LIST OF UPDATES FOR
DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023
(March 2023 Updates)

There are three (3) amendments for the March 2023 DRGD Updates as follows:

Main Body of DRGD Third Edition, Fourth Revision January 2023

Section B: Product Registration Process

1. Amendment of information, 6.3.7 Second or Third Source, Page 29

Appendix of DRGD Third Edition, Fourth Revision January 2023

Appendix 18: List of Permitted, Prohibited and Restricted Substances

2. Addition of new ingredient, 1.1 List of Prohibited Active Ingredients and Combinations, a) Prohibited Active Ingredients, Page 2

Appendix 19: General Labelling Requirements

3. Amendment of information, 1. Label for Immediate Container and Outer Carton, Additional Requirements, Page 4

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023

(March 2023 Updates)

Amendment of Section B: Product Registration Process

1. Amendment of 6.3.7 Second or Third Source on Page 29 by –

(a) deleting the following statement,

"g) Biologics are highly sensitive to manufacturing condition. If any of the conditions outlined below are not fulfilled, the application is automatically considered as a new application:

(i) The proposed facility is approved for manufacturing activities for the same company/ sponsor

(ii) No change in the composition, manufacturing process and drug substance as well as drug product specifications

(iii) No change in the container/ closure system

(iv) The same validated manufacturing process is used

(v) The newly introduced product is in the same family of product(s) or therapeutic classification as those already approved at the site and uses the same filling process/ equipment

(vi) Only one Final Release Site"

(b) adding the following information after f):

"6.3.7.1 Biologics

a) A second source biologic product is defined as a product which is the same as the first source in all aspects including the manufacture of drug substance, except for the site of final product manufacture. Some minor adaptations due to the new site may be accepted. An application for a new product from a second source may be considered by the Authority subject to justification. A third source may also be considered if justified.

b) Biologics are highly sensitive to manufacturing condition. Therefore, second or third source products are considered as new product applications. If all the conditions outlined are fulfilled, the product can be considered for registration via a facilitated pathway. If the conditions outlined are not fulfilled, the application will be processed by the normal pathway. The following procedures apply:

Second or third source for biologic products		
	Facilitated Pathway	Normal Pathway
Conditions	**All** the following **conditions are fulfilled:** 1. Products which fulfill either one of the following conditions: i. Treatment/prevention in pandemic/endemic situations, for the interest of public health ii. Emergency supply/crucial for treatment purpose according to the current needs in the country iii. Products manufactured by local manufacturer 2. The proposed facility is approved for manufacturing activities for the same company/PRH 3. No change in the composition, manufacturing process and drug substance & final drug product specifications 4. No change in the container/closure system	Conditions 1. to 6. are **not fulfilled**

Second or third source for biologic products		
	Facilitated Pathway	Normal Pathway
	5. The same validated manufacturing process is used 6. The newly introduced product is in the same family of product(s) or therapeutic classification as the products already approved at the site and uses the same filling process/equipment	
Supporting data	1. GMP certification issued by PIC/S authority 2. Updated relevant sections in ACTD Part II (P) 3. Confirmation that the information on the drug product has not change as a result of the submission (e.g., other than change in facility) or revised information of the drug product, if any of the attributes have changed 4. Name, address and responsibility of the proposed production facility involved in manufacturing and testing 5. Process validation and/or evaluation studies (e.g., equipment qualification, media fills, as appropriate), to	1. A complete product dossier specific to the new drug product manufacturing site is to be made available (ACTD Parts I, II; ACTD Parts III, IV can refer to the first source product registered with DCA) 2. Manufacturer's declaration of no change in formulation, specification of active ingredient(s) and excipient(s), and finished product for the second source compared to the first source 3. Quality comparability data (manufacturing process validation data, batch analyses, stability) 4. Real-time stability data to support proposed shelf-life (no extrapolation allowed by ICH

Second or third source for biologic products		
	Facilitated Pathway	Normal Pathway
	demonstrate comparability between both current and proposed manufacturing sites 6. Process validation study reports. The data should include transport between sites, if relevant. 7. Description of the batches and summary of results in the form of comparative tabulated quantitative data, for at least 3 consecutive commercial scale batches of the approved and proposed drug product, to demonstrate comparability between both current and proposed manufacturing sites 8. Summary of stability testing and results (e.g., studies conducted, protocols used, results obtained), to demonstrate comparability between both current and proposed manufacturing sites 9. Stability test results from: accelerated testing (usually a minimum of 3 months), or preferably, forced degradation studies under appropriate time and temperature conditions for	Q5C: Stability Testing of Biotechnological/Biological Products)

