

Abatacept

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Generic Name:

ABATACEPT

Proprietary Name: **Orencia**
(Bristol-Myers Squibb)

Approval Rating: **1P**

Therapeutic Class: **Immunomodulator, Selective T-Cell Co-Stimulation Modulator**

Similar Drugs: **Adalimumab, Anakinra, Etanercept, Infliximab**

Sound- or Look-Alike Names:

Aptosyn, Orinase, Ornex, Alefacept

INDICATION(S)

Abatacept is indicated for reducing the signs and symptoms

of rheumatoid arthritis, inducing major clinical response, slowing the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs), including methotrexate or tumor necrosis factor (TNF)-blocking agents. Abatacept may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists. Abatacept should not be used concomitantly with TNF antagonists or anakinra.¹

Indications for other similar biologic agents used in the treatment of rheumatoid arthritis are summarized in Table 1.

CLINICAL PHARMACOLOGY

The development of rheumatoid arthritis is the result of multiple destructive inflammatory processes (eg, increased levels of anti-immunoglobulin G [IgG] Fc antibodies, TNF, IL-1, IL-2, IL-6, IL-15). One of these processes is a direct consequence of naïve T-cell activation and the production of inflammatory molecules (eg, IL-2). The activation of naïve T cells requires two distinct signals; one from the exposure to an antigen and the other from costimulators. The antigen-presenting cells (APCs; eg, dendritic cells, macrophages, B cells) interact with the antigen through the human leukocyte antigen (HLA) molecules of the APCs. The signal from this interaction is not sufficient to fully activate the naïve T cell, but when the signal from this interaction is combined with the signal from the costimulator (eg, CD28), the naïve T cell is maximally activated. The activated T cell is then responsible for the increased production of IL-2 and cell proliferation. The activity of another modulator, cytotoxic T-lymphocyte antigen-4 (CTLA-4), is upregulated on the T cell following its activation. The CTLA-4 also interacts with the CD80 and CD86 to help modulate T-cell function by interrupting the CD28 pathway.³⁻⁵

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Table 1. FDA-Approved Indications for Selected Biological Agents Used in the Treatment of Rheumatoid Arthritis^{1,2}

Generic	Brand	Major Mechanism	Indications						
			Ankylosing spondylitis	Crohn disease	Ulcerative colitis	Plaque psoriasis	Psoriatic arthritis	Juvenile rheumatoid arthritis	Rheumatoid arthritis
Abatacept	Orencia	T-cell co-stimulation modulator							X
Adalimumab	Humira	TNF- α inhibitor				X ^a	X		X
Anakinra	Kineret	Interleukin-1 (IL-1) receptor antagonist							X
Etanercept	Enbrel	TNF- α inhibitor	X			X	X	X	X
Infliximab	Remicade	TNF- α inhibitor	X	X	X	X ^a	X	X ^a	X

^aOff-label use

Abatacept is a recombinant fusion protein comprising the extracellular domain of human CTLA-4 and a fragment of the Fc domain of human IgG1, which has been modified to prevent complement fixation. It is produced by recombinant deoxyribonucleic acid (DNA) technology in a mammalian expression system. Abatacept, like endogenous CTLA-4, competes with CD28 for CD80 and CD86 binding, and thereby can be used to selectively modulate T-cell activation.^{3,4,6} Abatacept selectively modulates the CD28–CD80/86 costimulatory signal required for full naïve T-cell activation by competitively blocking the binding of the co-stimulator (eg, CD28) to the APC ligand. This allows the drug to modulate T-cell activation without completely blocking its function.^{3,4}

Abatacept binds CD80 more avidly than CD86. A second-generation version of abatacept (LEA29Y) has increased affinity for CD86, which appears to be the

dominant co-stimulatory ligand in several experimental animal models for autoimmune disease (eg, systemic lupus erythematosus, multiple sclerosis, collagen-induced arthritis).⁴ Abatacept exhibited inhibition of the onset and progression of disease in a rat collagen-induced arthritis model with reductions in inflammation, inflammatory mediators (interferon gamma, IL-2, monocyte chemoattractant protein-1 [MCP-1], MCP-3, IL-1 α , and IL-6), and bone and joint destruction.

