Australian Government
Department of Health
Therapeutic Goods Administration

Australian Rheumatology Association

Arthritis AUSTRALIA

Tocilizumab (Actemra) shortage: Patient management

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

Updated 28 September 2021

Shortage of tocilizumab (Actemra)

The supply of tocilizumab (Actemra), sponsored by Roche Products Pty Ltd (Roche), has changed significantly. This joint statement has been updated to reflect the current supply situation.

Multiple presentations of tocilizumab products are in shortage until early 2022 due to global demand in response to the COVID-19 pandemic.

Due to extremely limited stock of intravenous (IV) tocilizumab until early 2022, supply must be tightly constrained to conserve stock for patients with no alternatives.

There is sufficient stock of subcutaneous (SC) tocilizumab (pre-filled syringe and pre-filled pen autoinjector) for only existing patients. However, supply of SC tocilizumab pre-filled syringe and ACTPen pre-filled pen autoinjector may fluctuate during the shortage. Wholesaler portals will likely show zero stock quantity for both medicines, even if they are available. Instructions for pharmacists to assist with ordering and substituting during the shortage is available on the TGA website.

For details of the supply status of different formulations of tocilizumab, please refer to the Shortages of tocilizumab (Actemra) medicines page on 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 the shortage 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 shortages of all tocilizumab (Actemra) products until early 2022. See web statement for details.
- **Patients taking tocilizumab (Actemra)** should contact their specialist as soon as possible about their treatment.
- **Prescribers** should:
  - immediately **reserve IV tocilizumab** stock for patients with certain priority indications (CRS, sJIA and pJIA).
  - change RA patients on IV tocilizumab to alternate treatments as soon as possible.
  - consider reducing the frequency of SC tocilizumab dose where appropriate.
  - consider alternative treatments for new patients and **do not initiate new patients** on tocilizumab, except where no alternatives or no suitable alternatives are available e.g. for GCA, CRS, sJIA or pJIA.
  - demonstrate to patients using SC presentations of tocilizumab how to use both the pre-filled syringe and pre-filled pen autoinjector in case they need to be switched.
  - be aware of PBS arrangements during the tocilizumab shortage
- **Pharmacists** should be aware of the Serious Scarcity Substitution Instrument (SSSI) for SC tocilizumab formulations.
- **General Practitioners and pharmacists** should advise patients using tocilizumab to contact their rheumatologist as soon as possible.
- **Pharmacists** will need to call wholesalers to order tocilizumab (Actemra). Wholesaler portals will likely show zero stock quantity for both subcutaneous medicines, even if they are available.

Summary by condition

Rheumatoid arthritis (RA)

- Avoid initiating new patients on tocilizumab. Consider alternative treatments as outlined in Table 1.
- Change IV tocilizumab patients to alternate treatments as outlined in Table 1.
- Do not change patients from IV to SC tocilizumab unless all alternate treatments have been exhausted.
- Consider reducing SC tocilizumab dose frequency for established patients, where appropriate.
- Ensure patients taking SC tocilizumab 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.
- Patients under 18 years cannot be offered a substitute SC medicine by a pharmacist under the Serious Scarcity Substitution Instrument. If the patient's usual SC medicine is unavailable, prescribers will need to issue a new prescription. If switching patients to the alternate SC presentation, ensure patients have been instructed on its use.

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.
- Patients under 18 years cannot be offered a substitute SC medicine by a pharmacist under the Serious Scarcity Substitution Instrument. If the patient's usual SC medicine is unavailable, prescribers will need to issue a new prescription. If switching patients to the alternate SC presentation, ensure patients have been instructed on its use.

Giant cell arteritis (GCA)

- Consider reducing the frequency of tocilizumab dose for some adult GCA patients.
- Prescribers should initiate SC tocilizumab 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.

Prescribers of IV tocilizumab are advised to immediately reserve stock for patients with few or no alternative treatments (see priority indications).

Adult patients should be advised on the possibility of switching between SC tocilizumab presentations depending on availability. Patients taking subcutaneous presentations of tocilizumab may need to switch between the pre-filled syringe and ACTPen pre-filled pen autoinjector and should be instructed on how to use both. Only patients over the age of 18 can be offered a substitute subcutaneous medicine by a pharmacist under the Serious Scarcity Substitution Instrument.

Priority indications

All patients who can, should be moved from IV tocilizumab to an alternative treatment. Prescribers should prioritise use of their existing and new stock for the priority conditions listed below.

The Australian Rheumatology Association and the Therapeutic Goods Administration (TGA) have agreed on priority registered indications for each presentation based on severity of the condition and lack of alternative treatments.

Priority indications for IV tocilizumab

Priority conditions for intravenous presentations are:

- Cytokine Release Syndrome (CRS)
- Systemic juvenile idiopathic arthritis (sJIA)
- Polyarticular juvenile idiopathic arthritis (pJIA)

Patients with the above indications have no or very few alternative treatments. Therefore, prescribers should ensure stock of IV tocilizumab is reserved for these patients.

Patients who are prescribed IV tocilizumab for rheumatoid arthritis should be switched to alternate treatments immediately wherever possible.

Priority indications for SC tocilizumab

Priority conditions for subcutaneous presentations are:

- Systemic juvenile idiopathic arthritis (sJIA)
- Giant cell arteritis (GCA)
- Polyarticular juvenile idiopathic arthritis (pJIA)

Patients with the above indications for SC tocilizumab have no or very few alternative treatments. Therefore, supply of SC tocilizumab should be prioritised for patients with these indications.

