SELECTED THERAPIES FOR THE TREATMENT OF RHEUMATOID ARTHRITIS*

RA

Refer to the individual Product Monographs for complete indications and information about contraindications, warnings, precautions, adverse reactions, interactions, dosing and conditions of clinical use.

ACTEMRA® (tocilizumab)[1] is indicated for reducing signs and symptoms in adult patients with moderately to severely active RA. ACTEMRA (IV only) in combination with MTX has been shown to reduce the rate of progression of radiographic joint damage at week 52.

CIMZIA® (certolizumab)[2] is, in combination with MTX, indicated for reducing signs and symptoms, inducing major clinical response, and reducing the progression of joint damage as assessed by X-ray, in adult patients with moderately to severely active RA. CIMZIA may be used alone for reducing signs and symptoms in adult patients with moderately to severely active RA who do not tolerate MTX.

ENBREL® (etanercept)[3] is indicated for the treatment of moderately to severely active RA in adults. Treatment is effective in reducing the signs and symptoms of RA, inducing major clinical response, inhibiting the progression of structural damage and improving physical function. ENBREL can be initiated in combination with MTX in adult patients or used alone.

HUMIRA® (adalimumab)[4] is indicated for reducing the signs and symptoms, inducing major clinical response and clinical remission, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active RA. HUMIRA can be used alone or in combination with MTX or other DMARDs. When used as first-line treatment in recently diagnosed patients who have not been previously treated with MTX, should be given in combination with MTX. HUMIRA can be given as monotherapy in case of intolerance to MTX or when treatment with MTX is contraindicated.

ORENCIA® (abatacept)[5] is indicated in the treatment of RA for reducing the signs and symptoms and inducing clinical responses. ORENCIA may be also used long-term, to inhibit the progression of structural damage, and improve physical function in adult patients with moderately to severely active RA who have had an inadequate response to one or more DMARDs or to TNF antagonists or to both. ORENCIA may be administered by IV or SC route. It is expected, based on pharmacokinetic information, that the SC route of administration will be beneficial in the long-term. ORENCIA may be used as monotherapy or in combination with DMARD therapy. When used as first-line treatment in recently diagnosed patients who have not been previously treated with MTX, ORENCIA should be given in combination with MTX.

REMICADE® (infliximab)[6] is indicated for use in combination with MTX for the reduction in signs and symptoms, inhibition of the progression of structural damage and improvement in physical function in adult patients with moderately to severely active RA.

SIMPONI® (golimumab)[7] SC is, in combination with MTX, indicated for reducing signs and symptoms and improving physical function in adult patients with moderately to severely active RA and inhibiting the progression of structural damage in adult patients with moderately to severely active RA who had not previously been treated with MTX. SIMPONI I.V. is, in combination with MTX, indicated for treatment of adult patients with moderately to severely active RA.

XELJANZ™ (tofacitinib)[8], in combination with MTX, is indicated for reducing the signs and symptoms of RA in adult patients with moderately to severely active RA who have had an inadequate response to MTX. In cases of intolerance to MTX, physicians may consider the use of XELJANZ as monotherapy.

DMARD=disease-modifying antirheumatic drug; **IV=**intravenous; **JAK=**Janus-associated kinase; **MTX=**methotrexate; **RA=**rheumatoid arthritis; **SC=**subcutaneous; **TNF=**tumour necrosis factor

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* Comparative clinical significance has not been established.
† Time taken for plasma concentration of the drug to fall by 50%.[10]