PHARMACOKINETICS

The mean terminal half-life of abatacept was 16.7 days (range, 12 to 23 days) following administration of a single 10 mg/kg IV dose in healthy subjects.¹ Multiple IV doses on days 1, 15, and 30, and monthly thereafter in patients with rheumatoid arthritis produced proportional increases in peak concentration and area under the curve over the dosing range of 2 to 10 mg/kg. The mean

terminal half-life was 13.1 days (range, 8 to 25 days). However, accumulation was not observed with monthly administration of 10 mg/kg in these patients with rheumatoid arthritis.¹

A trend toward greater clearance with increasing body weight has been observed. Age and gender did not influence abatacept pharmacokinetics, nor did coadministration with methotrexate, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, or TNF-blocking agents.¹

The pharmacokinetics of abatacept have not been studied in children and adolescents, nor in patients with renal or hepatic impairment.¹

COMPARATIVE EFFICACY

Abatacept was evaluated in several phase 2 and 3 studies that were published or presented in meeting abstracts and summarized in the prescribing information.

The Abatacept Trial in Treat-

ment of Anti-TNF Inadequate Responders (ATTAIN) was a 6-month, randomized, double-blind study enrolling 391 patients with active rheumatoid arthritis and an inadequate response to at least 3 months of therapy with etanercept or infliximab, or both. Patients were randomly assigned, in a 2:1 ratio, to receive abatacept (n = 258) or placebo (n = 133) as a 30-minute IV infusion on days 1, 15, and 29, and every 28 days thereafter for 6 months. Abatacept was dosed based on body weight; 500 mg for patients weighing less than 60 kg, 750 mg for those weighing 60 to 100 kg, and 1,000 mg for those weighing more than 100 kg. Abatacept treatment was in addition to at least one DMARD; 78% were receiving concomitant methotrexate. Patients discontinued previous TNF-alpha inhibitor therapy before randomization; etanercept was discontinued at least 28 days prior to randomization and infliximab was discontinued at least 60 days prior to randomization. Randomization was stratified according to current use of TNF-alpha inhibitors at the time of screening for current users and former users. At randomization, patients had to have at least 10 swollen joints, at least 12 tender joints, and C-reactive protein levels of at least 1 mg/dL. Patients had to have been taking an oral DMARD or anakinra for at least 3 months, and the dose of this medication had to have been stable for at least 28 days. Oral corticosteroids were also allowed if the dose had been stable for at least 28 days and was less than 10 mg/day equivalent of prednisone. Changes in the doses of background DMARDs were not allowed during the study period, except to avoid adverse effects. The primary end points for the study were the

proportion of patients with an American College of Rheumatology 20 response (ACR20; indicating a clinical improvement of 20% or greater) and the proportion of patients with an improvement of at least 0.3 from baseline in the Health Assessment Questionnaire (HAQ) disability index at 6 months. After 6 months, ACR20 was achieved in 50.4% of abatacept-treated patients, compared with 19.5% of patients treated with placebo ($P < 0.001$; number needed to treat [NNT], 3.2). Response rates for ACR50 were 20.3% with abatacept, compared with 3.8% with placebo ($P < 0.001$; NNT, 6.1). Response rates for ACR70 were 10.2% with abatacept and 1.5% with placebo ($P = 0.003$; NNT, 11.5). ACR response rates were similar in patients with disease duration of 5 years or less and patients with disease duration greater than 5 years. Response rates were also consistent in groups of patients with inadequate responses to etanercept, infliximab, or both. At 6-months, significant improvements were observed for each component of the ACR compared with placebo (tender joint count, swollen joint count, patient-reported pain, patient global assessment, physician global assessment, patient assessed disability [HAQ], and C-reactive protein). Improvements in tender joints, patients' and physician global assessments, and C-reactive protein were observed after the first dose (day-15 assessment). An improvement from baseline of at least 0.3 in the HAQ disability index was achieved in 47.3% of abatacept-treated patients, compared with 23.3% of placebo-treated patients ($P < 0.001$; NNT, 4.2). At 6 months, improvements in pain, sleep quality, and fatigue were greater in the

abatacept group than in the placebo group. Abatacept was also associated with greater improvements than placebo in all eight domains of the health-related quality of life Short-Form 36 (SF-36; physical function, role-physical, bodily pain, general health, vitality, social function, role-emotional, and mental health), as well as the physical and mental component summary scores. Greater reductions in serum levels of several serum biomarkers (rheumatoid factor, IL-6, matrix metalloproteinase-3) were also observed with abatacept, compared with placebo.⁶⁻¹²

