

TABLE 18

Stability of BH4 Dihydrochloride Sachet Packaged in Foil Pouches 40° C./75% RH				
Sample	T = 1 Month		T = 3 Month	
	Lot 11434-50 Orange (Sucrose base)	Lot 11434-51 Orange (Mannitol base)	Lot 11434-50 Orange (Sucrose base)	Lot 11434-51 Orange (Mannitol base)
Biopterin (RRT = .5) %	0.029	0.026	0.106	0.138
BH2 (RRT = .6) %	0.132	0.123	0.162	0.304
R-THBL (RRT = .79) %	0.038	0.082	0.093	0.154
S-THBL (RRT = .88) %	ND	ND	ND	0.057
BH4%	91.75	97.74	48.48	96.37
S-BH4 (RRT = 1.2) %	ND	ND	0.009	0.010
THP (RRT = 1.4) %	ND	ND	0.057	0.105
Unknown Impurity (RRT = 1.4) %	ND	ND	0.012	0.036
Unknown Impurity (RRT = .54) %	ND	ND	0.030	0.068
Unknown Impurity (RRT = .58) %	ND	ND	0.018	0.013
Unknown Impurity (RRT = .72) %	0.062	ND	0.079	0.018
Unknown Impurity (RRT = .81) %	ND	ND	0.064	ND
Total Unknown Impurity	0.062	ND	0.203	0.135
Total Impurity	0.261	0.231	0.629	0.903

ND = Not Detected

Example 10

Sachet Dosage Form Data without Flavoring

Certain embodiments of the sachet dosage forms of the present disclosure are illustrated in Table 19, wherein the sachet formulation may consist of a BH4 or BH4-related compound, a sweetener, and flavor enhancers without a flavoring agent.

It is understood that every embodiment described herein can optionally be combined with any one or more of the other embodiments described herein.

Every patent literature and every non-patent literature cited herein are incorporated herein by reference in their entirety.

TABLE 19

Sachet dosage formulation without flavoring agents		
Ingredient	g/sachet	%
Sapropterin HCl	0.2	32
Mannitol	0.35	56
Potassium Citrate	0.065	10.4
Ascorbic Acid	0.01	1.6
TOTAL	0.625	100

Numerous modifications and variations to the disclosure, as set forth in the embodiments and illustrative examples described herein, are expected to occur to those skilled in the art. Consequently, only such limitations as appear in the accompanying claims should be placed on the disclosure.

Example 11

Sachet Dosage Form Containing 200 mg BH4 Dihydrochloride

Table 20 describes the formulation of a stable sachet dosage form comprising 200 mg (6R)-L-erythro-tetrahydrobiopterin dihydrochloride in polymorphic form B. This sachet dosage form was prepared in a manner as provided in the Detailed Description.

TABLE 20

Sachet dosage formulation containing 200 mg BH4 Dihydrochloride		
Ingredient	mg/sachet	%
Sapropterin 2HCl	200	32
Sucralose micronized	11.9	1.9
Potassium citrate monohydrate	65	10.4
Ascorbic acid fine powder	10	1.6
TOTAL	625	100

The examples set forth above are provided to give those of ordinary skill in the art with a complete disclosure and description of how to make and use the claimed embodiments, and are not intended to limit the scope of what is disclosed herein. Modifications that are obvious to persons of skill in the art are intended to be within the scope of the following claims. All publications, patents, and patent applications cited in this specification are incorporated herein by reference as if each such publication, patent or patent application were specifically and individually indicated to be incorporated herein by reference.

What is claimed is:

1. A pharmaceutical composition, comprising a dry blend powder that comprises about 32% by weight of (6R)-L-erythro-tetrahydrobiopterin dihydrochloride, about 54% by weight of mannitol, about 1.9% by weight of sucralose, about 10.4% by weight of potassium citrate, and about 1.6% by weight of ascorbic acid; wherein at least 90% of the initial amount of (6R)-L-erythro-tetrahydrobiopterin dihydrochloride in the pharmaceutical composition remains after the pharmaceutical composition is stored at 40° C. and 75% relative humidity for a period of three months.

2. The pharmaceutical composition of claim 1, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin dihydrochloride in the pharmaceutical composition is in a range from about 100 mg to about 500 mg.

3. The pharmaceutical composition of claim 1, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin dihydrochloride in the pharmaceutical composition is about 100 mg.

4. The pharmaceutical composition of claim 1, wherein the initial amount of (6R)-L-erythro-tetrahydrobiopterin dihydrochloride in the pharmaceutical composition is about 500 mg.

\* \* \* \* \*