Trade name (generic name)	Therapeutic classification	Available for RA in Canada	Terminal half-life†	Dosage & route of administration	Storage
ACTEMRA® (tocilizumab)[1]	Interleukin receptor inhibitor[1]	**2010**[9]	Half-life 21 days	**IV infusion:** When used in combination with DMARDs or as monotherapy, the recommended starting dose is 4 mg/kg IV every 4 weeks, followed by an increase to 8 mg/kg based on clinical response **SC injection:** <100 kg weight: starting dose 162 mg SC every other week, followed by an increase to every week based on clinical response ≥100 kg weight: 162 mg SC every week	Store in a refrigerator at 2°C to 8°C. Do not freeze. Keep the vial in the outer carton to protect it from light.
CIMZIA® (certolizumab)[2]	Biological response modifier[2]	**2009**[9]	Half-life 14 days	Loading dose 400 mg SC given at weeks 0, 2 and 4 Maintenance dose of 200 mg given every other week, or 400 mg given every 4 weeks	Store at 2°C to 8°C (36°F to 46°F). Do not freeze. Protect from light.
ENBREL® (etanercept)[3]	Biological response modifier[3]	**2000**[9]	Mean half-life 4.25±1.25 days	50 mg SC per week A 50 mg dose can also be given as two 25 mg SC injections either on the same day once weekly or 3 or 4 days apart	Store refrigerated at 2°C to 8°C. Do not freeze. Keep the product in the original carton to protect from light until the time of use. May be transferred to room temperature storage (≤27°C) for a period not to exceed 60 days. Once transferred to room temperature storage, ENBREL must be used within 60 days.
HUMIRA® (adalimumab)[4]	Biological response modifier[4]	**2004**[9]	Mean half-life ~2 weeks Range: 10-20 days	40 mg SC administered every other week	Must be refrigerated between 2°C and 8°C. Store in original carton until time of administration. Do not freeze. Protect from light. Option to store at temperatures up to a maximum of 25°C (77°F) for a single period of up to 14 days. Must be discarded if not used within the 14-day period.
ORENCIA® (abatacept)[5]	Selective co-stimulation modulator[5]	**2006**[9]	**IV infusion:** Mean half-life 13.1 days Range: 8-25 days **SC injection:** Mean half-life 14.3 days	■ **IV infusion:** Weight range-based dosing: <60 kg=500 mg, 60-100 kg=750 mg and >100 kg=1 g. Following initial IV infusion, IV infusion at 2 and 4 weeks and every 4 weeks thereafter ■ **SC injection:** After initial IV loading dose (dosing as per above), first 125 mg SC given within a day followed by 125 mg SC once weekly Patients who are unable to receive an infusion may initiate weekly injections of SC ORENCIA without an intravenous loading dose.	Must be refrigerated at 2°C to 8°C. Protect the vials from light by storing in the original package until time of use.
REMICADE® (infliximab)[6]	Biological response modifier[6]	**2001**[9]	Half-life 7.7-10 days	3 mg/kg IV followed by 3 mg/kg doses at 2 and 6 weeks after first IV infusion, then every 8 weeks thereafter	Store in original carton under refrigeration at 2°C to 8°C (36°F to 46°F). At the location of reconstitution, REMICADE may also be stored in the original carton up to a maximum of 30°C for a single period of up to 6 months. Since no preservative is present, it is recommended that the administration of the infusion solution should begin within 3 hours of reconstitution and dilution.
SIMPONI® (golimumab)[7]	TNFα inhibitor[7]	**IV infusion: 2013**[9] **SC injection: 2011**[9]	**IV infusion:** Mean half-life 14±4 days **SC injection:** Mean half-life 12±3 days	**IV infusion:** 2 mg/kg given as a 30-minute IV infusion at weeks 0 and 4, then every 8 weeks thereafter **SC injection:** 50 mg SC once a month, on the same date each month	Store refrigerated at 2°C to 8°C (36°F to 46°F). Keep the product in original carton until time of use to protect from light. Do not freeze. Do not shake.
XELJANZ™ (tofacitinib)[8]	Antirheumatic, immunomodulator agent[8]	**2014**[9]	Half-life ~3 hours	5 mg administered orally twice daily, with or without food	Store between 15°C and 30°C.

