

LIST OF UPDATES FOR DRGD SECOND EDITION, SEPTEMBER 2016, REVISION JULY 2018
(June 2018 Updates)

* Please note that this monthly list of updates will only be updated in the full version of DRGD in July 2018 revision. However, the effective dates are as stated below in the respective column.

NO.	UPDATES			EFFECTIVE DATE	REFERENCE									
	SECTION/ APPENDIX	DETAILS												
1.	(i) APPENDIX 4: Guideline On Registration Of Health Supplement	<u>Addition</u> of the wording “graphics/ images” in the table for <u>Prohibited Visual/Graphics/Statements on Label/Packaging Material</u> as below;			1 July 2018	Drug Evaluation Committee Meeting No. 10/2018								
	(ii) APPENDIX 5: Guideline On Registration Of Natural Products	<table border="1"> <thead> <tr> <th>No.</th> <th>Issue</th> <th>Example</th> <th>Note</th> </tr> </thead> <tbody> <tr> <td>16.</td> <td>Indecent photographs/ pornography/ graphics/ images</td> <td></td> <td>Prohibited on product label</td> </tr> </tbody> </table>					No.	Issue	Example	Note	16.	Indecent photographs/ pornography/ graphics/ images		Prohibited on product label
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(iii) APPENDIX 9: Labelling Requirements														

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2.	<p>APPENDIX 9 : LABELLING REQUIREMENTS</p> <p>(9.2 : SPECIFIC LABELLING REQUIREMENTS)</p>	<p>Addition of the following substance and safety information/ statements regarding Severe Cutaneous Adverse Reactions (SCARs);</p> <table border="1"> <thead> <tr> <th>NO.</th> <th>SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)</th> </tr> </thead> <tbody> <tr> <td></td> <td> <p>ACETAZOLAMIDE</p> <p>(Please refer Attachment 1)</p> </td> </tr> </tbody> </table>	NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)		<p>ACETAZOLAMIDE</p> <p>(Please refer Attachment 1)</p>	1 July 2018	<p>Directive No. 16 Year 2018. (Ref: BPFK/PPP/07/25 (16) Jld.2)</p> <p>Direktif Untuk Semua Produk Yang Mengandungi Acetazolamide : Pengemaskinian Sisip Bungkusan Dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan <i>Severe Cutaneous Adverse Reactions</i> (SCARs)</p>
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3.	APPENDIX 9 : LABELLING REQUIREMENTS (9.2 : SPECIFIC LABELLING REQUIREMENTS)	<p><u>Addition</u> of the following substance and <u>safety information/ statements</u> regarding Scleroderma Renal Crisis;</p> <table border="1"> <thead> <tr> <th>NO.</th> <th>SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)</th> </tr> </thead> <tbody> <tr> <td></td> <td> <p>PREDNISONE AND PREDNISOLONE (EXCEPT TOPICAL PREPARATIONS)</p> <p>(Please refer Attachment 2)</p> </td> </tr> </tbody> </table>	NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)		<p>PREDNISONE AND PREDNISOLONE (EXCEPT TOPICAL PREPARATIONS)</p> <p>(Please refer Attachment 2)</p>	1 July 2018	<p>Directive No. 17 Year 2018. (Ref: BPFK/PPP/07/25 (17) Jld.2)</p> <p>Direktif Untuk Semua Produk Yang Mengandungi Prednisone Dan Prednisolone (Kecuali Persediaan Topikal) : Pengemaskinian Sisip Bungkusan Dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan <i>Scleroderma Renal Crisis</i></p>
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4.	APPENDIX 9 : LABELLING REQUIREMENTS (9.2 : SPECIFIC LABELLING REQUIREMENTS)	<p><u>Addition of the following substances and safety information/ statements regarding QTc prolongation:</u></p> <table border="1"> <thead> <tr> <th>NO.</th> <th>SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)</th> </tr> </thead> <tbody> <tr> <td></td> <td> <p>EFAVIRENZ</p> <p>(Please refer Attachment 3)</p> </td> </tr> </tbody> </table>	NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)		<p>EFAVIRENZ</p> <p>(Please refer Attachment 3)</p>	1 July 2018	<p>Directive No. 18 Year 2018. (Ref: BPFK/PPP/07/25 (18) Jld.2) Direktif Untuk Semua Produk Yang Mengandungi Efavirenz : Pengemaskinian Sisip Bungkus dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan QTc Prolongation</p>
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Attachment 1

NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)
	<p>ACETAZOLAMIDE</p> <p>The following statements shall be <u>included in the package insert and Consumer Medication Information Leaflet (RiMUP)</u> for products containing Acetazolamide;</p> <p><u>Package Insert</u></p> <p>a) Warnings and Precautions:</p> <p>Adverse reactions common to all sulfonamide derivatives may occur such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), erythema multiforme (EM) and acute generalised exanthematous pustulosis (AGEP). If signs of serious reactions or hypersensitivity occur, discontinue use of this preparation.</p> <p>b) Adverse Effects / Undesirable Effects:</p> <p><u>Skin and Subcutaneous Tissue Disorders</u></p> <p>Frequency not known: Severe skin reactions [including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), erythema multiforme (EM) and acute generalised exanthematous pustulosis (AGEP)]</p> <p><u>Consumer Medication Information Leaflet (RiMUP)</u></p> <p>a) Side Effects:</p> <p>[Product name] may cause severe allergy and serious skin reactions. Stop using [Product name] and seek medical assistance immediately if you experience any of the following symptoms:</p> <ul style="list-style-type: none">• severe skin reaction: skin reddening, blisters, rash, fever, sore throat

or eye irritation

Reference: Directive No. 16 Year 2018. Ref. [BPFK/PPP/07/25 \(16 \) Jld 2.](#) Direktif Untuk Semua Produk Yang Mengandungi Acetazolamide : Pengemaskinian Sisip Bungkus dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan *Severe Cutaneous Adverse Reactions* (SCARs)

