Australian Government
Department of Health
Therapeutic Goods Administration

Australian Rheumatology Association

Arthritis AUSTRALIA

Tocilizumab (Actemra) shortage: Patient management

Joint statement from the Therapeutic Goods Administration, the Australian Rheumatology Association and Arthritis Australia

Shortage of tocilizumab (Actemra)

The sponsor of tocilizumab (Actemra), Roche Products Pty Ltd (Roche), has notified the Therapeutic Goods Administration (TGA) of shortages of multiple presentations of their tocilizumab products due to global demand in response to the COVID-19 pandemic.

From July 2021 to January 2022 there will be various shortages across different strengths of intravenous (IV) tocilizumab. There will also be up to 6 weeks where subcutaneous (SC) tocilizumab presentations (pre-filled syringe and pre-filled pen autoinjector) will be out of stock at patient level.

For details of the supply status of different formulations of tocilizumab, please refer to the TGA website.

The advice in this document may change depending on supply updates for tocilizumab.

This document contains:

- Advice for prescribers about managing patients prescribed tocilizumab during a period of supply constraints and shortage at patient level for the following registered indications:
    - rheumatoid arthritis (RA),
    - polyarticular juvenile idiopathic arthritis (pJIA)
    - systemic juvenile idiopathic arthritis (sJIA)
    - giant cell arteritis (GCA)
    - cytokine release syndrome (CRS)

Summary

- There are multiple shortages of tocilizumab (Actemra) products, with an anticipated shortage at patient level of the subcutaneous presentations for up to 6 weeks. See web statement for details.
- **Patients taking tocilizumab (Actemra)** should contact their specialist as soon as possible about their treatment.
- **Prescribers** should review the shortage dates for each formulation and then review their potentially affected patients.
- **Prescribers** should consider reducing the frequency of tocilizumab SC dose where appropriate (not for Cytokine Release Syndrome (CRS) patients).
- **Prescribers** should delay initiating any new patients on tocilizumab, except where no alternatives or no suitable alternatives are available e.g. for giant cell arteritis (GCA), Cytokine Release Syndrome (CRS) or systemic juvenile idiopathic arthritis (sJIA).
- **Prescribers** should demonstrate to patients using subcutaneous presentations of tocilizumab how to use both the pre-filled syringe and pre-filled pen autoinjector in case they need to be switched.
- **General Practitioners and pharmacists** should advise patients using tocilizumab to contact their rheumatologist as soon as possible.

Summary by condition

Rheumatoid arthritis (RA)

- Avoid initiating new patients on tocilizumab where possible
- Consider reducing dose frequency for established patients, where appropriate
- Consider alternative treatments as outlined in Table 1 for new patients or those who cannot reduce dose frequency
- Ensure patients taking tocilizumab SC formulations have been instructed on how to use both presentations in case they need to switch

Polyarticular juvenile idiopathic arthritis (pJIA)

- Avoid initiating new patients on tocilizumab where possible
- Consider reducing dose frequency for established patients, where appropriate
- Consider alternative treatments as outlined in Table 1 for new patients or those who cannot reduce dose frequency
- Ensure patients taking tocilizumab SC formulations have been instructed on how to use both presentations in case they need to switch

Systemic juvenile idiopathic arthritis (sJIA)

- Consider reducing dose frequency for established patients, where appropriate
- Ensure patients taking tocilizumab SC formulations have been instructed on how to use both presentations in case they need to switch
- Initiate patients on tocilizumab only when no other options are available

Giant cell arteritis (GCA)

- Consider reducing the frequency of tocilizumab dose for some adult GCA patients
- Prescribers should initiate tocilizumab SC in GCA patients where it is not possible to delay treatment

Cytokine release syndrome (CRS)

- Prescribers should not make any changes to treatment plans for CRS patients.

Clinical management advice

Global supply of tocilizumab is unstable during the shortage period with different presentations of the medicine available at different times. Patients should be advised on the possibility of switching subcutaneous tocilizumab presentations if the supply situation changes. Patients taking subcutaneous presentations of tocilizumab may need to switch between the pre-filled syringe and pre-filled pen autoinjector and should be instructed on how to use both.

