

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**210874Orig1s000**

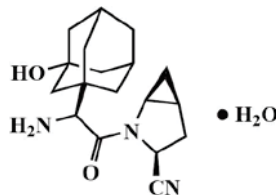
**PRODUCT QUALITY REVIEW(S)**



**Labeling Addendum to NDA 210874**

The API saxagliptin (b) (4) the revised language pertaining to saxagliptin is in Section 11 'DESCRIPTION' of the label has been revised as follows:

Saxagliptin is an active inhibitor of the dipeptidyl-peptidase-4 (DPP-4) enzyme. It is isolated in the monohydrate form chemically known as (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxytricyclo [3.3.1.1] dec-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile, monohydrate or (1S,3S,5S)-2-[(2S)-2-amino-2-(3-hydroxy-1-adamantan-1-yl)acetyl]-2-azabicyclo[3.1.0]hexane-3-carbonitrile hydrate. The empirical formula is C<sub>18</sub>H<sub>25</sub>N<sub>3</sub>O<sub>2</sub>•H<sub>2</sub>O and the molecular weight is 333.43. The structural formula is:



Furthermore, as the above structural formula clearly indicates that the API (b) (4) Therefore, the description of the 4 individual strengths of the drug product now contain a revised statement for saxagliptin: “exists in the form of HCl salt” (b) (4). The description of the four strengths of the drug product is now as follows:

QTERNMET XR is available as film-coated tablets of four strengths:

- 2.5 mg dapagliflozin/2.5 mg saxagliptin/1000 mg metformin HCl: Each tablet contains 2.5 mg dapagliflozin (equivalent to 3.08 mg dapagliflozin propanediol), 2.5 mg saxagliptin (exists in the form of HCl salt), and 1000 mg metformin HCl (equivalent to 779.86 mg metformin).
- 5 mg dapagliflozin/2.5 mg saxagliptin/1000 mg metformin HCl: Each tablet contains 5 mg dapagliflozin (equivalent to 6.15 mg dapagliflozin propanediol), 2.5 mg saxagliptin (exists in the form of HCl salt) and 1000 mg metformin HCl (equivalent to 779.86 mg metformin).
- 5 mg dapagliflozin/5 mg saxagliptin/1000 mg metformin HCl: Each tablet contains 5 mg dapagliflozin (equivalent to 6.15 mg dapagliflozin propanediol), 5 mg saxagliptin (exists in the form of HCl salt) ) and 1000 mg metformin HCl (equivalent to 779.86 mg metformin).
- 10 mg dapagliflozin/5 mg saxagliptin/1000 mg metformin HCl: Each tablet contains 10 mg dapagliflozin (equivalent to 12.3 mg dapagliflozin propanediol), 5 mg saxagliptin (exists in the form of HCl salt) ) and 1000 mg metformin HCl (equivalent to 779.86 mg metformin).

**Christopher  
Galliford -S**

Digitally signed by Christopher Galliford -S  
DN: c=US, o=U.S. Government, ou=HHS,  
ou=FDA, ou=People,  
0.9.2342.19200300.100.1.1=2001708703,  
cn=Christopher Galliford -S  
Date: 2019.04.24 12:09:42 -04'00'

Christopher Galliford ATL

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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CHRISTOPHER GALLIFORD  
04/30/2019 03:04:58 PM

**Recommendation:**  
**NDA: Approval**

## NDA 210874 Review 1

<b>Drug Name/Dosage Form</b>	Qtemmet, Dapagliflozin, saxagliptin and metformin hydrochloride extended release tablets (Dapa/Saxa/Met XR)
<b>Strength</b>	Dapa/Saxa/Met XR 2.5/2.5/1000 mg, 5/2.5/1000 mg, 5/5/1000 mg and 10/5/1000 mg
<b>Route of Administration</b>	Oral
<b>Rx/OTC Dispensed</b>	Rx
<b>Applicant</b>	ASTRAZENECA AB

SUBMISSION(S) REVIEWED	DOCUMENT DATE
0001	07/02/2018
0002	07/26/2018
0013	12/28/2018
0015	01/11/2019
0016	01/22/2019
0017	02/14/2019

### Quality Review Team

DISCIPLINE	REVIEWER	BRANCH/DIVISION
Drug Substance	Ramsharan Mittal	OPQ/ONDP/DNDAPI/NDBI
Drug Product	Christopher Galliford	OPQ/ONDP/DNDPII/NDPBVI
Process	Ted Chang	OPQ/OPF/DPAII/PABIV
Facility	Ted Chang	OPQ/OPF/DPAII/PABIV
Biopharmaceutics	Sarah Ibrahim	OPQ/ONDP/DB/BBII
Regulatory Business Process Manager	Anika Lalmansingh	OPQ/OPRO/DRBPMI/RBPMBI
Application Technical Lead	Christopher Galliford	OPQ/ONDP/DNDPII/NDPBVI
Environmental Assessment (EA)	James Laurenson	OPQ/ONDP

## Quality Review Data Sheet

### 1. RELATED/SUPPORTING DOCUMENTS:

#### A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	STATUS <sup>1</sup>	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	Type II		(b) (4)	Adequate		Based on information provided in the NDA
	Type III			Adequate		Based on information provided in the NDA
	Type III			Adequate		Based on information provided in the NDA
	Type III			Adequate		Based on information provided in the NDA

<sup>1</sup>Adequate, Adequate with Information Request, Deficient, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

#### B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	202293	Dapagliflozin (Farxiga® Tablets)
NDA	205649	Dapagliflozin/ Metformin hydrochloride (Xigduo™ XR Tablets)
NDA	22350	Saxagliptin (Onglyza® Tablets)
NDA	200678	Saxagliptin/Metformin hydrochloride (Kombiglyze® XR Tablets)
NDA	209091	Dapagliflozin/Saxagliptin (Qtem® Tablets)

### 2. CONSULTS:

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