Attachment 2

NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)
	<p>PREDNISONONE AND PREDNISOLONE (EXCEPT TOPICAL PREPARATIONS)</p> <p>The following statements shall be <u>included in the package insert and Consumer Medication Information Leaflet (RiMUP)</u> for products containing Prednisone dan Prednisolone (except topical preparations);</p> <p><u>Package Insert</u></p> <p>a) Warnings and Precautions:</p> <p><u>Scleroderma renal crisis</u></p> <p>Caution is required in patients with systemic sclerosis because of an increased incidence of (possibly fatal) scleroderma renal crisis with hypertension and decreased urinary output observed with a daily dose of 15 mg or more prednisolone.</p> <p><u>Consumer Medication Information Leaflet (RiMUP)</u></p> <p>a) Before you start to use it:</p> <p>Talk to your doctor before taking <product name>, if you have:</p> <p>Systemic sclerosis (an autoimmune disorder). Taking daily doses of 15 mg or more may increase the risk of a serious complication called scleroderma renal crisis which may cause your blood pressure to increase and reduce urination.</p> <p>Reference: Directive No. 17 Year 2018. Ref. BPFK/PPP/07/25 (17) Jld 2. Direktif Untuk Semua Produk Yang Mengandungi Prednisone Dan Prednisolone (Kecuali Persediaan Topikal) : Pengemaskinian Sisip Bungkusan Dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan <i>Schleroderma Renal Crisis</i></p>

Attachment 3

NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)
	<p data-bbox="321 394 506 426">EFAVIRENZ</p> <p data-bbox="321 478 1433 594">The following statements shall be <u>included in the package insert and Consumer Medication Information Leaflet (RiMUP)</u> for products containing Efavirenz;</p> <p data-bbox="321 688 548 720"><u>Package Insert</u></p> <p data-bbox="321 772 792 804">a) Warnings and Precautions:</p> <p data-bbox="378 856 1433 1056">QTc prolongation has been observed with the use of efavirenz (see Section Pharmacodynamics and Section Interaction with Other Medicaments). Consider alternatives to [Product name] when coadministered with a drug with a known risk of Torsade de Pointes or when administered to patients at higher risk of Torsade de Pointes.</p> <p data-bbox="321 1108 695 1140">b) Pharmacodynamics:</p> <p data-bbox="378 1192 751 1224">Cardiac Electrophysiology</p> <p data-bbox="378 1276 1433 1808">The effect of [Product name] on the QTc interval was evaluated in an open-label, positive and placebo controlled, fixed single sequence 3-period, 3-treatment crossover QT study in 58 healthy subjects enriched for CYP2B6 polymorphisms. The mean Cmax of efavirenz in subjects with CYP2B6 *6/*6 genotype following the administration of 600 mg daily dose for 14 days was 2.25-fold the mean Cmax observed in subjects with CYP2B6 *1/*1 genotype. A positive relationship between efavirenz concentration and QTc prolongation was observed. Based on the concentration-QTc relationship, the mean QTc prolongation and its upper bound 90% confidence interval are 8.7 ms and 11.3 ms in subjects with CYP2B6*6/*6 genotype following the administration of 600 mg daily dose for 14 days. (see Section Warnings and Precautions & Section Interaction with Other Medicaments).</p>

c) Interactions with Other Medicaments:

QT Prolonging Drugs

There is limited information available on the potential for a pharmacodynamic interaction between [Product name] and drugs that prolong the QTc interval. QTc prolongation has been observed with the use of efavirenz (see Section Pharmacodynamics and Section Warnings and Precautions). Consider alternatives to [Product name] when coadministered with a drug with a known risk of Torsade de Pointes.

Consumer Medication Information Leaflet (RiMUP)

a) Before You Use <product name>:

Before you start to use it:

Tell your doctor if you have any heart disorder.

Reference: Directive No. 18 Year 2018. Ref. [BPFK/PPP/07/25 \(18 \) Jld 2](#). Direktif Untuk Semua Produk Yang Mengandungi Efavirenz : Pengemaskinian Sisip Bungkus dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan QTc *Prolongation*

Attachment 4

NO.	SPECIFIC LABELLING REQUIREMENTS (SUBSTANCE SPECIFIC)
	<p>DOXYCYCLINE</p> <p>The following statements shall be <u>included in the package insert and Consumer Medication Information Leaflet (RiMUP)</u> for products containing Doxycycline;</p> <p><u>Package Insert</u></p> <p>a) Warnings and Precautions:</p> <p>Some patients with spirochete infections may experience a Jarisch-Herxheimer reaction shortly after doxycycline treatment is started. Patients should be reassured that this is a usually self-limiting consequence of antibiotic treatment of spirochete infections.</p> <p>b) Adverse Effects/Undesirable Effects:</p> <p><u>Immune system disorders</u></p> <p>Frequency not known: Jarisch-Herxheimer reaction (see Section Warnings and Precautions)</p> <p><u>Consumer Medication Information Leaflet (RiMUP)</u></p> <p>a) Side Effects:</p> <p>[Product name] may cause Jarisch-Herxheimer reaction which usually consists of fever, chills, headache, muscle pain, and skin rash. The reaction occurs shortly after starting [product name] for spirochete infections and is often self-limiting.</p> <p>Reference: Directive No. 19 Year 2018. Ref. BPFK/PPP/07/25 (19) Jld 2. Direktif Untuk Semua Produk Yang Mengandungi Doxycycline : Pengemaskinian Sisip Bungkusan Dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan <i>Jarisch-Herxheimer Reaction</i></p>