Managing stabilised/long-term patients during supply constraints

Rheumatoid arthritis (RA) patients

SC formulations – prefilled syringe and pre-filled pen autoinjector

Prescribers should consider reducing the frequency of dose from weekly to every two weeks where appropriate to conserve their patient's supply of tocilizumab SC as there will be an out of stock at patient level for tocilizumab SC. Reduction in frequency for a short period is expected to have minimal impact on patients who are stabilised on tocilizumab SC.

There are few data on flare rates with dose reduction over this time period; there is some evidence that increasing the dosing interval to 2 weeks is associated with loss of remission over a 24-week period, although up to 3/4 of patients may maintain remission[1]. There is another small study of 45 patients that demonstrated 45% maintained remission at 12 months following cessation of tocilizumab IV[2]. Prescribers should consider the individual risks and benefits of dose modification during this period of stock shortage.

IV formulation

Prescribers should consider the current supply constraints of various tocilizumab IV strengths, when prescribing tocilizumab IV. Other strengths of tocilizumab IV may need to be used to make up a patient's appropriate dose.

Alternative treatments

Prescribers who have assessed the above considerations as not appropriate for their patients with rheumatoid arthritis (RA) may consider alternative treatments (see Table 1).

[1] Sanmarti et al Arthritis and Rheumatology Vol.71, No. 10, October 2019, pp1616-1625
[2] Aguilar-Lozano et al J Rheumatol. 2013 Jul;40(7):1069-73

Systemic juvenile idiopathic arthritis (sJIA) and polyarticular juvenile idiopathic arthritis (pJIA) patients

SC formulations – prefilled syringe and pre-filled pen autoinjector

Where appropriate, prescribers should consider reducing the frequency of dose to a suitable individualised dose interval. This may assist in conserving their patient's supply of tocilizumab SC as there will be an out of stock at patient level for tocilizumab SC. Prescribers should consider the individual risks and benefits of dose modification during this period of stock shortage.

The pre-filled syringe with needle safety device can be used to treat paediatric patients of all approved ages. The pre-filled pen autoinjector (ACTPen) should not be used to treat children and adolescent patients less than 12 years of age.

IV formulation

Prescribers should consider the current supply constraints of various tocilizumab IV strengths, when prescribing tocilizumab IV. Other strengths of tocilizumab IV may need to be used to make up a patient's appropriate dose.

Giant cell arteritis (GCA) patients

SC formulation only – prefilled syringe and pre-filled pen autoinjector

There are no therapeutic alternative biologic treatments for GCA patients. However, prescribers may consider reducing the frequency of tocilizumab dose for some adult GCA patients.

The recommended dose of tocilizumab for adult patients with GCA is 162 mg given once every week as a subcutaneous injection, in combination with a tapering course of glucocorticoids. A dose of 162 mg given once every two weeks as a subcutaneous injection, in combination with a tapering course of glucocorticoids, may be prescribed based on clinical considerations.

Tocilizumab IV formulation is not registered with the TGA for GCA and is not intended for subcutaneous administration.

Switching patients between tocilizumab presentations

Switching between SC pre-filled syringe and pre-filled pen autoinjector

If only one presentation of tocilizumab SC is available at a time, patients may need to switch between the pre-filled syringe and pre-filled pen autoinjector.

Prescribers should ensure patients taking tocilizumab SC formulations have been instructed on how to use both presentations.

The pre-filled syringe with needle safety device can be used to treat paediatric patients of all approved ages. The pre-filled pen autoinjector (ACTPen) should not be used to treat children and adolescent patients less than 12 years of age.

Tocilizumab IV to SC

Prescribers should not switch patients prescribed tocilizumab IV to tocilizumab SC formulations as tocilizumab SC is expected to be out of stock at patient level.

The tocilizumab IV formulation is not intended for subcutaneous administration.

Tocilizumab SC to IV

Prescribers should consider reducing the frequency of tocilizumab SC dosing as initial management as advised under Managing stabilised/long term patients.

Prescribers should only consider switching patients prescribed tocilizumab SC formulations to tocilizumab IV if other options are not available or not appropriate.