The Abatacept in Inadequate responders to Methotrexate (AIM) study was a randomized, double-blind, placebo-controlled study assessing the efficacy and safety of abatacept in patients treated with abatacept 10 mg/kg (n = 433) or placebo (n = 219) for active rheumatoid arthritis despite methotrexate therapy. Abatacept or placebo was administered on day-1, -15, and -29, and every 28 days thereafter. Methotrexate was continued during the study; one nonbiologic DMARD (hydroxychloroquine, sulfasalazine, gold) could be added between 6 and 12 months. Co-primary end points included the ACR20 response at 6 months and structural damage progression (Genant-modified Sharp score) at 1-year. Secondary end points included ACR50 and ACR70 responses at 6 months and all ACR responses at 1-year. Improvement in ACR20 responses was observed as early as day-15. For individual ACR components, tender joints and physical function were improved, compared with placebo at 3-, 6-, and 12-months; swollen joints, pain, patient global assessment, physician global assessment, and C-reactive protein

Table 2. The Abatacept in Inadequate Responders to Methotrexate Study: Response Rates, Abatacept vs Placebo^{1,18,28}

Parameter	Abatacept	Placebo
ACR20		
Month-6	67.9% ^a	39.7%
Month-12	73% ^a	40%
ACR50		
Month-6	39.9% ^a	16.8%
Month-12	48% ^a	18%
ACR70		
Month-6	19.8% ^a	6.5%
Month-12	29% ^a	6%
DAS28 < 3.2 (low disease activity)	42.5%	9.9%
DAS28 < 2.6 (remission)	23.8% ^a	1.9%
Major clinical response^b	14% ^a	2%

^a $P < 0.001$
^bDefined as achieving an ACR70 response for a continuous 6-month period

were improved, compared with placebo at 1-, 3-, 6-, and 12-months. ACR responses and scores for the Disease Activity Score in 28 joints (DAS28) are summarized in Table 2. An improvement from baseline of at least 0.3 in the HAQ disability index was achieved in 63.7% of abatacept-treated patients, compared with 39.3% of placebo-treated patients at 1-year ($P < 0.001$; NNT, 4.1). Abatacept-treated patients also demonstrated improvements in all eight subscales and both mental and physical component summaries of the health-related quality of life SF-36. Abatacept was also associated with improvements in sleep quality and reduced fatigue, compared with placebo. Mean improvement from baseline in ability to perform daily activities was 7.79 with abatacept, compared with 3.88 with placebo at 6-months ($P < 0.001$), and 8.39 with abatacept and 4.45

with placebo at 12-months ($P < 0.001$). At 1-year, paired radiographs revealed inhibition of structural damage progression with abatacept compared with placebo, as shown by reductions in erosion scores ($P = 0.029$), joint space narrowing scores ($P = 0.009$), and total scores ($P = 0.012$). The greatest inhibition of progression of erosions was seen in the subset of patients with disease duration of 2 years or less; although, improvements were seen in all subsets of disease duration (2 years or less, more than 2 years to 5 years or less, greater than 5 years to 10 years or less, and greater than 10 years). Reductions in serum levels of multiple proinflammatory mediators, including rheumatoid factor, IL-6, and matrix metalloproteinase-3, were also seen with abatacept, compared with placebo.^{8,13-20} Similarly, pain scores and quality of life SF-36 scores showed consistent

results through year-3.¹⁵

The Abatacept Study of Safety in Use with other Rheumatoid arthritis therapies (ASSURE) assessed the safety of abatacept in patients with active rheumatoid arthritis during 1 year of therapy with abatacept add-on to treatment with one or more traditional nonbiologic DMARDs and/or biologic DMARDs currently approved for rheumatoid arthritis. Patients were randomized to therapy with abatacept 10 mg/kg or placebo for 1 year. A total of 1,441 patients were randomized and treated (856 with abatacept and nonbiologic DMARD, 103 with abatacept and biologic DMARD, 418 with placebo and nonbiologic DMARD, and 64 with placebo and biologic DMARD). Adverse effects occurred most frequently in the patients treated with abatacept plus a biologic DMARD. Adverse effects in the group treated with abatacept plus a nonbiologic DMARD did not differ from those treated with placebo and a nonbiologic DMARD. An improvement from baseline of at least 0.3 in the HAQ disability index was achieved in 47.3% of abatacept-treated patients, compared with 34.6% of placebo-treated patients ($P < 0.001$; NNT, 7.9).^{21,22}