Subcutaneous presentations of tocilizumab are available for existing patients, but supply may fluctuate, with only one presentation available at certain times. New patients should not be

initiated on SC tocilizumab unless they have no suitable alternative treatments or alternative treatment is not available.

Rheumatoid arthritis (RA) patients

RA existing patients

IV formulation

Patients on IV tocilizumab should temporarily be changed to alternate treatments as soon as possible due to extremely limited stock of IV tocilizumab. All classes of biological and targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) should be considered as an alternative.

For patients on IV tocilizumab who have previously exhausted all other suitable treatments, a switch to SC tocilizumab could be considered as there is inadequate supply of IV tocilizumab to ensure continued treatment. Prescribers should check with their supplier of IV tocilizumab as to current availability. The switch from IV tocilizumab to SC tocilizumab should only be necessary in a very small percentage of patients. Please note it is not an action that is recommended for all patients on IV tocilizumab.

SC formulations – prefilled syringe and pre-filled pen autoinjector

There is only sufficient stock of SC tocilizumab for existing patients. Supply of SC tocilizumab pre-filled syringe and ACTPen pre-filled pen autoinjector may fluctuate during the shortage. The TGA has issued a Serious Scarcity Substitution Instrument to allow a pharmacist to dispense either product to a patient when one is available without prior approval to substitute from the prescriber. Further information is in the Switching between SC pre-filled syringe and pre-filled pen autoinjector section of this document.

For patients who have difficulty obtaining supply of SC tocilizumab and where tocilizumab is their first biologic treatment, prescribers could consider temporarily switching to an alternative b/tsDMARD.

For some stable RA patients, prescribers could consider reducing the frequency of dose to every two weeks to conserve supply of SC tocilizumab.

There are few data on flare rates with dose reduction over this time period; there is some evidence that remission is maintained in 75% of patients when the dose interval is increased to 2 weeks. Prescribers should consider the individual risks and benefits of dose modification during this period of reduced availability.

PBS arrangements have been put in place to facilitate access to alternative treatments during the shortage and re-commencement of tocilizumab if appropriate when the shortage is resolved. If the interval is increased and the patient fails to sustain a response this will not be included in the 5 in a life fails for RA.

Further information is on the PBS website.

RA new patients

Prescribers should not initiate RA patients on SC or IV tocilizumab until supply has stabilised to avoid interruptions in the first months of treatment. Prescribers should consider alternative treatments as outlined in Table 1.

Systemic juvenile idiopathic arthritis (sJIA) patients

sJIA existing patients

Where appropriate, prescribers should consider reducing the frequency of dose to a suitable individualised dose interval to assist in conserving supply. 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 ACTPen pre-filled pen autoinjector should not be used to treat children and adolescent patients less than 12 years of age.

sJIA new patients

Prescribers should consider alternative treatments as outlined in Table 1.

Prescribers should only 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 ACTPen pre-filled pen autoinjector should not be used to treat children and adolescent patients less than 12 years of age.

Polyarticular juvenile idiopathic arthritis (pJIA) patients

pJIA existing patients

Where appropriate, prescribers should consider reducing the frequency of dose to a suitable individualised dose interval. This may assist in conserving supply of SC or IV tocilizumab. 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 ACTPen pen autoinjector should not be used to treat children and adolescent patients less than 12 years of age.

pJIA new patients

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

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

Giant cell arteritis (GCA) patients - SC formulation only

GCA existing patients

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.

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

GCA new patients

Prescribers should initiate SC tocilizumab 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 IV tocilizumab for CRS.

IV tocilizumab 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 IV tocilizumab 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.

Additional information

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

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

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

The TGA has issued a Serious Scarcity Substitution Instrument to allow a pharmacist to dispense either product to a patient when one is available without prior approval to substitute from the prescriber.

The instrument only applies to patients 18 years or older. Patients should be made aware of the substitution instrument in the event their prescribed SC tocilizumab presentation is not available.

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

Further information about the substitution instrument is on the TGA website. Further information about Pharmaceutical Benefits Scheme (PBS) subsidy arrangements for SC tocilizumab under the instrument is on the PBS website.

PBS arrangements for tocilizumab shortage

In response to this shortage, the Department of Health has been working with Services Australia to facilitate patient access to appropriate continuing treatment options via the PBS.

The following PBS arrangements have been put in place to facilitate access to appropriate continuing treatment for patients currently prescribed tocilizumab who are unable to access their medicine due to the shortage.

PBS information for existing patients with severe active rheumatoid arthritis or severe active juvenile idiopathic arthritis:

- Switching from tocilizumab to an alternative biological/targeted synthetic disease modifying drug (b/tsDMARD)
- Switching back to tocilizumab from an alternative b/tsDMARD
- Patients continuing on alternative therapy

Further information is on the PBS website.

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
IV Tocilizumab 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	No		Tocilizumab should be prioritised in these patients.
IV Tocilizumab 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	No		Tocilizumab should be prioritised in these patients.
IV Tocilizumab 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	No		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
SC Tocilizumab 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.
SC Tocilizumab 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
V2.0	Revised advice based on updated supply situation	Therapeutic Goods Administration, the Australian Rheumatology Association and Arthritis Australia	28/09/2021

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