Extreme temperature stability assessment for omadacycline tablets and intravenous vials

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Background

Physical storage conditions outside of the recommended range may affect drug stability and chemistry[1]

Reduction in quality of antibiotics due to changes during storage may decrease their effectiveness and thus contribute to the development of antimicrobial resistance[2]

Omadacycline is an aminomethylcycline antibiotic approved in oral and intravenous formulations for the treatment of adults with acute bacterial skin and skin structure infections or community-acquired bacterial pneumonia[3–5]

Both the omadacycline tablets and lyophilized vials for injection should be stored at 20°C to 25°C, with excursions permitted to 15°C to 30°C[6]

Methods

Omadacycline tablets (150 mg; 72 blister packs of 6 tablets) and sterile lyophilized vials for injection (100 mg/vial; 186 vials) were powdered and placed in a calibrated laboratory oven at 50°C with ambient laboratory humidity (6.7% to 46.9%); samples were reconstituted for testing

Tablets and vials were removed at 24, 48, and 72 hours, and were tested for appearance, assay and related substances (by high-performance liquid chromatography), water content, dissolution, and microbial matter. The lyophilized injection vials were also tested for visible particles, pH, particulate matter, bacterial endotoxins, and container closure integrity (CCIT)

All analyses were performed on the day of sample removal from the oven, except for microbial and particulate matter, bacterial endotoxins, and CCIT, which were stored at room temperature until the final time point, when all samples were tested

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Omadacycline remains stable at 50°C for up to 72 hours in the original packaging

Objective

To assess the effect of physical storage conditions outside of the recommended temperature range on omadacycline stability and chemistry

Conclusions

Omadacycline met prespecified acceptance criteria for all parameters, including appearance, assay and related substances, moisture content, dissolution, pH and particulate matter (injection only), and microbial analyses

Both the omadacycline tablets and the lyophilized injection vials were stable without any indication of significant degradation when stored at 50°C (122°F) for up to 72 hours in the original packaging

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Results

Omadacycline tablets and lyophilized injection vials stored at 50°C met the acceptance criteria for all parameters at all time points, for up to 3 days (**Table 1**)

4-Beta epimer omadacycline was the most common related substance. All related substances were within prespecified acceptance criteria

Table 1. Initial and testing results for omadacycline tablets and lyophilized injection vials stored at 50°C

	Initial	24 hours	48 hours	72 hours	Acceptance criteria
Omadacycline tablets (150 mg)					
Appearance	Conforms	Conforms	Conforms	Conforms	[a]
Mean water content (% w/w)	3.01	3.09	2.97	2.94	≤7.0
Mean % dissolved at 15 min	96	97	96	96	≥85
Total aerobic microbial count (CFU/g)	<10	<10	<10	<10	$\leq 10^3$
Total combined yeasts and molds (CFU/g)	<10	<10	<10	<10	$\leq 10^2$
Escherichia coli in 1 g	Absent	Absent	Absent	Absent	Absent
Omadacycline for injection (100 mg/vial)					
Appearance of lyophilisate	Yellow cake	Yellow cake	Yellow cake	Yellow cake	Yellow to dark orange cake
Appearance of reconstituted solution	Conforms	Conforms	Conforms	Conforms	[b]
pH	4.0	4.0	4.0	4.0	3.3–4.8
Particles ≥10 nm	47	46	28	27	6,000
Particles ≥25 nm	0	<1	0	0	600
Mean moisture content (% w/w)	1.52	1.68	1.70	1.70	≤3.0
Bacterial endotoxins (EU/mg)	<0.1	<0.1	<0.1	<0.1	<0.6
CCIT	Conforms	Conforms	Conforms	Conforms	[c]

[a]Conforming result: yellow, diamond-shaped, film-coated tablet with "OMC" on one side and "150" on the other side.
[b]Conforming result: clear yellow solution practically free of visible particles.
[c]Conforming result: <1 µL dye ingress.
CCIT = container closure integrity; CFU = colony-forming unit; EU = endotoxin unit.

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