Six- and 12-month results from a phase 2b, double-blind, randomized, placebo-controlled study were also published. In this study, 339 patients with active rheumatoid arthritis despite methotrexate therapy for at least 6 months were randomly assigned therapy with abatacept 10 mg/kg ($n = 115$), abatacept 2 mg/kg ($n = 105$), or placebo ($n = 119$) administered IV over 30 minutes on day-1, -15, and -30, and every 30 days thereafter. Methotrexate therapy was continued at a dose of 10 to

30 mg/week. All other DMARDs were discontinued before study entry; corticosteroid doses were reduced to the equivalent of prednisone 10 mg/day or less. Corticosteroids were continued in 79.8% of patients and NSAIDs were continued in 88.1%. At 6-months, ACR20 response was achieved in 60% treated with abatacept 10 mg/kg, compared with 35% treated with placebo ($P < 0.001$). At 1-year, ACR20 response was achieved in 62.6% of patients treated with abatacept 10 mg/kg, compared with 36.1% treated with placebo ($P < 0.001$). An ACR50 response was achieved in 41.7% treated with abatacept 10 mg/kg and 20.2% treated with placebo ($P < 0.001$). An ACR70 response was achieved in 20.9% treated with abatacept 10 mg/kg and 7.6% treated with placebo ($P = 0.003$). Higher ACR response rates were observed in patients with disease duration of 3 years than those with longer disease duration; although, abatacept was more effective than placebo in both patient populations. Patients treated with abatacept 10 mg/kg also exhibited improvement in modified HAQ scores (49.6% vs 27.7% with placebo; $P < 0.001$), an increase in rates of remission as assessed with the DAS28 (34.8% vs 10.1% with placebo; $P < 0.001$), and improvement in all eight subscales of the SF-36.^{20,23-25} A 2-year, open-label extension of this study included 84 abatacept 10 mg/kg-treated patients. At 2-years, ACR20 response was achieved in 77.3% of patients, ACR50 response was achieved in 54.7% of patients, and ACR70 response was achieved in 29.3% of patients.²⁶ An improvement from baseline of at least 0.3 in the modified HAQ disability index was achieved in 54.8% of abata-

cept-treated patients at 1-year and 53.1% of patients at 3-years.¹⁴ Remission (DAS28 score less than 2.6) was achieved in 25.3% of abatacept-treated patients at 1-year, 27.8% at 2-years, and 26.6% at 3-years.²⁰

Abatacept was also assessed in a double-blind, placebo-controlled, dose-finding study enrolling 214 patients with rheumatoid arthritis. Patients received four infusions of abatacept (0.5, 2, or 10 mg/kg) or placebo IV on days 1, 15, 29, and 57, and were evaluated on day-85. ACR20 response was achieved in 23%, 44%, and 53% of patients treated with abatacept 0.5, 2, and 10 mg/kg, respectively, and 31% treated with placebo.²⁷

Abatacept is also undergoing assessment in the treatment of relapsing-remitting multiple sclerosis.²⁸

CONTRAINDICATIONS

Abatacept is contraindicated in patients with a history of hypersensitivity to any of the product ingredients.¹

WARNINGS AND PRECAUTIONS

Concomitant use of abatacept with TNF antagonists is not recommended. Patients receiving concomitant abatacept and TNF antagonist therapy in clinical trials experienced more infections (63%) and more serious infections (4.4%) compared with patients receiving TNF antagonists only (43% and 0.8%, respectively). Efficacy was not improved with concomitant use.¹

Hypersensitivity reactions occurred in some patients treated with abatacept in clinical trials. Among 2,688 patients treated with abatacept, there were two cases of anaphylaxis or anaphylactoid reactions. Other events possi-

bly associated with hypersensitivity reactions, such as hypotension, urticaria, and dyspnea, occurred in fewer than 0.9% of abatacept-treated patients.¹ Acute infusion-related events occurred in 9% of abatacept-treated patients and 6% of placebo recipients. The most frequently reported infusion-related events included dizziness, headache, and hypertension at rates of 1% to 2%. Other acute infusion-related events included hypotension, increased blood pressure, dyspnea, nausea, flushing, urticaria, cough, hypersensitivity, pruritus, rash, and wheezing.¹