Second or third source for biologic products		
	Facilitated Pathway	Normal Pathway
	the product; and 3 months of real time testing at time of submission (6 months real time testing data at time of registration approval) on three commercial scale batches of the drug product manufactured using the proposed manufacturing facility, or longer if less than 3 time points are available (including the zero time point), as well as commitment to notify NPRA of any failures in the ongoing long term stability studies. 10. Certificates of analysis for drug products manufactured at the new manufacturing site 11. Rationale for considering the proposed formulation/filling site as equivalent 12. Information on the proposed production facility involved in the manufacture of the drug product, including the complete set of floor plans and flow charts (drawings, room classification, water systems, HVAC systems), as well as the cleaning and	

Second or third source for biologic products		
	Facilitated Pathway	Normal Pathway
	shipping validation, as appropriate [if applicable] 13. Information describing the change-over procedures for shared product-contact equipment or the segregation procedures, as applicable. If no revisions, a signed attestation that no changes were made to the change-over procedures [if applicable] 14. Results of the environmental monitoring studies in classified areas [if applicable]	
Fees	RM1,000 (processing fee) + RM3,000 (analysis fee – single active ingredient) OR + RM4,000 (analysis fee – two or more active ingredients)	
Processing timeline	120 working days	245 working days
NOTE: There can only be one Final Release Site for each MAL no.		

”

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(March 2023 Updates)

Amendment of Appendix 18: List of Permitted, Prohibited and Restricted Substances

2. Amendment of 1.1 List of Prohibited Active Ingredients and Combinations, a) Prohibited Active Ingredients on Page 2 by –

   (a) adding a new prohibited active ingredient, Pholcodine.

Amendment of Appendix 19: General Labelling Requirements

3. Amendment of 1. Label for Immediate Container and Outer Carton, Additional Requirements on Page 4 by –

   (b) substituting the following statement, “e) Only a single label artwork is permitted for all pack sizes of a registered product.” with the following statement, “e) A registered product is required to have the same label artwork for all pack sizes, but may have **minor** differences in colour code to differentiate pack sizes.”

LIST OF UPDATES FOR
DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023
(April 2023 Updates)

There are eight (8) amendments for the April 2023 DRGD Updates as follows:

Main Body of DRGD Third Edition, Fourth Revision January 2023

Section B: Product Registration Process

1. Addition of information, 7.10 Proposed Package Insert, Page 35
2. Addition of information, 7.11 Consumer Medication Information Leaflet (RiMUP), Page 36

Appendix of DRGD Third Edition, Fourth Revision January 2023

Appendix 19: General Labelling Requirements

3. Addition of information, 1. Label for Immediate Container and Outer Carton, Additional Requirements, Page 4

Appendix 20: Specific Labelling Requirements

4. Addition of new ingredient and safety information, No. 23, Azacitidine, Page 28
5. Addition of new ingredient and safety information, No. 97, Griseofulvin, Page 98
6. Addition of new ingredient and safety information, No. 215, Valaciclovir, Page 213

Appendix 27: Inspection

7. Addition of information, Table A. Examples of Immediate Notification, Page 4
8. Addition of information, Table B. Examples of Periodical Notification, Page 8

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023

(April 2023 Updates)

Amendment of Section B: Product Registration Process

1. Addition of new information in 7.10 Proposed Package Insert on Page 35 by –

   (a) adding the statement,

   "For information regarding **e-labelling**, refer to:

   (i) **Directive No. 3, 2023**. *NPRA.600-1/9/13(21) Jld.1 Direktif Berkenaan Pelaksanaan Electronic Labelling (E-labelling) Ke Atas Produk Farmaseutikal Di Malaysia*

   (ii) Guideline on Electronic Labelling (E-labelling) for Pharmaceutical Products in Malaysia"

2. Addition of new information in 7.11 Consumer Medication Information Leaflet (RiMUP) on Page 36 by –

   (a) adding the statement,

   "g) For information regarding **e-labelling**, refer to:

   (i) **Directive No. 3, 2023**. *NPRA.600-1/9/13(21) Jld.1 Direktif Berkenaan Pelaksanaan Electronic Labelling (E-labelling) Ke Atas Produk Farmaseutikal Di Malaysia*

   (ii) Guideline on Electronic Labelling (E-labelling) for Pharmaceutical Products in Malaysia"