Initiating treatment

Rheumatoid arthritis (RA) and polyarticular juvenile idiopathic arthritis (pJIA) patients

Prescribers should consider delaying initiating RA and pJIA patients on tocilizumab SC or IV until supply has stabilised to avoid interruptions in the first months of treatment.

Alternative treatments

When delaying treatment initiation is not appropriate for RA or pJIA patients, prescribers should consider alternative treatments as outlined in Table 1.

Systemic juvenile idiopathic arthritis (sJIA) patients

Prescribers should initiate tocilizumab (SC or IV depending on availability) in sJIA patients where it is not possible to delay treatment and there is no suitable therapeutic alternative available, for example, patients with severe glucocorticoid toxicity, severe serositis or those at risk of macrophage activation syndrome.

The pre-filled syringe with needle safety device can be used to treat paediatric patients of all approved ages. The pre-filled pen autoinjector (ACTPen) should not be used to treat children and adolescent patients less than 12 years of age.

Giant cell arteritis (GCA) patients

Prescribers should initiate tocilizumab SC in GCA patients where it is not possible to delay treatment, as GCA patients have no therapeutic alternatives, for example, patients with severe glucocorticoid toxicity or at high risk of glucocorticoid toxicity.

Treatment of Cytokine Release Syndrome (CRS) (IV formulation only)

Prescribers should not make any changes to the treatment plan for patients prescribed tocilizumab IV for CRS.

Tocilizumab IV for the treatment of CRS should be given the highest priority over all other indications of tocilizumab due to the nature and urgency of the condition.

Ensure adequate tocilizumab IV is available at pharmacy before chimeric antigen receptor (CAR) T cell treatment initiation, in case of the need to initiate tocilizumab for the management of severe or life-threatening CRS.

Table 1: Alternative treatments for tocilizumab

Product	TGA approved indication	PBS approved indication	Alternative biologics on PBS	Alternative biologics recommended but not necessarily PBS listed	Considerations
Tocilizumab IV 80mg/4mL	RA	Yes	Yes	Multiple	
	Polyarticular JIA	Yes	Yes	Adalimumab Etanercept	
	Systemic JIA	Yes	No	Anakinra Canakinumab	Alternatives not available on the PBS.
	CRS	No	Yes	Anakinra	Tocilizumab should be prioritised in these patients.
Tocilizumab IV 200mg/10mL	RA	Yes	Yes	Multiple	
	Polyarticular JIA	Yes	Yes	Adalimumab Etanercept	
	Systemic JIA	Yes	No	Anakinra Canakinumab	Alternatives not available on the PBS.
	CRS	No	Yes	Anakinra	Tocilizumab should be prioritised in these patients.
Tocilizumab IV 400mg/20mL	RA	Yes	Yes	Multiple	
	Polyarticular JIA	Yes	Yes	Adalimumab Etanercept	
	Systemic JIA	Yes	No	Anakinra Canakinumab	Alternatives not available on the PBS.
	CRS	No	Yes	Anakinra	Tocilizumab should be prioritised in these patients.

Table 1: Alternative treatments for tocilizumab (continued)

Product	TGA approved indication	PBS approved indication	Alternative biologics on PBS	Alternative biologics recommended but not necessarily PBS listed	Considerations
Tocilizumab SC 162mg/0.9mL pre-filled syringe, pack of 4	RA	Yes	Yes	Multiple	
	GCA	Yes	No		Tocilizumab should be prioritised in these patients.
	Polyarticular JIA	Yes	Yes	Adalimumab Etanercept	
	Systemic JIA	Yes	No	Anakinra Canakinumab	Alternatives not available on the PBS.
Tocilizumab SC 162mg/0.9mL pre-filled pen, pack of 4	RA	Yes	Yes	Multiple	
	GCA	Yes	No		Tocilizumab should be prioritised in these patients.
	Polyarticular JIA	Yes	Yes	Adalimumab Etanercept	
	Systemic JIA	Yes	No	Anakinra Canakinumab	Alternatives not available on the PBS.

Version history

Version	Description of change	Author	Effective date
V1.0	Original publication – Joint statement	Therapeutic Goods Administration, the Australian Rheumatology Association and Arthritis Australia	04/08/2021