As with other biologic DMARD agents used in the treatment of rheumatoid arthritis, abatacept carries the potential for increased risk of infection.¹ Caution is advised when administering abatacept in patients with a history of recurrent infections, underlying conditions that may predispose to infection or chronic, latent, or localized infections. Patients developing a new infection while receiving abatacept therapy should be closely monitored. Abatacept should be discontinued if a patient develops a serious infection. Administration with concomitant biologic rheumatoid arthritis therapy (eg, etanercept, infliximab, adalimumab, anakinra) may be associated with an increased incidence of infections.¹

Prior to initiating therapy with abatacept, patients should be screened for latent tuberculosis infection with a tuberculin skin test. Patients testing positive should be treated by standard medical practice prior to initiating therapy with abatacept.¹

In patients with chronic obstructive pulmonary disease (COPD), abatacept was associated with an increased incidence of adverse effects, including COPD

Table 3. Adverse Reactions Occurring in More than 3% of Patients and More Frequently with Abatacept than Placebo¹

<i>Adverse Reaction</i>	<i>Abatacept (n = 1,955)</i>	<i>Placebo (n = 989)</i>
Headache	18%	13%
Nasopharyngitis	12%	9%
Dizziness	9%	7%
Cough	8%	7%
Back pain	7%	6%
Hypertension	7%	4%
Dyspepsia	6%	4%
Urinary tract infection	6%	5%
Rash	4%	3%

exacerbations, cough, rhonchi, and dyspnea. Abatacept should be used with caution in patients with COPD and rheumatoid arthritis. Such patients should be monitored for worsening of respiratory status.¹

As with other biologic DMARD agents used in the treatment of rheumatoid arthritis, abatacept may also impact the development and course of malignancies.¹

The safety and efficacy of abatacept have not been established in patients with renal or hepatic impairment, or in pediatric patients.¹

Abatacept is in Pregnancy Category C. Animal studies have not revealed evidence of teratogenicity. At doses 11-fold higher than the recommended human dose based on systemic exposure, alterations in immune function and inflammation of the thyroid were observed in some offspring. There are no studies in pregnant women. Abatacept should be used in pregnancy only if clearly needed.¹

Abatacept is excreted in the milk of lactating rats. It is not known whether abatacept is

excreted in human milk or absorbed systemically after ingestion. Because of the potential for effects on the developing immune system in breast-feeding infants, a decision should be made to discontinue either breast-feeding or abatacept.¹

ADVERSE REACTIONS

Most frequently observed adverse reactions in clinical studies included headache, upper respiratory infections, nasopharyngitis, and nausea.¹ The adverse reactions occurring in more than 3% of patients treated with abatacept and at least 1% more frequently in patients treated with abatacept than those treated with placebo are summarized in Table 3. Other common adverse reactions included cough, bronchitis, dyspepsia, dizziness, back pain, hypertension, and infusion reactions.^{1,6,23,29}

In placebo-controlled studies with abatacept, infections were reported in 54% of abatacept-treated patients and 48% of placebo-treated patients. Serious infections were reported in 3% of patients treated with abatacept and 1.9% treated with placebo.¹

DRUG INTERACTIONS

Live vaccines should not be given concurrently with abatacept or within 3 months of its discontinuation.¹

Methotrexate, NSAIDs, corticosteroids, and TNF-blocking agents did not alter abatacept clearance. The majority of patients in abatacept studies received one or more of the following agents concomitantly with abatacept: methotrexate, NSAIDs, corticosteroids, TNF-blocking agents, azathioprine, chloroquine, gold, hydroxychloroquine, leflunomide, sulfasalazine, or anakinra.¹

Concurrent therapy with TNF antagonists and abatacept is not recommended. Concurrent use of TNF antagonists with abatacept is associated with increased risk of serious infections, with no additional efficacy over the use of TNF antagonists alone.¹ There is insufficient experience with the use of abatacept with anakinra; therefore, the concomitant use of anakinra with abatacept is also not recommended.¹

RECOMMENDED MONITORING

Patients should be monitored for improvement in the signs and symptoms of their rheumatoid arthritis. They should also be closely monitored during the infusion for signs and symptoms of an infusion reaction and throughout therapy for signs and symptoms of an infection.