Subcutaneous injection using prefilled autoinjector, pen, prefilled syringe or vial
Intravenous infusion
Oral tablet
Store refrigerated at 2°C to 8°C
Store at room temperature between 15°C and 30°C

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SELECTED THERAPIES FOR THE TREATMENT OF PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS*

Refer to the individual Product Monographs for complete indications and information about contraindications, warnings, precautions, adverse reactions, interactions, dosing and conditions of clinical use.

PsA AS

Trade name (generic name)	Therapeutic classification	Available for PsA/AS in Canada	PsA		AS		Terminal half-life†	Storage
			Indication	Dosage & route of administration	Indication	Dosage & route of administration		
CIMZIA® (certolizumab)[2]	Biological response modifier[2]	**2014** (PsA, AS)[9]	Alone or in combination with MTX, indicated for reducing signs and symptoms and inhibiting the progression of structural damage as assessed by X-ray, in adult patients with moderately to severely active PsA who have failed one or more DMARDs.	Loading dose 400 mg SC given at weeks 0, 2 and 4 Maintenance dose 200 mg SC every 2 weeks, or 400 mg SC every 4 weeks	Reducing signs and symptoms in adult patients with active AS who have had an inadequate response to conventional therapy.	Loading dose 400 mg SC given at weeks 0, 2 and 4 Maintenance dose 200 mg SC every 2 weeks, or 400 mg SC every 4 weeks	Half-life 14 days	Store at 2°C to 8°C (36°F to 46°F). Do not freeze. Protect from light.
ENBREL® (etanercept)[3]	Biological response modifier[3]	**2004** (PsA), **2005** (AS)[9]	Reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in adult patients with PsA. ENBREL can be used in combination with MTX in adult patients who do not respond adequately to MTX alone.	50 mg SC per week A 50 mg dose can also be given as two 25 mg SC injections either on the same day once weekly or 3 or 4 days apart	Reducing signs and symptoms of active AS.	50 mg SC per week A 50 mg dose can also be given as two 25 mg SC injections either on the same day once weekly or 3 or 4 days apart	Mean half-life 4.25±1.25 days	Store refrigerated at 2°C to 8°C. Do not freeze. Keep the product in the original carton to protect from light until the time of use. May be transferred to room temperature storage (≤27°C) for a period not to exceed 60 days. Once transferred to room temperature storage, ENBREL must be used within 60 days.
HUMIRA® (adalimumab)[4]	Biological response modifier[4]	**2006** (PsA, AS)[9]	Reducing the signs and symptoms of active arthritis and inhibiting the progression of structural damage and improving the physical function in adult PsA patients. HUMIRA can be used in combination with MTX in patients who do not respond adequately to MTX alone.	40 mg SC every other week	Reducing signs and symptoms in patients with active AS who have had an inadequate response to conventional therapy.	40 mg SC every other week	Mean half-life ~2 weeks Range: 10-20 days	Must be refrigerated between 2°C and 8°C. Store in original carton until time of administration. Do not freeze. Protect from light. Option to store at temperatures up to a maximum of 25°C (77°F) for a single period of up to 14 days. Must be discarded if not used within the 14-day period.
OTEZLA® (apremilast)[11]	Selective immunosuppressant[11]	**2015** (PsA)[12]	Alone or in combination with MTX, indicated for the treatment of active PsA in adult patients who have had an inadequate response, intolerance or contraindication to a prior DMARD.	30 mg orally twice daily, with or without food. An initial titration schedule is required to reduce the risk of gastrointestinal symptoms.	Not indicated for AS		Mean half-life 8.88 hours CV: 25.4%	Store at 15°C to 30°C.
REMICADE® (infliximab)[6]	Biological response modifier[6]	**2005** (AS), **2006** (PsA)[9]	Reduction of signs and symptoms, induction of major clinical response, and inhibition of the progression of structural damage of active arthritis, and improvement in physical function in patients with PsA.	5 mg/kg IV followed by additional similar doses at 2 and 6 weeks after first IV infusion, then every 8 weeks thereafter. Can be used with or without MTX. If a patient shows no response at 24 weeks, no additional treatment with REMICADE should be given.	Reduction of signs and symptoms and improvement in physical function in patients with active AS who have responded inadequately, or are intolerant to, conventional therapies.	5 mg/kg IV followed by 5 mg/kg doses at 2 and 6 weeks after first IV infusion, then every 6-8 weeks thereafter	Median half-life 7.7-10 days	Store in original carton under refrigeration at 2°C to 8°C (36°F to 46°F). At the location of reconstitution, REMICADE may also be stored in the original carton up to a maximum of 30°C for a single period of up to 6 months. Since no preservative is present, it is recommended that the administration of the infusion solution should begin within 3 hours of reconstitution and dilution.
SIMPONI® (golimumab)[7]	TNFα inhibitor[7]	**2011** (PsA, AS)[9]	Reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active PsA. SIMPONI can be used in combination with MTX in patients who do not respond adequately to MTX alone.	50 mg SC once a month, on the same date each month	Reducing signs and symptoms in adult patients with active AS who have had an inadequate response to conventional therapies.	50 mg SC once a month, on the same date each month	Mean half-life 12±3 days	Store refrigerated at 2°C to 8°C (36°F to 46°F). Keep the product in original carton until time of use to protect from light. Do not freeze. Do not shake.
STELARA® (ustekinumab)[13]	Selective immunomodulating agent[13]	**2014** (PsA)[9]	Treatment of adult patients with active PsA. STELARA can be used alone or in combination with MTX.	45 mg SC at weeks 0 and 4, then every 12 weeks thereafter 90 mg SC may be used in patients with body weight >100 kg	Not indicated for AS		Median half-life ~3 weeks Range: 15-32 days	Must be refrigerated at 2°C to 8°C and protected from light. Keep the product in the original carton to protect from light until time of use. Do not freeze. Do not shake.

