Bezlotoxumab (zinplava) with mayo clinic

Group 4: Rafi Saadallah, Anthony Hill, Alex Nedved, Angel Withrow

Bezlotoxumab (Zinplava)

BLT with MAYO Clinic

Pharmacy and Therapeutic committee

Drug Evaluation Monograph:

Generic Name	Bezlotoxumab
Brand Name	Zinplava
Manufacturer	MERCK SHARP DOHME
Therapeutic Category	80: 04 Antitoxins and Immune Globulins
Classification	J06BB: Specific Immunoglobulins
FDA	

Classification:	
Approved (rating not specified)	
Status: Rx only	
Similar Agents on Market	None

Summary:

Zinplava is the first and only monoclonal antibody FDA approved for prevention of recurrent C. Diff infections. It is used as an add on therapy to decrease risk of recurrent C. Diff. Zinplava is currently the only drug in its class because it’s currently the only drug in the market that prevents the recurrence of CDI instead of treating the actual infection. The drugs mechanisms of action is unique due to its ability to inhibit Toxin B and stopping its effects on the cell. After looking at the trials, it’s hard to see any side effects that can prevent people from taking this drug. Most of the Zinplava’s side effects were nausea, headaches, and infusion problems. It is recommended to not use this drug with people who have congestive heart failure.

Recommendations:

It is recommended to add Zinplava to the drug formulary for add on therapy. It is usefull for those patients that are at especially high risk of a recurrent C. Diff infection. Zinplava currently costs $4, 560. 00 per vial and while it has been proven to reduce the risk of recurrent zinplava the use of this medication can only be justified in patients that meet criteria that would put them at high risk of recurrent C. Difff. With other options available to prevent recurrent C. Diff it can only be justified to use zinplava in a particular group of patients that cannot tolerate alternative medical interventions and are at an increased risk of recurrent C. Diff.

Pharmacological Data:

Mechanism of action : A monoclonal antibody that inhibits Toxin B (does not bind to Toxin A) and stops the effect on Mammalian cells. This drug should not be used alone, instead it needs to be used in conjunction with other antibiotics to treat recurrence cases of C. Diff.

Therapeutic Indications:

FDA approved on June 9th, 2016 for the prevention and treatment of recurrent C. diff in patients > 18 years of age that are undergoing antimicrobial therapy for the treatment of C. Diff.

Evidence Based Guidelines

–Zinplava was approved in October 2016 and its place in guideline therapy has not yet been determined. It is the first monoclonal antibody approved for the prevention of recurrent C. Diff. and guidelines do not yet reflect therapy

with zinplava for the prevention of primary or recurrent C. Diff. All guidelines available are only for the treatment of C. diff and do not yet include zinplava.

Clinical Studies:

The safety of Zinplava was evaluated in two placebo-controlled Phase 3 trials. Patients received a single Zinplava dose with antimicrobial treatment for C. diff infection. Between the experimental group and placebo group, mortality rates were slightly lower in the experimental group at 7. 1% compared to 7. 6% at a 12 week follow-up. Common side effects noted were nausea, pyrexia, and headache. Heart failure was listed as a serious adverse reaction, as it occurred in 2. 3% of the experimental group compared to 1% in the placebo group. Infusion related reactions were reported in 10% of patients treated with Zinplava compared to 8% of placebo patients.

In terms of recurrence prevention efficacy, Trial 1 had 386 patients in the Zinplava group and 395 patients in the control group. Disease recurrence was found in 67 patients (17. 4%) treated with Zinplava and in 109 patients (27. 6%) of the control group. In Trial 2, there were 395 patients in the Zinplava group and 378 patients in the control group. Disease recurrence was found in 62 patients (15. 7%) treated with Zinplava and in 97 patients (25. 7%) of the control group. There was no statistical significance

1. Merck Sharp & Dohme Corp. A study of MK-3415, MK-6072, and MK-3415A in participants receiving antibiotic therapy for clostridium difficile infection (MK-3415A-001) (MODIFY I). NLM Identifier: NCT01241552. Last updated November 30, 2015. Available at:

https://www. clinicaltrials. gov/ct2/show/NCT01241552? term= NCT01241552&rank= 1 .

2. Merck Sharp & Dohme Corp. A study of MK-6072 and MK-3415A in participants receiving antibiotic therapy for clostridium difficile infection (MK-3415A-002) (MODIFY 11). NLM Identifier: NCT01513239. Last updated October 29, 2015. Available at: https://www. clinicaltrials. gov/ct2/show/NCT01513239? term= NCT01513239&rank= 1 .