DOSING

The recommended weight-based abatacept dose (500 mg for patients weighing less than 60 kg, 750 mg for those weighing 60 to 100 kg, and 1,000 mg for patients weighing more than 100 kg) should be administered as an IV infusion over 30 minutes, at week-2 and -4 after the first infusion,

and every 4 weeks thereafter.¹ The infusion set should include a sterile, nonpyrogenic, low-protein-binding filter (pore size 0.2 to 1.2 μm).¹

Abatacept lyophilized powder must be reconstituted with 10 mL of sterile water for injection, USP, using only the silicone-free disposable syringe provided with each vial and an 18 to 21 gauge needle. If the powder is accidentally reconstituted with a siliconized syringe, the solution may develop translucent particles and must be discarded.¹

To minimize foam formation during reconstitution, the vial should be rotated gently until the contents are completely dissolved. Upon complete dissolution, the vial should be vented with a needle to dissipate any foam that may be present.¹

The reconstituted solution containing abatacept 25 mg/mL (250 mg per 10 mL) must be further diluted to 100 mL. From an 100 mL infusion bag or bottle, withdraw a volume of 0.9% sodium chloride injection, USP, equal to the volume of the reconstituted vials (two vials [500 mg] remove 20 mL, three vials [750 mg] remove 30 mL, four vials [1 g] remove 40 mL). The reconstituted abatacept solution from each vial should be added into the infusion bag or bottle using the silicon-free disposable syringe provided with the vial. The resulting diluted solution will contain abatacept 5, 7.5, or 10 mg/mL.¹ Infusion must be completed within 24 hours of reconstitution of the abatacept vials. Fully diluted abatacept solution may be stored at room temperature or refrigerated at 2° to 8°C (36° to 46°F) prior to use.¹

PRODUCT AVAILABILITY AND STORAGE

Abatacept received FDA approval in December 2005. It is available as a sterile, white, preservative-free, lyophilized powder for parenteral administration. Each single-use vial provides abatacept 250 mg, maltose 500 mg, sodium phosphate monobasic 17.2 mg, and sodium chloride 14.6 mg. Following reconstitution with 10 mL of sterile water for injection, USP, the solution has a pH of 7 to 8.¹ The individually packaged vial is packaged with a silicone-free disposable syringe.¹

Abatacept vials should be stored under refrigeration at 2° to 8°C (36° to 46°F) and protected from light by storing in the original package until the time of use.¹

CONCLUSION

Abatacept is a biologic DMARD agent. It appears effective in patients failing to adequately respond to methotrexate, etanercept, or infliximab when used in combination with methotrexate or other nonbiological DMARD therapy. Additional clinical efficacy and adverse effect information is necessary to identify the best place for abatacept in the treatment of rheumatoid arthritis.

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Continuing Education Case Study Quiz

Goal — The goal of this program is to educate the reader about the use of abatacept in the treatment of rheumatoid arthritis.

Objectives — At the completion of this program, the reader will be able to:

1. Describe the pharmacology and pharmacokinetics of abatacept.
2. Discuss the risks associated with abatacept use.
3. Be able to discuss the potential benefit of abatacept for an individual patient.
4. Apply the information on the use of abatacept to a case study.

Key Words — rheumatoid arthritis; immunomodulators; DMARDs

1. Abatacept is FDA approved for the treatment of rheumatoid arthritis in:

- A. Conjunction with infliximab
- B. Conjunction with methotrexate and etanercept
- C. Patients with an inadequate response to one or more DMARDs
- D. Pediatric and adult patients

2. Abatacept exerts its activity in rheumatoid arthritis by:

- A. Blocking tumor necrosis factor alpha
- B. Inhibiting dihydroorotate dehydrogenase
- C. Inhibiting interleukin-1
- D. Modulating T-cell activation

3. The mean terminal elimination half-life of abatacept is:

- A. 24 to 48 hours
- B. 3 to 5 days
- C. 10 to 20 days
- D. 3 to 4 weeks

4. Upon initiation of therapy in clinical studies, improvement in tender joints, patient assessments, and C-reactive protein have been observed:

- A. After the first dose
- B. After the third dose

- C. After three to 6 months of therapy
- D. After 1 year of therapy

Case History

KC is a 63-year-old female with rheumatoid arthritis, type 2 diabetes, and COPD. She has been treated with regimens including NSAIDs, sulfasalazine, hydroxychloroquine, prednisone, methotrexate, and etanercept. Recently, the use of etanercept plus methotrexate provided slight reductions in joint pain and swollen joints compared with the use of methotrexate alone; however, the changes were not sufficient to improve her ability to conduct daily activities. Her physician has decided to try abatacept therapy. KC is 5'2" tall and weighs 149 pounds.

