen contains glass. Do not drop or crush the Pen because the glass inside may break.
- Each HUMIRA Pen has 2 caps on it. Do not remove the gray cap (Cap #1) or the plum-colored cap (Cap #2) until right before your injection.
- When the plum-colored button on the HUMIRA Pen is pressed to give your dose of HUMIRA, you will hear a loud "click" sound.
  - You must practice injecting HUMIRA with your doctor or nurse so that you are not startled by this click when you start giving yourself the injections at home.
  - The loud click sound means the start of the injection.
  - You will know that the injection has finished when the yellow indicator appears fully in the window view and stops moving.

See the section below called **"Preparing the HUMIRA Pen"**.

Gather the Supplies for Your Injection

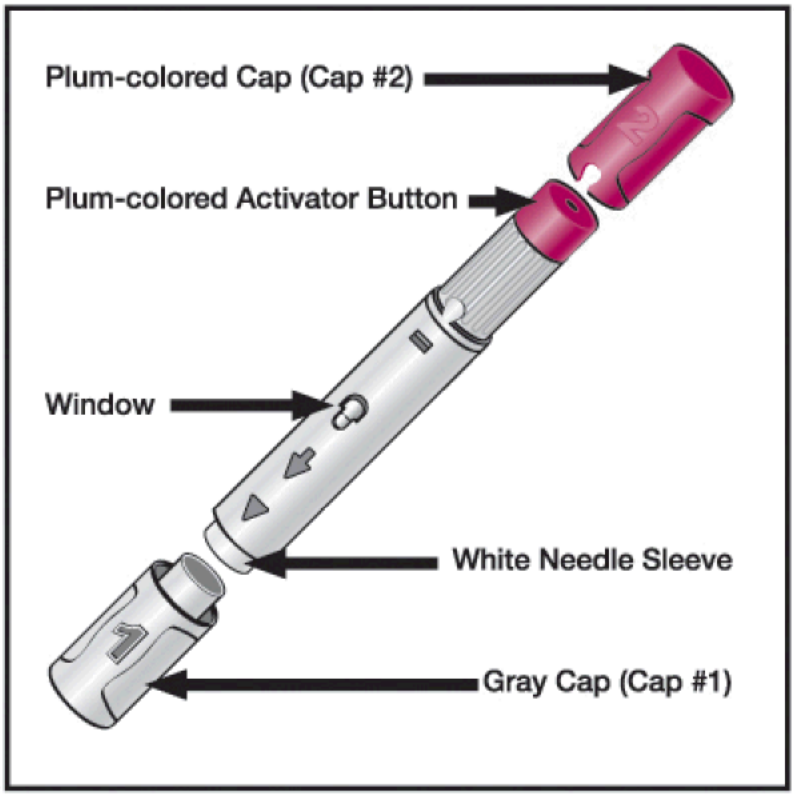
- You will need the following supplies for each injection of HUMIRA.
  Find a clean, flat surface to place the supplies on.
  - 1 alcohol swab
  - 1 cotton ball or gauze pad (not included in your HUMIRA carton)
  - 1 HUMIRA Pen (See Figure A)
  - Puncture-resistant sharps disposal container for HUMIRA Pen disposal (not included in your HUMIRA carton). See the **"How should I throw away (dispose of) the used HUMIRA Pen?"** section at the end of this Instructions for Use.

If more comfortable, take your HUMIRA Pen out of the refrigerator **15 to 30 minutes** before injecting to allow the liquid to reach room temperature. **Do not** remove the gray cap (Cap #1) or the plum-colored cap (Cap #2) while allowing it to reach room temperature. **Do not** warm HUMIRA in any other way (for example, **do not** warm it in a microwave or in hot water).

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If you do not have all the supplies you need to give yourself an injection, go to a pharmacy or call your pharmacist. The figure below shows what the HUMIRA Pen looks like. See Figure A.

Figure A



Check the carton, dose tray, and HUMIRA Pen.

1. Make sure the name HUMIRA appears on the carton, dose tray, and HUMIRA Pen label.

2. **Do not use** and **do call** your doctor or pharmacist if:
   - you drop or crush your HUMIRA Pen.
   - the seals on the top or bottom of the carton are broken or missing.
   - the expiration date on the carton, dose tray, and Pen has passed.
   - the HUMIRA Pen has been frozen or left in direct sunlight.
   - HUMIRA has been kept at room temperature for longer than **14** days or HUMIRA has been stored above 77°F (25°C).

See the **"How should I store HUMIRA?"** section at the end of this Instructions for Use.

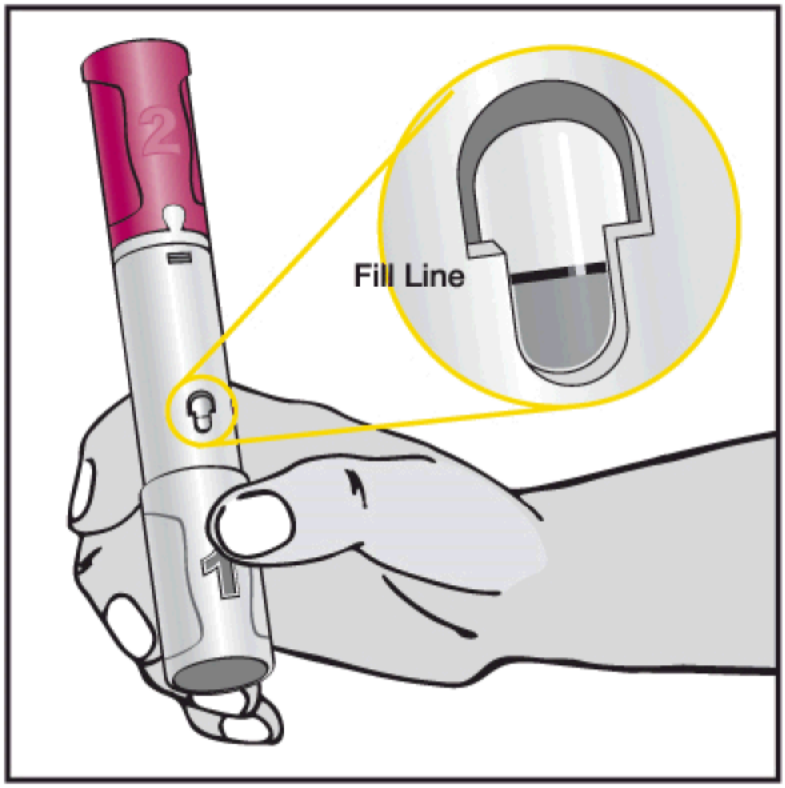
3. Hold the Pen with the gray cap (Cap # 1) pointed down.