AS=ankylosing spondylitis; **CV=**coefficient of variation; **DMARD=**disease-modifying antirheumatic drug; **IV=**intravenous; **MTX=**methotrexate; **PsA=**psoriatic arthritis; **SC=**subcutaneous; **TNF=**tumour necrosis factor

* Comparative clinical significance has not been established.
† Time taken for plasma concentration of the drug to fall by 50%.[10]

Subcutaneous injection using prefilled autoinjector, pen, prefilled syringe or vial
Intravenous infusion
Store refrigerated at 2°C to 8°C
Store at room temperature between 15°C and 30°C

References: 1. ACTEMRA (tocilizumab) Product Monograph. Hoffmann-La Roche Limited, December 23, 2014. **2.** CIMZIA (certolizumab) Product Monograph. UCB Canada Inc., October 2, 2015. **3.** ENBREL® (etanercept) Product Monograph, manufactured by Immunex Corporation, marketed by Amgen Canada Inc. October 19, 2015. **4.** HUMIRA (adalimumab) Product Monograph. AbbVie Corporation, July 3, 2015. **5.** ORENCIA (abatacept) Product Monograph. Bristol-Myers Squibb Canada, June 22, 2015. **6.** REMICADE (infliximab) Product Monograph. Janssen Inc., July 22, 2015. **7.** SIMPONI/SIMPONI IV (golimumab) Product Monograph. Janssen Inc., November 25, 2014. **8.** XELJANZ (tofacitinib) Product Monograph. Pfizer Canada Inc., April 16, 2014. **9.** Health Canada Notice of Compliance Database. Accessed May 5, 2014. www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/noc-acc/index-eng.php. **10.** Griffin JP, Posner J, Barker GR, eds. *The Textbook of Pharmaceutical Medicine*, 7th ed. West Sussex, UK: John Wiley & Sons, Ltd.; 2013. **11.** OTEZLA (apremilast) Product Monograph. Celgene Inc., June 9, 2015. **12.** Health Canada Notice of Compliance Database. Accessed August 14, 2015. http://webprod5.hc-sc.gc.ca/noc-acc/search-recherche.do?lang=eng. **13.** STELARA (ustekinumab) Product Monograph. Janssen Inc., March 9, 2015.

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