Amendment of Appendix 19: General Labelling Requirements

3. Addition of new information in 1. Label for Immediate Container and Outer Carton, Additional Requirements on Page 4 by –

   (a) adding the statement,

   "m) For information regarding **e-labelling**, refer to:

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023

(April 2023 Updates)

(i) **Directive No. 3, 2023**. *NPRA.600-1/9/13(21) Jld.1 Direktif Berkenaan Pelaksanaan Electronic Labelling (E-labelling) Ke Atas Produk Farmaseutikal Di Malaysia*

(ii) Guideline on Electronic Labelling (E-labelling) for Pharmaceutical Products in Malaysia"

Amendment of Appendix 20: Specific Labelling Requirements

4. **Addition of new ingredient 23. Azacitidine and safety information on page 28** as follows in accordance with Directive No. 5, 2023: *Direktif Untuk Semua Produk Yang Mengandungi Azacitidine: Pengemaskinian Sisip Bungkusan Dengan Maklumat Keselamatan Berkaitan Risiko Differentiation Syndrome (DS)* as decided in DCA Meeting No. 383, which takes effect on 1 May 2023 –

"**23. AZACITIDINE**

The following statements shall be included in the package insert for products containing azacitidine;

Package Insert

a) Warnings & Precautions:

Differentiation syndrome

Cases of differentiation syndrome (also known as retinoic acid syndrome) have been reported in patients receiving injectable azacitidine. Differentiation syndrome may be fatal and symptoms and clinical finding include respiratory distress, pulmonary infiltrates, fever, rash, pulmonary oedema, peripheral oedema, rapid weight gain, pleural effusions, pericardial effusions, hypotension and renal dysfunction. Treatment with high-dose IV corticosteroids and haemodynamic monitoring should be considered at first onset of symptoms or signs suggestive of differentiation syndrome. Temporary discontinuation of injectable azacitidine should be considered until resolution of symptoms and if resumed, caution is advised.

b) Adverse Effects/ Undesirable Effects:

Neoplasms benign, malignant and unspecified (including cysts and polyps)
Frequency 'Not known': Differentiation syndrome*
*= rarely fatal cases have been reported

Reference: Directive No. 5, 2023. ***NPRA.600-1/9/13 (23)Jld.1*** *Direktif Untuk Semua Produk Yang Mengandungi Azacitidine: Pengemaskinian Sisip Bungkusan Dengan Maklumat Keselamatan Berkaitan Risiko Differentiation Syndrome (DS)"*

5. **Addition of new ingredient 97. Griseofulvin and safety information on page 98** as follows in accordance with Directive No. 4, 2023: *Direktif Untuk Semua Produk Yang Mengandungi Griseofulvin: Pengemaskinian Sisip Bungkusan dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan Risiko Severe Cutaneous Adverse Reactions (SCARs)* as decided in DCA Meeting No. 383, which takes effect on 1 May 2023 –

"**97. GRISEOFULVIN**

The following statements shall be included in the package insert and Consumer Medication Information Leaflet (RiMUP) for products containing griseofulvin;

Package Insert

a) Warnings & Precautions:

Severe cutaneous adverse reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalised exanthematous pustulosis) and erythema multiforme have been reported with griseofulvin use. These reactions may be serious and may result in hospitalisation or death. If severe skin reactions occur, griseofulvin should be discontinued.

b) Adverse Effects/ Undesirable Effects:

Skin and subcutaneous tissue disorders

Frequency 'not known': Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalised exanthematous pustulosis, erythema multiforme.

Consumer Medication Information Leaflet (RiMUP)

a) While You Are Using It:

If you experienced a severe skin reaction, including bumps under the skin, blisters, redness and peeling with or without fever, swollen glands and abnormal blood test results, see your doctor straight away.

b) Side effects:

Rare skin reactions which may be serious: widespread rash with blisters and peeling of the skin, especially around the mouth, nose and in the genital area causing severe skin peeling, fever, enlargement of the lymph nodes, or abnormal blood test (elevated eosinophil level or liver enzyme level). If you have such signs, consult your doctor immediately.