Pharmacokinetics and Bioavailability

Absorption	Immediately and 100% bioavailable
Distribution	Vd is 7. 33 L
Metabolism	By Catabolism
Excretion	Primarily by Catabolism

Dosage Forms:

Drug	Bezlotoxumab
Formulation	Solution

Strength	1000 mg/40 ml (25 mg/ml)
Storage	2-8 °C (Do not freeze)
Special considerations	Solutions diluted for infusion may be stored at room temperature for up to 16 hours or under refrigeration for up to 24 hours.
Administration	Infusion over a 60 minute period through a sterile, low protein binding 0. 2

	to 5 micro line or add on filter. Can be administered through a central line or a peripheral catheter.

Dosage Range:

Adults	IV 10 mg/kg (single dose)
Children	Only studied in 18 years or older
Elderly	Same as adult dosing
Hepatic Failure	No dose adjustments
Renal Impairment	No dose adjustments

Adverse Effects

Adverse Effects	Nausea, Pyrexia, Headache, Infusion related reactions, Immunogenicity Serious: Congestive Heart Failure exacerbation

Special Precautions: In congestive heart failure patients, Bezlotoxumab should be reserved for patients where benefit outweighs the risk in order to reduce risk of worsening heart failure.

Contraindications:

–None

Drug Interactions:

-Belimumab: Monoclonal Antibodies may enhance the adverse/toxic effect of Belimumab(Brand name: Benlysta).

Drug Food interactions:

–None.

Drug Laboratory Test interactions:

–None.

Patient Safety:

-Zinplava has a good side effect profile with the most common side effect being nausea. The patient should tell their doctor if they have or have had a history of congestive heart failure, as it can be a serious side effect of the zinplava.

Monitoring Guidelines :

–Monitor for signs and symptoms of adverse reactions.

Patient Information:

-Zinplava doesn’t take the place of their antibacterial treatment for CDI. Patient must continue to take their treatment regimen as directed. You will need to have a doctors appointment to receive Zinplava. Administration will take one hour via IV route. If you miss an appointment, contact your doctor right away.

Cost Comparison:

Drug (Strength)	Daily Dose/Dosing	AWP
Zinplava 1000 mg/40 mL (25 mg/mL)	10 mg/kg infusion over 1 hour	$4560.00(per vial: 1000

	mg/40 ml)	
Vancomycin HCL in dextrose IV	-1g/ 200ml	$27. 65
	-500 mg/10 0 ml	$7. 92
	-750 mg/15 0 ml	$14. 50
Vancomycin HCL in NaCl IV	-1g/ 200 ml	$28. 55
	-500 mg/10 0 ml	$8. 82
	-750 mg/15 0 ml	$15. 40
Vancomycin HCL IV	10 g	$206. 40
	500 mg	$8. 40
	750	$11.

mg	63
1000 mg	$15. 60
5000 mg	$85. 50

Pharmacoeconomic Analysis:

Problem definition:

-The objective of this analysis is to determine if Zinplava should be used as an add on to antimicrobial therapy.

Perspective:

-Will be from the perspective of the institution.

Specific treatment alternatives and outcomes:

-Zinplava can only be used as an add on to antimicrobial therapy for the treatment and prevention of recurrent Clostridium Difficile. The treatment options are either antimicrobial therapy without zinplava and antimicrobial therapy with zinplava.

Pharmacoeconomic model:

–Number need to treat with zinplava will be used in order to detail the effects that zinplava has in order to make a realistic judgement as to whether or not zinplava is worth the extra cost to add on therapy in terms of determining if adding on zinplava can be justified from an economic perspective. .

-NNT (Vancomycin and Zinplava) = 5. 5

Drugs:	Average Cost:
Vancomycin	$25. 6 (per 1 gram)
Vancomycin + Zinplava	$25. 6 (per 1 gram) + $4, 560 (1000mg/40 ml) = $4, 585. 6

[Note to reader: Number needed to treat data was extrapolated from a randomized, double blind controlled study using 200 patients during a phase 2 trial. Recurrence of C. Diff. (measured after 84 days) between the monoclonal antibody and placebo group was 7% and 25%, respectively with a 95% confidence interval and a p-value <0. 001. Since zinplava is a new drug to the market (FDA approved June 2016) there is not a wide variety of economic analysis available at this time.]

Presented by Rafi Saadallah, Anthony Hill, Alex Nedved, Angel Withrow to the Pharmacy and Therapeutics committee on March 10th, 2017

Reference:

Lowy I, Molrine DC, Leav BA, Blair BM, Baxter R, Gerding DN, Nichol G, Thomas WD, Jr., Leney M, Sloan S, Hay CA, Ambrosino DM: Treatment with

monoclonal antibodies against Clostridium difficile toxins. N Engl J Med 2010, 362: 197-205.(Economic analysis refrence)