4. Make sure the amount of liquid in the Pen is at the fill line or close to the fill line seen through the window. This is the full dose of HUMIRA that you will inject. See Figure B.

5. If the Pen does not have the full amount of liquid, **do not use that Pen**. Call your pharmacist.

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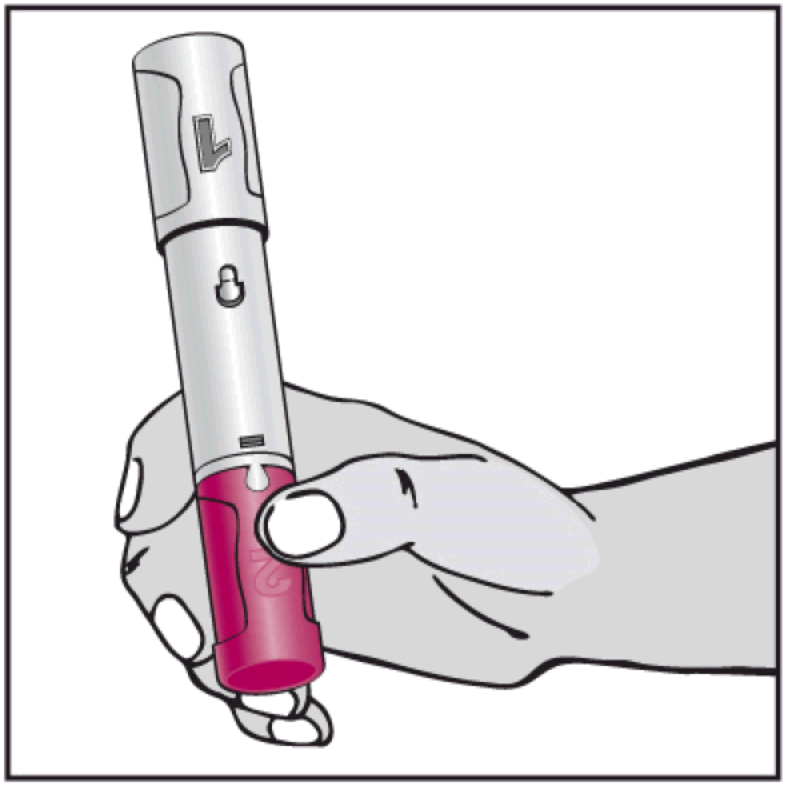
Figure B



6. Turn the Pen over and hold the Pen with the gray cap (Cap # 1) pointed up. See Figure C.

7. Check the solution through the windows on the side of the Pen to make sure the liquid is clear and colorless. **Do not use** your HUMIRA Pen if the liquid is cloudy, discolored, or if it has flakes or particles in it. Call your pharmacist. It is normal to see one or more bubbles in the window.

Figure C



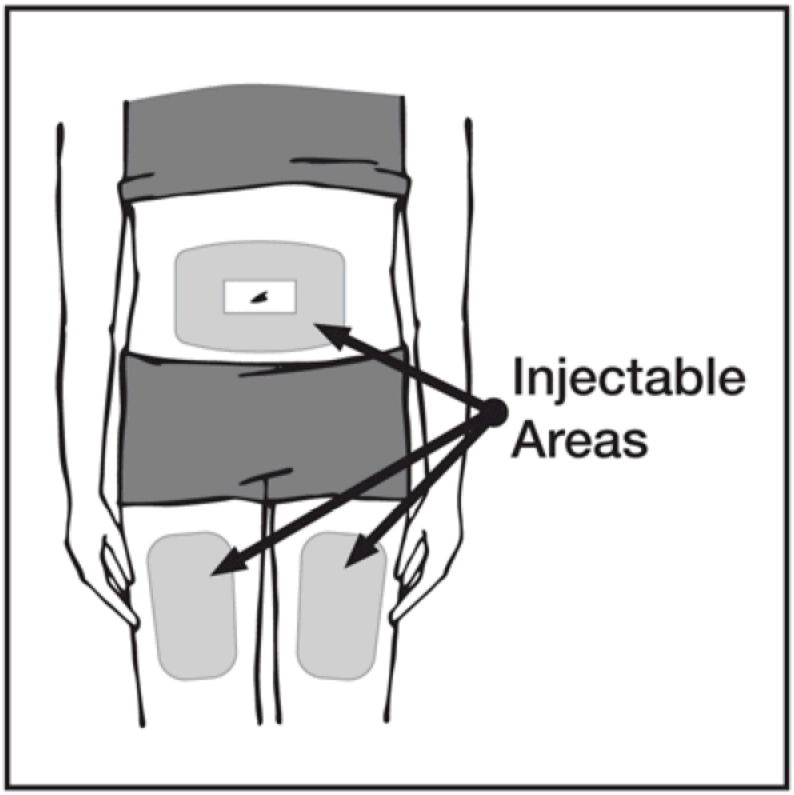
Choose the Injection Site

8. Wash and dry your hands well.

9. Choose an injection site on:
   - the front of your thighs or
   - your lower abdomen (belly). If you choose your abdomen, do not use the area 2 inches around your belly button (navel). See Figure D.

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Figure D



- Choose a different site each time you give yourself an injection. Each new injection should be given at least one inch from a site you used before.
- **Do not** inject HUMIRA into skin that is:
  - sore (tender)
  - bruised
  - red
  - hard
  - scarred or where you have stretch marks
- If you have psoriasis, **do not** inject directly into any raised, thick, red or scaly skin patches or lesions on your skin.
- Do not inject through your clothes.

