PDL DRUG REVIEW

Proprietary Name: Tremfya®
Common Name: guselkumab
PDL Category: Anti-Inflammatories, Non-NSAID

Comparable Products	Preferred Drug List Status
Cosentyx	Preferred with Conditions

Summary

Pharmacology/Usage: Guselkumab, the active ingredient of Tremfya®, is a human immunoglobulin G1 lambda monoclonal antibody produced using recombinant DNA technology. It selectively binds to the p19 subunit of interleukin 23 (IL-23) and inhibits its interaction with the IL-23 receptor. IL-23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Guselkumab inhibits the release of pro-inflammatory cytokines and chemokines.

Indications: For the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

There is no pregnancy category for this product; however, the risk summary indicates that there are no available data on use in pregnant women to inform a drug associated risk of adverse developmental outcomes. Human IgG antibodies are known to cross the placental barrier; thus, Tremfya® may be transmitted from the mother to the developing fetus. The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Single-dose prefilled syringe: 100mg/ml. Store in refrigerator but allow to reach to room temperature before injection (about 30 minutes)

Recommended Dosage: Prior to starting treatment, assess for tuberculosis (TB) infection. May be self-injected once proper training in technique has been completed.

Inject 100mg subcutaneously (SC) at week 0, week 4, and every 8 weeks thereafter. There have been no studies conducted on use in renal or hepatic impairment.

Drug Interactions: Avoid live vaccines if treated with Tremfya®. In addition, upon starting Tremfya® in those receiving concomitant CYP450 substrates, especially those with a narrow therapeutic index, consider monitoring for therapeutic effect or drug concentration. Consider dose adjustments as needed.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Tremfya®) minus reported % incidence for placebo/adalimumab. Please note that an incidence of 0% means the incidence was the same as or that the active drug was less than its comparator.* The most frequently reported adverse events included upper respiratory infections (1.5%/3.6%), headache (1.3%/3.6%), injection site reactions

(1.7%/0%), arthralgia (0.6%/0.7%), diarrhea (0.7%/0.1%), gastroenteritis (0.4%/0%), tinea infections (1.1%/1.1%), and herpes simplex infections (0.6%/1.1%).

Tremfya® may increase the risk of infections. In clinical trials, infections occurred more with Tremfya® than placebo (23% vs 21%). The rate of serious infections for each treatment group was ≤0.2%. Treatment should not be started in those with any clinically important active infection until the infection resolves or is adequately treated. It is recommended to consider the risks and benefits prior to use in patients with a chronic infection or history of a recurrent infection. Do not administer to patients with active TB.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Janssen Biotech, Inc

Analysis: The safety and efficacy of Tremfya® were assessed in 3 randomized, double-blind, studies that included adults ≥18 years of age with moderate-to-severe plaque psoriasis who were eligible for systemic therapy or phototherapy. All had an Investigator's Global Assessment (IGA) score of ≥3 (moderate) on a 5-point scale of overall disease severity, a Psoriasis Area and Severity Index (PASI) score ≥12, and a minimum affected body surface area of 10%.

Study 1 (VOYAGE 1) and Study 2 (VOYAGE 2) included adults randomized to either Tremfya®, placebo or adalimumab and had the same co-primary endpoints when compared to placebo, which included: the proportion of subjects who achieved an IGA score of 0 (cleared) or 1 (minimal) AND the proportion who achieved at least a 90% reduction from baseline in the PASI composite score (PASI 90). Secondary outcomes included comparisons between Tremfya® and adalimumab, and included the proportion who achieved an IGA score of 0 or 1, a PASI 90, and a PASI 75 response at week 16 AND the proportion achieving an IGA score of 0, an IGA score of 0 or 1, and a PASI 90 response at week 24 (both studies) and at week 48 (study 1).

Results of the primary outcome can be seen in the table below, which was adapted from the prescribing information.

	VOYAGE 1		VOYAGE 2	
Endpoint	Tremfya® (N=329)	Placebo (N=174)	Tremfya® (N=496)	Placebo (N=248)
IGA response 0/1	85% (N=280)	7% (N=12)	84% (N=417)	8% (N=21)
PASI 90	73% (N=241)	3% (N=5)	70% (N=347)	2% (N=6)

The table below includes results with Tremfya® compared with adalimumab, which was adapted from the prescribing information.

	VOYAGE 1		VOYAGE 2	
Endpoint	Tremfya® (N=115)	Adalimumab (N=115)	Tremfya® (N=160)	Adalimumab (N=81)
IGA response of 0/1 (cleared or minimal)				
Week 16	84% (N=97)	61% (N=70)	74% (N=119)	62% (N=50)
Week 24	84% (N=97)	54% (N=62)	74% (N=119)	57% (N=46)
Week 48	79% (N=91)	54% (N=62)	NA	NA
IGA response of 0 (cleared)				
Week 24	53% (N=61)	23% (N=27)	48% (N=76)	28% (N=23)
Week 48	47% (N=54)	24% (N=28)	NA	NA

	VOYAGE 1		VOYAGE 2	
PASI 75 response				
Week 16	91% (N=105)	70% (N=80)	83% (N=132)	63% (N=51)
PASI 90 response				
Week 16	73% (N=84)	41% (N=47)	64% (N=102)	42% (N=34)
Week 24	80% (N=92)	44% (N=51)	71% (N=113)	51% (N=41)
Week 48	73% (N=84)	46% (N=53)	NA	NA

To assess maintenance of response, subjects in VOYAGE 2 randomized to Tremfya® at week 0 and who were PASI 90 responders at week 28 were re-randomized to either continue treatment with Tremfya® or be withdrawn from therapy (i.e. receive placebo). At week 48, 89% who continued Tremfya® maintained PASI 90 as compared with 37% who were re-randomized to placebo. For those re-randomized to placebo and withdrawn from Tremfya®, the median time to loss of PASI 90 was about 15 weeks.

The NAVIGATE study was a study of Tremfya® in subjects who had not achieved an adequate response, defined as IGA ≥2 at week 16 after initial treatment with ustekinumab. Subjects were randomized to continue ustekinumab or switch to Tremfya®. In subjects with an inadequate response with ustekinumab, greater proportions on Tremfya® compared to ustekinumab achieved an IGA score of 0 or 1 with a ≥2-grade improvement at week 28 (31% vs 14%, respectively, 12 weeks after randomization).

Place in Therapy: Tremfya® is a human monoclonal antibody indicated for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. In phase 3 clinical trials, it was found to be more effective as compared to placebo for the co-primary endpoints, and more effective as compared to adalimumab with secondary endpoints of PASI 90 and PASI75 response, as well as IGA score of 0 or 1. In addition, it was found to be more effective as compared with ustekinumab in subjects with an inadequate response with ustekinumab for achieving an IGA score of 0 or 1.

There is some evidence at this time to support that Tremfya® is more effective than adalimumab and ustekinumab (in ustekinumab non-responders) in phase 3 clinical trials for certain endpoints assessed; however, there is no evidence that it is safer or more effective than other agents indicated for plaque psoriasis. It is therefore recommended that Tremfya® remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Tremfya [package insert]. Horsham, PA: Janssen Biotech, Inc; 2017.