5. Based on her recent regimen, KC should receive abatacept:

- A. As monotherapy
- B. In conjunction with the etanercept
- C. In conjunction with the methotrexate
- D. In conjunction with the methotrexate and etanercept

6. The recommended dose of abatacept for KC is:

- A. 500 mg
- B. 750 mg
- C. 1,000 mg
- D. 1,500 mg

7. The dose should be administered:

- A. As a subQ infusion over 24 hours
- B. As an IV infusion over 2 hours
- C. As an IV infusion over 30 minutes
- D. As an IM injection

8. Prior to initiation of therapy, KC should be screened for:

- A. Hepatic impairment
- B. Tuberculosis
- C. Pneumonia
- D. Pregnancy

9. Because KC also has type 2 diabetes, she is at increased risk for developing:

- A. A positive tuberculin skin test
- B. Hypersensitivity reactions
- C. Infections
- D. Malignancies

10. If abatacept therapy is initiated, KC should be monitored closely for:

- A. Hepatotoxicity
- B. Neutropenia
- C. Decreased respiratory function
- D. Poor glycemic control

11. KC should also be monitored for acute infusion-related events including:

- A. Dizziness, headache, and hypertension
- B. Flushing, cough, and rash
- C. Hypotension, urticaria, and dyspnea
- D. All of the above

12. The most common adverse effects observed with abatacept in clinical trials included:

- A. Dizziness, nausea, and diarrhea
- B. Headache, nasopharyngitis, and dizziness
- C. Hypertension, hypotension, and infection
- D. Wheezing, cough, and urticaria

13. Several weeks after starting abatacept therapy, she asks you if she should receive the new herpes zoster vaccine. She should be advised that she:

- A. Should not receive the vaccine ever, as it is contraindicated in patients with her medical history
- B. Should not receive the vaccine while she is receiving abatacept therapy, or within 3 months of stopping abatacept therapy
- C. Should receive the vaccine as soon as possible since she is at increased risk for developing herpes zoster
- D. Should receive the vaccine between abatacept doses, to improve her immune response to the vaccine

14. Abatacept should be reconstituted with the provided:

- A. Diluent containing dehydrated alcohol in water
- B. Filtered needle
- C. Latex-free syringe
- D. Silicone-free syringe

15. Unopened abatacept vials should be stored:

- A. In the freezer
- B. In the refrigerator
- C. In the refrigerator or at room temperature
- D. At room temperature

Drug Evaluations: Abatacept
ACPE # 071-999-06-016-H01 0.15 CEU
Program Expires: August 2009

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Note: Your answer sheet will be graded confidentially and you will receive prompt notification of your score. In order to receive continuing education credit for this program, you need a minimum correct response rate of 70%.

PROGRAM EVALUATION

Please rate our continuing education offering by responding to the following questions.

1. This program described the pharmacology and pharmacokinetics of abatacept:
 completely fairly well not at all

2. I was able to apply the knowledge from this educational program and other resources to answer questions associated with the case study:
 completely fairly well not at all
3. The program discussed the risks associated with the use of abatacept:
 completely fairly well not at all
4. After this program, I was able to discuss the potential benefit of abatacept for an individual patient:
 completely fairly well not at all
5. The overall quality of the program was:
 excellent good fair poor
6. Was the content of this article relevant to the practice of pharmacy?
 excellent good fair poor
7. How long did it take you to complete this continuing education program? _____ hours
8. What other continuing education programs or topics would you like to see?

<i>Answer Form</i>			
1. A B C D	9. A B C D		
2. A B C D	10. A B C D		
3. A B C D	11. A B C D		
4. A B C D	12. A B C D		
5. A B C D	13. A B C D		
6. A B C D	14. A B C D		
7. A B C D	15. A B C D		
8. A B C D			



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