Prepare the Injection Site

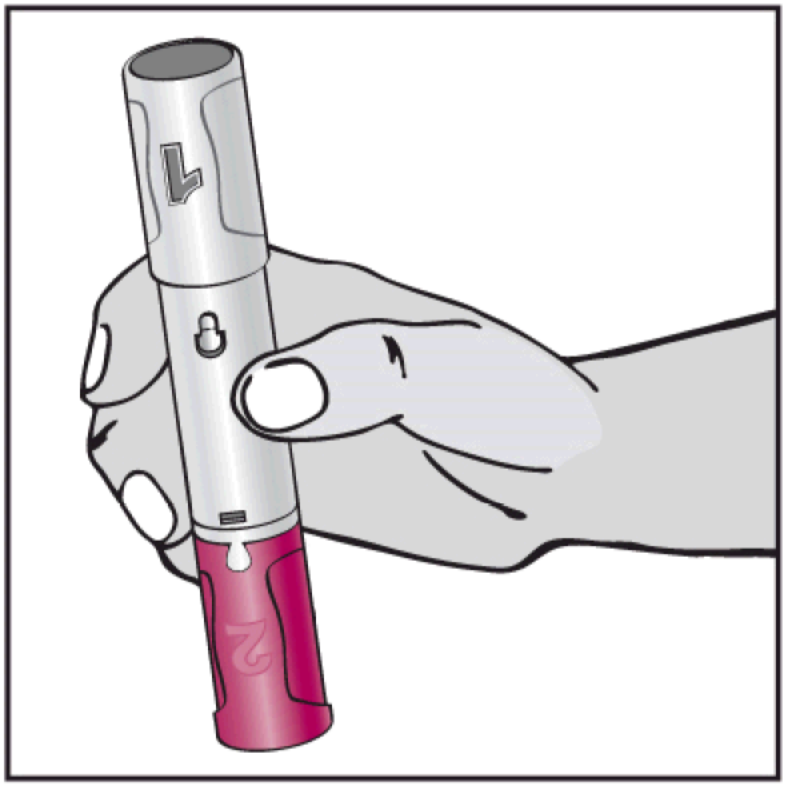
10. Wipe the injection site with an alcohol prep (swab) using a circular motion.
- **Do not** touch this area again before giving the injection. Allow the skin to dry before injecting. **Do not** fan or blow on the clean area.

Preparing the HUMIRA Pen

11. **Do not remove the gray cap (Cap # 1) or the plum-colored cap (Cap # 2) until right before your injection.**

12. Hold the middle of the Pen (gray body) with one hand so that you are not touching the gray cap (Cap # 1) or the plum-colored cap (Cap # 2). Turn the Pen so that the gray cap (Cap # 1) is pointing up. See Figure E.

Figure E

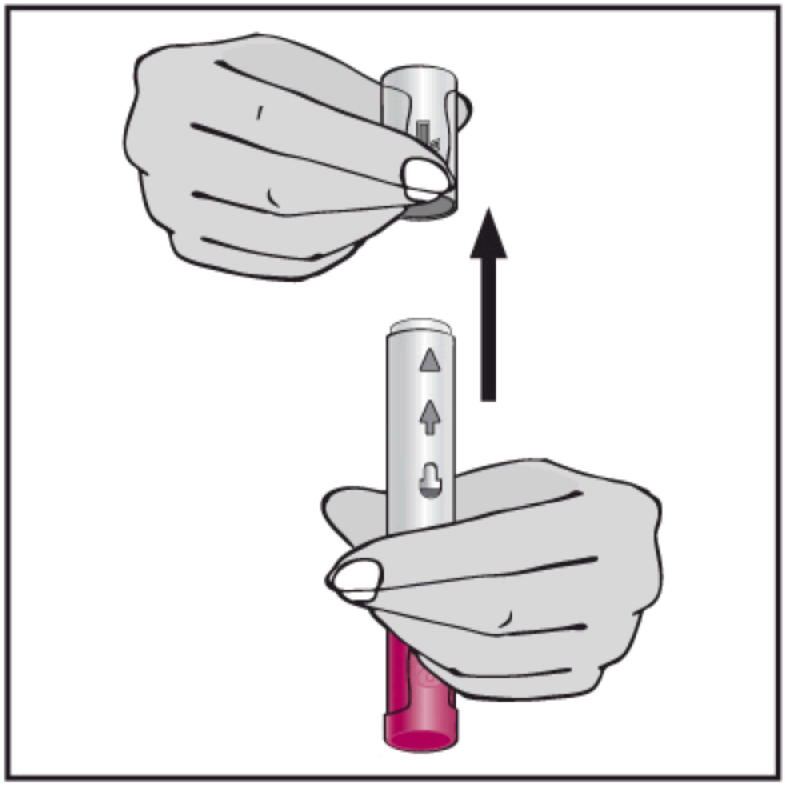


13. With your other hand, pull the gray cap (Cap # 1) straight off (do not twist the cap). Make sure the small needle cover of the syringe has come off with the gray cap (Cap # 1). See Figure F.