Reference: Directive No. 4, 2023. ***NPRA.600-1/9/13 (22)Jld.1*** *Direktif Untuk Semua Produk Yang Mengandungi Griseofulvin: Pengemaskinian Sisip Bungkusan dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan Risiko Severe Cutaneous Adverse Reactions (SCARs)"*

6. **Addition of new ingredient 215. Valaciclovir and safety information on page 213** as follows in accordance with Directive No. 6, 2023: *Direktif Untuk Semua Produk Yang Mengandungi Valaciclovir: Pengemaskinian Sisip Bungkusan dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan Risiko Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS)* as decided in DCA Meeting No. 383, which takes effect on 1 May 2023 –

"**215. VALACICLOVIR**

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(April 2023 Updates)

The following statements shall be included in the package insert and Consumer Medication Information Leaflet (RiMUP) for products containing valaciclovir;

Package Insert

a) Warnings & Precautions:

Immune: Drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, has been reported in association with valaciclovir treatment. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of DRESS appear, valaciclovir should be withdrawn immediately and an alternative treatment considered (as appropriate). If a patient has developed DRESS with the use of valaciclovir, treatment with valaciclovir must not be restarted in this patient at any time.

b) Adverse Effects/ Undesirable Effects:

Immune system disorders

Drug reaction with eosinophilia and systemic symptoms (DRESS).

Consumer Medication Information Leaflet (RiMUP)

a) Side Effects:

Drug reaction with eosinophilia and systemic symptoms (DRESS) (serious skin reaction that may affect one or more organs): fever, severe rash, peeling skin, swelling of the face, swollen lymph glands, flu-like feeling, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feel thirsty, urinating less often, less urine.

Reference: Directive No. 6, 2023. ***NPRA.600-1/9/13 (24)Jld.1*** *Direktif Untuk Semua Produk Yang Mengandungi Valaciclovir: Pengemaskinian Sisip Bungkusan dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) Dengan Maklumat Keselamatan Berkaitan Risiko Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS)"*

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(April 2023 Updates)

Amendment of Appendix 27: Inspection

7. Addition of new information in Table A. Examples of Immediate Notification on Page 4 by –

(a) adding the following items:

Items	Example	Description	Requirement of NPRA/431/12	Type of Application under NPRA/431/12	Documentation Required	Remarks (if any)
5.	Sharing of manufacturing facilities between traditional medicines and health supplements	No changes in manufacturing facility	No	Not applicable	1. Notification to PKKK, NPRA.	Verification of information via GMP inspection, if necessary.
6.	Sharing of manufacturing facilities between notified cosmetics and other non-cosmetics (e.g. household products, insect repellent or veterinary cosmetic)	No changes in manufacturing facility	No	Not applicable	1. Notification to PKKK, NPRA.	Verification of information via GMP inspection, if necessary.

8. Addition of new information in Table B. Examples of Periodical Notification on Page 8 by –

(a) adding the following item:

Items	Example	Description	Requirement of NPRA/431/12	Type of Application under NPRA/431/12	Documentation Required	Remarks (if any)
10.	Sharing of manufacturing facilities between medical devices and medicinal products	No changes in manufacturing facility	No	Not Applicable	1. Notification to PKKK, NPRA. 2. Establishment Licence from MDA	Verification of information via GMP inspection, if necessary

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(May 2023 Updates)

There are eight (8) amendments for the May 2023 DRGD Updates as follows:

Main Body of DRGD Third Edition, Fourth Revision January 2023

Section A: General Overview

1. Addition of information, 5.2 Responsibilities of the Applicant, Page 21

Appendix of DRGD Third Edition, Fourth Revision January 2023

Appendix 4: Guideline on Registration of Biologics

2. Addition of information, Page 1

Appendix 7: Guideline on Registration of Natural Products

3. Amendment of information, 2.3 Excipients, c) List of Restricted Excipients, Page 31
4. Amendment of information, 2.4.1 Indications Acceptable for Natural Products, e) Cough & Cold / *Batuk & Selsema*, Page 32
5. Amendment of information, Table 9: List of Prohibited Ingredients in Pregnancy, Page 45-47
6. Amendment of information, Recommended Presentation of the Summary Table of Stability Results, Page 61

Appendix 20: Specific Labelling Requirements

7. Amendment of information, No. 9, Alfalfa (*Medicago sativa*), Page 17
8. Amendment of information, No. 190, Senna (Cassia spp.) – fruit / pod / semen and leaf and Rhubarb / *Radix et Rhizoma Rhei* / *Rheum Palmatum* / *Rheum Officinalis* – root part, Page 182

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DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023

(May 2023 Updates)

Amendment of Section A: General Overview

1. Addition of information in 5.2 Responsibilities of the Applicant on Page 21 by –

   (a) adding the statements,

   "l) NPRA shall only correspond with the existing PRH and not with any other third party (including product owner and the law firm hired by any of the party) regarding product registration.

   m) NPRA shall not be involved in any dispute between the existing PRH and other third parties. The existing PRH is responsible for solving the dispute. For example, disputes between the PRH and the product owner in matters of COH or any contractual agreement between the two parties."