14. Throw away the gray cap (Cap # 1).

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Figure F



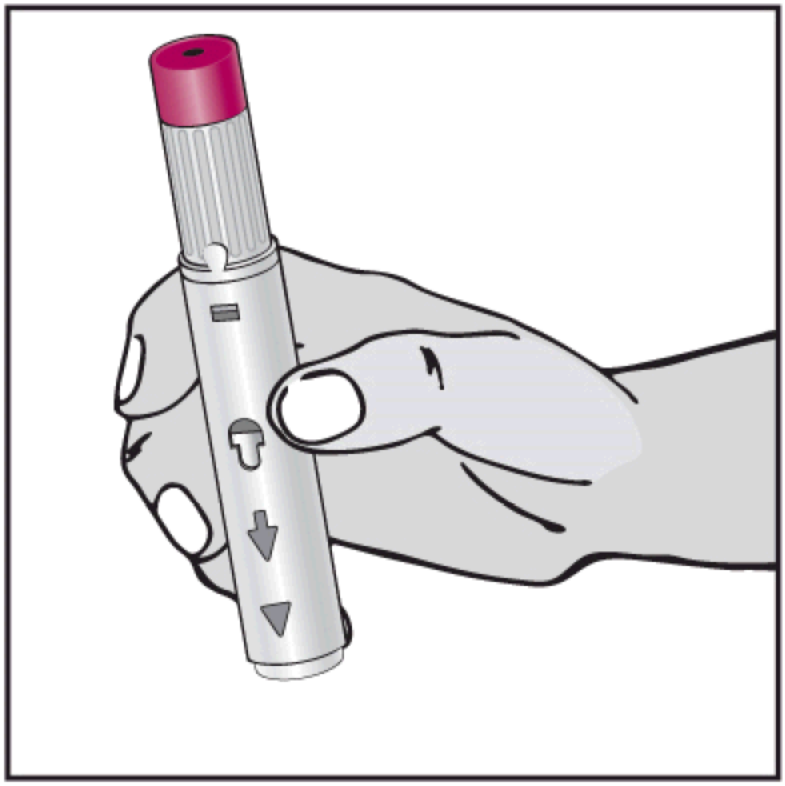
- **Do not** put the gray cap (Cap # 1) back on the Pen. Putting the gray cap (Cap # 1) back on may damage the needle.
- The white needle sleeve, which covers the needle, can now be seen.
- **Do not** touch the needle with your fingers or let the needle touch anything.
- You may see a few drops of liquid come out of the needle. This is normal.

15. Remove the plum-colored cap (Cap # 2) from the bottom of the Pen by pulling it straight off (do not twist the cap). The Pen is now activated. Throw away the plum-colored cap (Cap # 2).
- Do not put the plum-colored cap (Cap # 2) back on the Pen because it could cause medicine to come out of the syringe.

The plum-colored activator button:
- Turn the Pen so the plum-colored activator button is pointed up. See Figure G.

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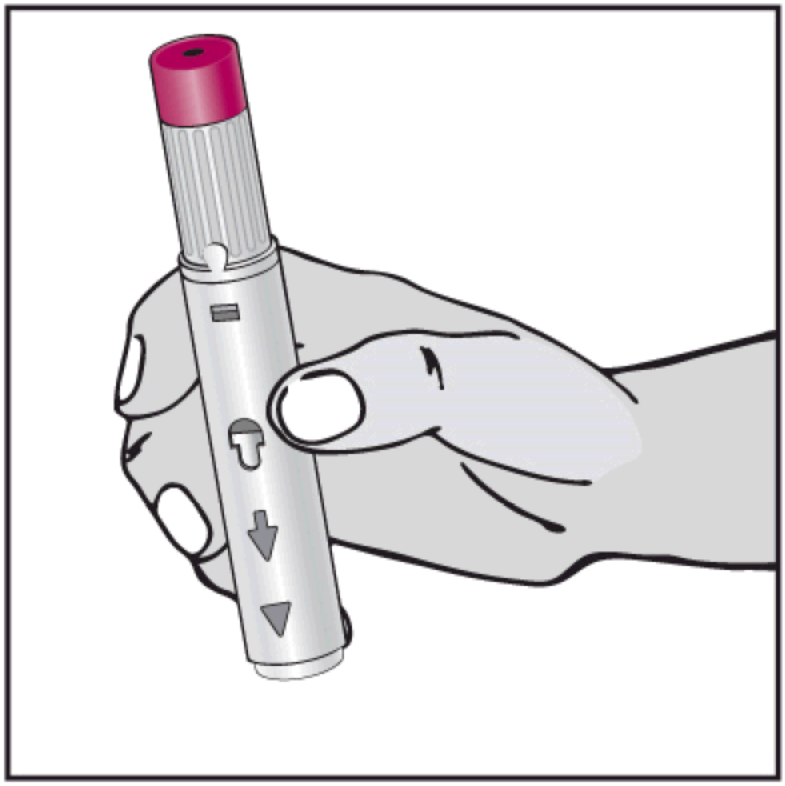
Figure G



- **Do not** press the plum-colored activator button until you are ready to inject HUMIRA. Pressing the plum-colored activator button will release the medicine from the Pen.
- Hold the Pen so that you can see the window. See Figure H. It is normal to see one or more bubbles in the window.

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Figure H



Position the Pen and Inject HUMIRA

16. Position the Pen:
    - **Squeeze** the area of the cleaned skin and hold it firmly until the injection is complete. See Figure I. You will inject into this raised area of skin.

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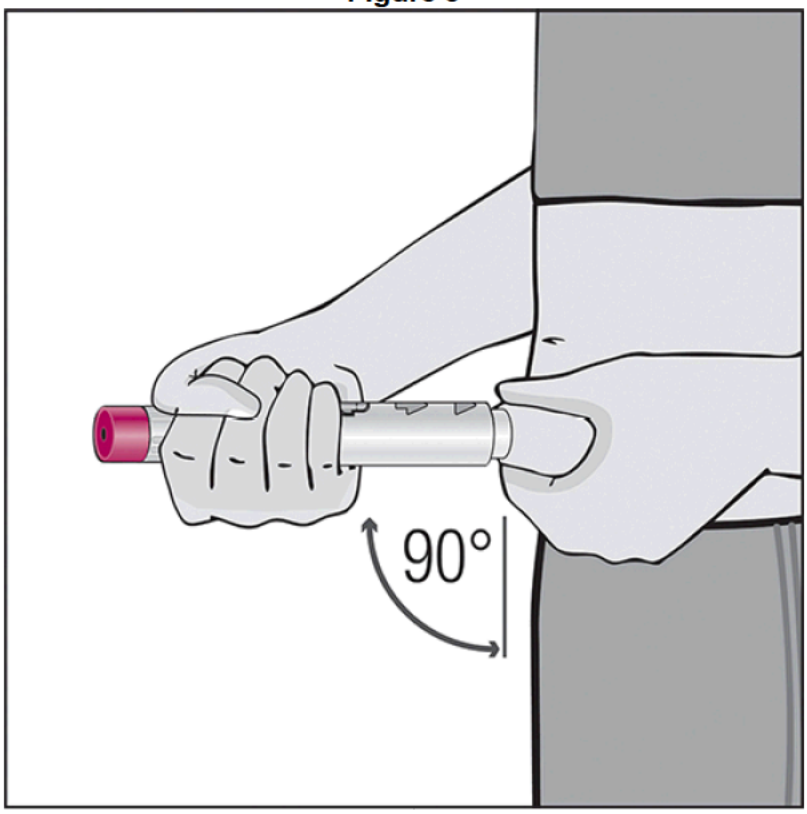
Figure I



17. Place the white end of the Pen straight (**at a 90° angle**) and flat against the raised area of your skin that you are squeezing. Place the Pen so that it will not inject the needle into your fingers that are holding the raised skin. See Figure J.

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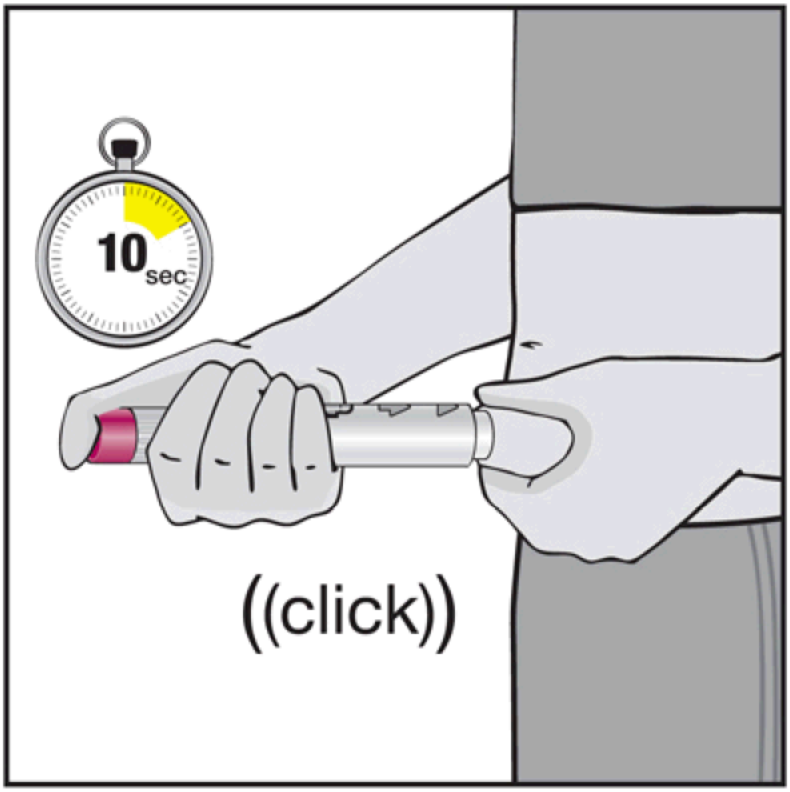
Figure J



18. Inject HUMIRA
    - **It is important that you firmly push the Pen down** all the way against the injection site before starting the injection.
    - **Keep pushing down** to prevent the Pen from moving away from the skin during the injection.
    - Press the plum-colored activator button with your thumb to begin the injection. Try not to cover the window. See Figure K.

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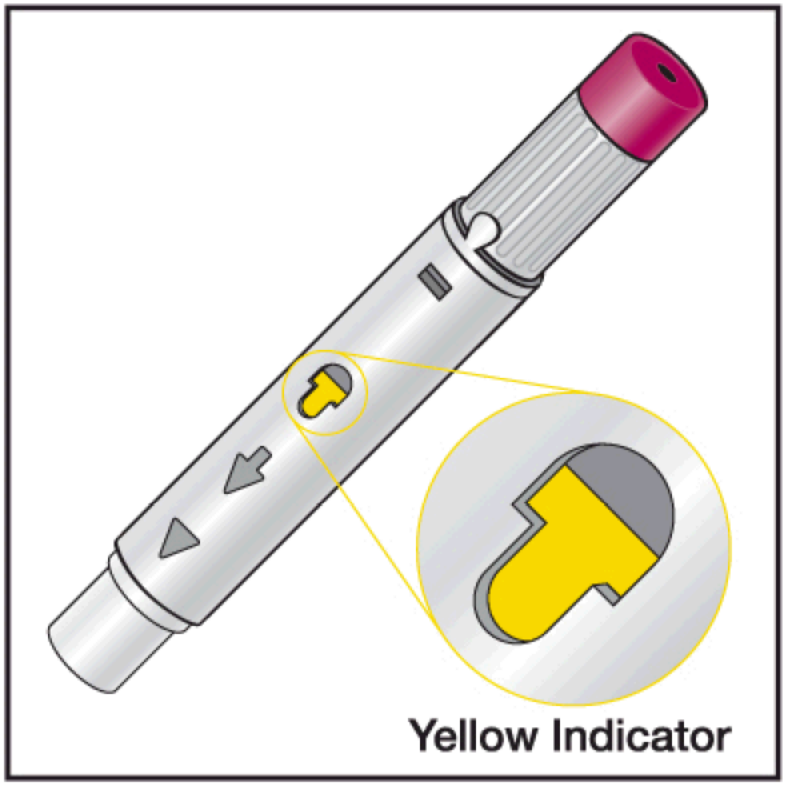
Figure K



- You will hear a loud ‘click’ when you press the plum-colored activator button. The loud click means the start of the injection.
- Keep pressing the plum-colored activator button and continue to push the Pen against your squeezed, raised skin until all the medicine is injected. This can take up to 10 seconds, so count slowly to ten. Keep pushing the Pen against the squeezed, raised skin of your injection site for the whole time so you get the full dose of medicine.
- You will know that the injection has finished when the yellow indicator fully appears in the window view and stops moving. See Figure L.

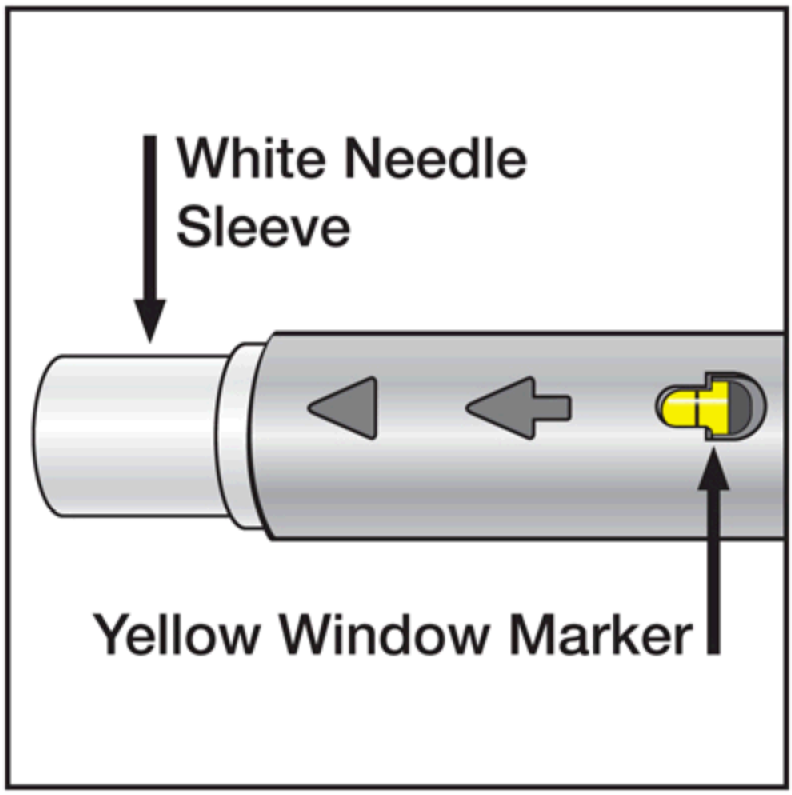
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Figure L



19. When the injection is finished, slowly pull the Pen from your skin. The white needle sleeve will move to cover the needle tip. See Figure M.
    - Do not touch the needle. The white needle sleeve is there to prevent you from touching the needle.

Figure M



- There may be a small amount of liquid on the injection site. This is normal.
- Press a cotton ball or gauze pad over the injection site and hold it for 10 seconds. Do **not** rub the injection site. You may have slight bleeding. This is normal.

20. Throw away (dispose of) your used HUMIRA Pen in a sharps disposal container right away after use. See the section **"How should I dispose of the used HUMIRA Pen?"**

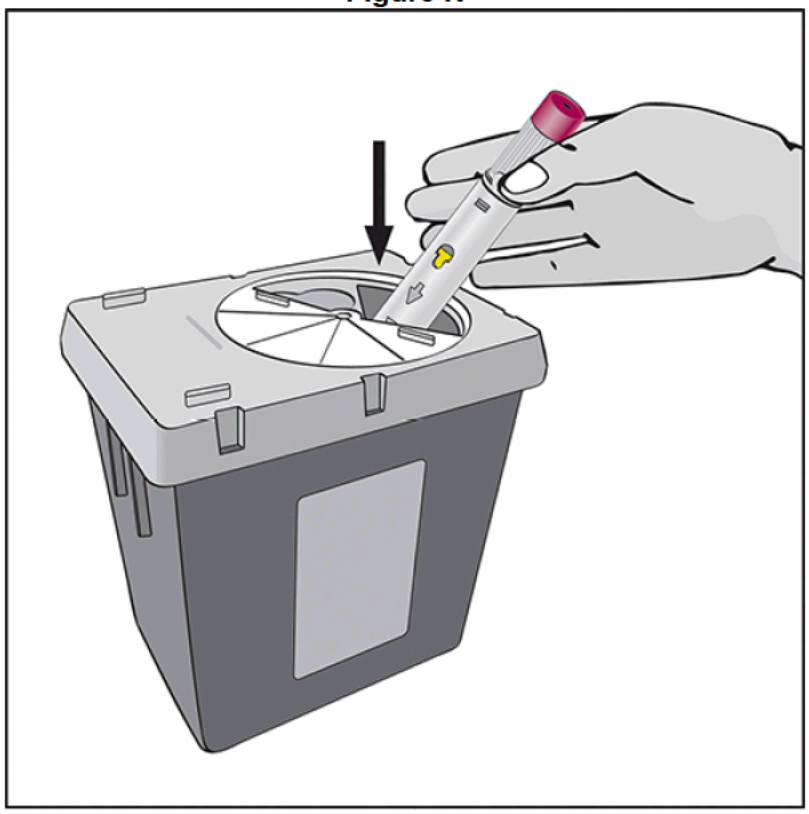
21. Keep a record of the dates and location of your injection sites. To help you remember when to take HUMIRA, you can mark your calendar ahead of time.

How should I throw away (dispose of) the used HUMIRA Pen?

- Put your Pen in a FDA-cleared sharps disposal container right away after use. See Figure N. **Do not throw away the Pen in your household trash.**
- Do not try to touch the needle. The white needle sleeve is there to prevent you from touching the needle.

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Figure N



- If you do not have a FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- For the safety and health of you and others, never re-use your HUMIRA Pens.
- The used alcohol pads, cotton balls, dose trays and packaging may be placed in your household trash.
- **Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.**
- **Always keep the sharps container out of the reach of children.**

How should I store HUMIRA?

- Store HUMIRA in the refrigerator between 36ºF to 46ºF (2ºC to 8ºC). Store HUMIRA in the original carton until use to protect it from light.

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- **Do not** freeze HUMIRA. **Do not** use HUMIRA if frozen, even if it has been thawed.
- Refrigerated HUMIRA may be used until the expiration date printed on the HUMIRA carton, dose tray or Pen. **Do not** use HUMIRA after the expiration date.
- If needed, for example when you are traveling, you may also store HUMIRA at room temperature up to 77°F (25°C) for up to **14** days. Store HUMIRA in the original carton until use to protect it from light.
- Throw away HUMIRA if it has been kept at room temperature and not been used within **14** days.
- Record the date you first remove HUMIRA from the refrigerator in the spaces provided on the carton and dose tray.
- Do not store HUMIRA in extreme heat or cold.
- Do not use a Pen if the liquid is cloudy, discolored, or has flakes or particles in it.
- Do not drop or crush HUMIRA.
- Keep HUMIRA, injection supplies, and all other medicines out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:

AbbVie Inc.

North Chicago, IL 60064, U.S.A.

US License Number 1889

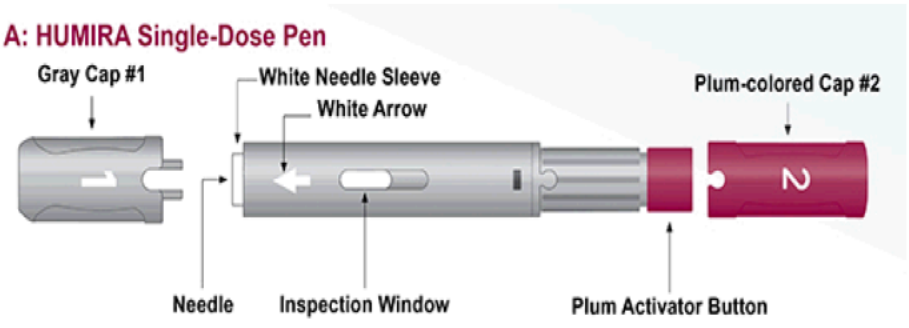
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Revised: 02/2021

INSTRUCTIONS FOR USE
HUMIRA® (Hu-MARE-ah)
(adalimumab)
40 mg/0.4 mL
Single-Dose Pen

Before Injecting: Your healthcare provider should show you how to use HUMIRA before you use it for the first time. Call your healthcare provider or **1-800-4HUMIRA** (1-800-448-6472) if you need help.

Figure A: HUMIRA Single-Dose Pen



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Important Information You Need to Know Before Injecting HUMIRA

Do not use the Pen and call your healthcare provider or pharmacist if:

- Liquid is cloudy, discolored, or has flakes or particles in it
- Liquid has been frozen (even if thawed) or left in direct sunlight
- Expiration date has passed
- The Pen has been dropped or crushed

Keep the caps on until right before your injection.

How should I store HUMIRA?

- Store HUMIRA in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store HUMIRA in the original carton until use to protect it from light.
- **Do not freeze**
- Refrigerated HUMIRA may be used until the expiration date printed on the HUMIRA carton, dose tray or Pen.
- If needed, for example when you are traveling, you may also store HUMIRA at room temperature up to 77°F (25°C) for up to **14** days.
- Throw away HUMIRA if it has been kept at room temperature and not used within **14** days.
- Record the date you first remove HUMIRA from the refrigerator in the spaces provided on the carton and dose tray.
- Do not store HUMIRA in extreme heat or cold.

Keep HUMIRA, injection supplies, and all other medicines out of reach of children.

Read Instructions on All Pages Before Using the HUMIRA Pen

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Take HUMIRA out of the refrigerator.
Leave HUMIRA at room temperature for **15 to 30 minutes** before injecting.

- **Do not** remove the Gray Cap (Cap #1) or Plum-colored Cap (Cap #2) while allowing HUMIRA to reach room temperature
- **Do not** warm HUMIRA in any other way. For example, **do not** warm it in a microwave or in hot water.
- **Do not** use the Pen if liquid has been frozen (even if thawed)



Check expiration date on the Pen label. **Do not** use the Pen if expiration date has passed.
Place the following on a clean, flat surface:

- 1 single-dose Pen and alcohol swab
- 1 cotton ball or gauze pad (not included)
- Puncture-resistant sharps disposal container (not included). See Step 9 at the end of this Instructions for Use for instructions on how to throw away (dispose of) your HUMIRA Pen

Wash and dry your hands.



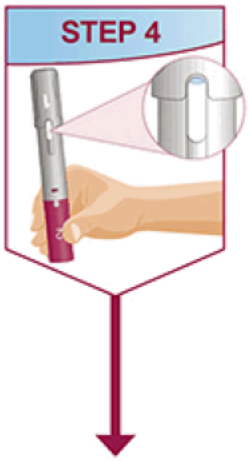
Choose an injection site:

- On the front of your thighs or
- Your abdomen (belly) at least 2 inches from your navel (belly button)
- Different from your last injection site

Wipe the injection site in a circular motion with the alcohol swab.

- **Do not** inject through clothes
- **Do not** inject into skin that is sore, bruised, red, hard, scarred, has stretch marks, or areas with psoriasis plaques

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Hold the Pen with the Gray Cap #1 facing up.
Check the window.

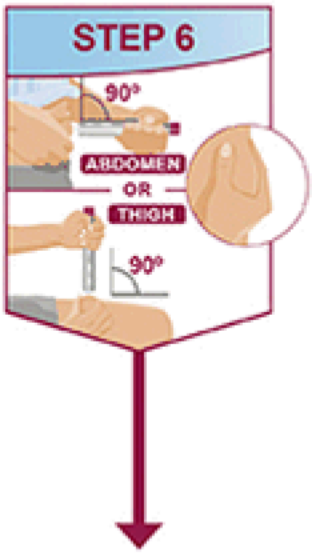
- It is normal to see 1 or more bubbles in the window
- Make sure the liquid is clear and colorless
- **Do not** use the Pen if the liquid is cloudy, discolored, or has flakes or particles in it
- **Do not** use the Pen if it has been dropped or crushed



Pull the Gray Cap #1 straight off.
Throw the cap away.

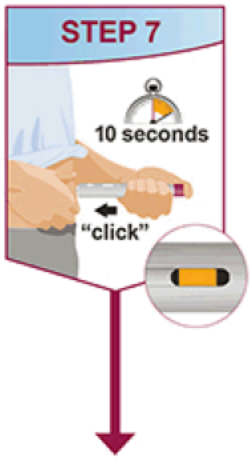
- It is normal to see a few drops of liquid come out of the needle

Pull the Plum-colored Cap #2 straight off.
Throw the cap away.
Turn the Pen so that the white arrow points toward the injection site.



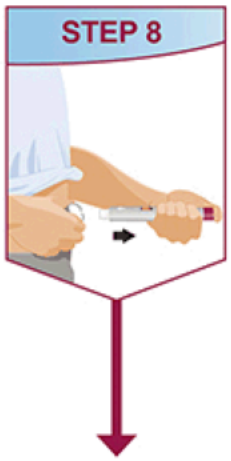
Squeeze the skin at your injection site to make a raised area and hold it firmly until the injection is complete.
Point the white arrow toward the injection site.
Place the white needle sleeve straight **(90° angle)** against the injection site.
Hold the Pen so that you can see the inspection window.
Do not press the plum activator button until you are ready to inject.

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It is important that you firmly push the Pen down all the way against the injection site before starting the injection.
Keep pushing down to prevent the Pen from moving away from the skin during the injection.
Press the plum activator button and count slowly for **10** seconds.

- A loud "click" will signal the **start** of the injection
- **Keep pushing** the Pen **down firmly** against the injection site until the injection is complete
- Injection is complete when the yellow indicator has stopped moving



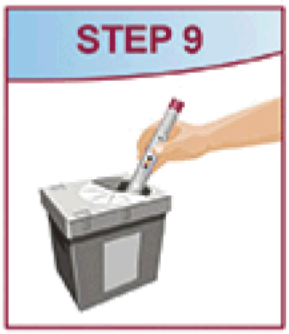
When the injection is completed, slowly pull the Pen from the skin. The white needle sleeve will cover the needle tip.

- A small amount of liquid on the injection site is normal

If there are more than a few drops of liquid on the injection site, call **1-800-4HUMIRA** (1-800-448-6472) for help.
After completing the injection, place a cotton ball or gauze pad on the skin of the injection site.

- **Do not** rub
- Slight bleeding at the injection site is normal

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How should I dispose of the used HUMIRA Pen?

- Put your used needles, Pens, and sharps in a FDA cleared sharps disposal container right away after use. **Do not throw away (dispose of) loose needles, syringes, and the Pen in the household trash.**
- If you do not have a FDA cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: http://www.fda.gov/safesharpsdisposal.
- Do not dispose of your used sharps disposal container in your household trash unless your community guidelines permit this. Do not recycle your used sharps disposal container.

The Pen caps, alcohol swab, cotton ball or gauze pad, dose tray, and packaging may be placed in your household trash.

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Questions About Using the HUMIRA Pen

What if I have not received in person training from a healthcare provider?
- Call your healthcare provider or **1-800-4HUMIRA (1-800-448-6472)** or visit www.HUMIRA.com if you need help

How do I know when the injection is complete?
- The yellow indicator has stopped moving. This takes up to **10** seconds.

What should I do if there are more than a few drops of liquid on the injection site?
- Call **1-800-4HUMIRA (1-800-448-6472)** for help

What if I do not have an FDA-cleared sharps disposal container or proper household container?
- Call **1-800-4HUMIRA (1-800-448-6472)** for a free FDA-cleared sharps disposal container

Always keep the Pen and the sharps disposal container out of reach of children.



Keep a record of the dates and locations of your injections. To help remember when to take HUMIRA, mark your calendar ahead of time.

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This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised 02/2021

Manufactured by AbbVie Inc. North Chicago, IL 60064 U.S.A.
US License Number 1889 20066945

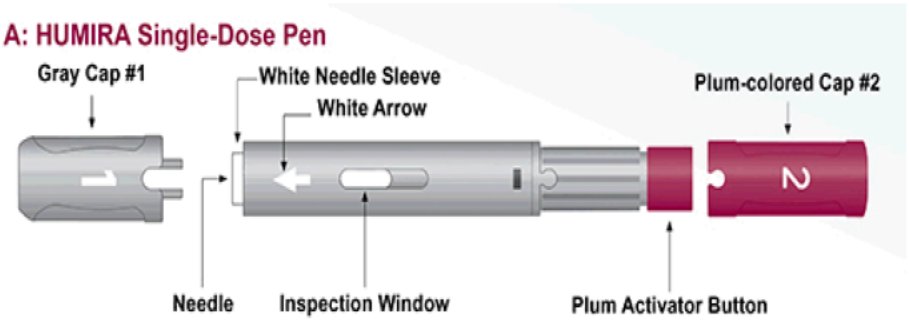
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INSTRUCTIONS FOR USE

HUMIRA® (Hu-MARE-ah)
(adalimumab)
Packages containing 80 mg/0.8 mL
Single-Dose Pen

Before Injecting: Your healthcare provider should show you how to use HUMIRA before you use it for the first time. Call your healthcare provider or **1-800-4HUMIRA** (1-800-448-6472) if you need help.

Figure A: HUMIRA Single-Dose Pen



Important Information You Need to Know Before Injecting HUMIRA

Do not use the Pen and call your healthcare provider or pharmacist if:

- Liquid is cloudy, discolored, or has flakes or particles in it
- Liquid has been frozen (even if thawed) or left in direct sunlight
- Expiration date has passed
- The Pen has been dropped or crushed

Keep the caps on until right before your injection.

How should I store HUMIRA?

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- Store HUMIRA in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store HUMIRA in the original carton until use to protect it from light.
- **Do not freeze**
- Refrigerated HUMIRA may be used until the expiration date printed on the HUMIRA carton, dose tray or Pen.
- If needed, for example when you are traveling, you may also store HUMIRA at room temperature up to 77°F (25°C) for up to **14** days.
- Throw away HUMIRA if it has been kept at room temperature and not used within **14** days.
- Record the date you first remove HUMIRA from the refrigerator in the spaces provided on the carton and dose tray.
- Do not store HUMIRA in extreme heat or cold.

Keep HUMIRA, injection supplies, and all other medicines out of reach of children.

Read Instructions on All Pages Before Using the HUMIRA Pen



Take HUMIRA out of the refrigerator.
Leave HUMIRA at room temperature for **15 to 30 minutes** before injecting.

- **Do not** remove the Gray Cap (Cap #1) or Plum-colored Cap (Cap #2) while allowing HUMIRA to reach room temperature
- **Do not** warm HUMIRA in any other way. For example, **do not** warm it in a microwave or in hot water
- **Do not** use the Pen if liquid has been frozen (even if thawed)

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