Amendment of Appendix 4: Guideline on Registration of Biologics

2. Addition of information on Page 1 by –

   (a) adding "through Deoxyribonucleic Acid (DNA) testing by Polymerase Chain Reaction (PCR) or any qualified and validated analytical method. If the analytical results are positive or DNA test on the final product is not submitted, labels should contain the information of the animal origin (specifying the name of the animal(s)) accordingly." to "Animal derived materials/ products are commonly used in the manufacture of biologics/ biopharmaceuticals. A detailed information regarding the rationale for use of such material e.g. the source, etc. shall be provided, as per **Checklist A** and **Checklist B**; and also provide a confirmation on the presence/ absence of the animal materials in the final product."

   (b) adding "**Reference:** NPRA.600-1/9/12(20): *Keperluan Ujian Deoxyribonucleic Acid (DNA) Ke Atas Produk Akhir Bagi Produk Biologik Yang Menggunakan Bahan Bersumberkan Haiwan Dalam Proses Pengilangan Produk* (24 May 2023)"

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(May 2023 Updates)

Amendment of Appendix 7: Guideline on Registration of Natural Products

3. Amendment of information in 2.3 Excipients, c) List of Restricted Excipients on Page 31 by –

   (a) substituting the term, “Limits (Not allowed)” with “Allowable Limits”.
   (b) substituting “(>10%)” with “(<10%)”.

4. Amendment of information in 2.4.1 Indications Acceptable for Natural Products, e) Cough & Cold / *Batuk & Selsema* on Page 32 by –

   (a) substituting the word, “*selsema*” with “*selesema*”.

5. Amendment of information in Table 9: List of Prohibited Ingredients in Pregnancy on Page 45-47 by –

   (a) substituting “Cortex Moutan Radicis” with “Cortex Paeonia suffruticosa (Cortex Moutan Radicis)”.
   (b) substituting “Fructus Aurantii Immaturus” with “Fructus Citrus Aurantium Immaturus (Fructus Aurantii Immaturus)”.
   (c) substituting “Moschus moschferus Linnaeus” with “Moschus moschiferus Linnaeus”.
   (d) substituting “Radix Achyranthis Bidentatae with “Radix Achyranthes bidentata”.

6. Amendment of information in Recommended Presentation of the Summary Table of Stability Results on Page 61 by –

   (a) adding “DRGD, e.g.” in the Specifications column for Microbial Contamination Test.

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(May 2023 Updates)

Amendment of Appendix 20: Specific Labelling Requirements

7. **Amendment of No. 9, Alfalfa (*Medicago sativa*) on Page 17** by –

(a) substituting "*Medico sativa*" with "*Medicago sativa*".

8. **Amendment of No. 190. Senna (Cassia spp.) – fruit / pod / semen and leaf and Rhubarb / *Radix et Rhizoma Rhei / Rheum Palmatum / Rheum Officinalis* – root part on page 182** by –

(a) substituting the substance name, "SENNA (CASSIA SPP.) – fruit / pod / semen and leaf and Rhubarb / Radix et Rhizoma Rhei / Rheum Palmatum / Rheum Officinalis – root part" with "SENNA (CASSIA SPP.) – fruit / pod / semen / leaf".

(b) substituting the statement, "The following statement shall be included on the labels of products containing Senna (Cassia spp.) – fruit / pod / semen and leaf and Rhubarb / *Radix et Rhizoma Rhei / Rheum Palmatum / Rheum Officinalis* – root part:" with "The following statement shall be included on the label and in the package insert and Consumer Medication Information Leaflet (RiMUP) of products containing Senna (Cassia spp.) – fruit / pod / semen / leaf (for oral use only):"

(c) listing as a separate entry for 179. Rhubarb (e.g. *Radix et Rhizoma Rhei / Rheum Palmatum / Rheum Officinalis*) – root part and safety information on page 175 as follows –

"**RHUBARB (e.g. *Radix et Rhizoma Rhei / Rheum Palmatum / Rheum Officinalis*) – root part**

The following statement shall be included on the label and in the package insert and Consumer Medication Information Leaflet (RiMUP) of products containing Rhubarb (e.g. *Radix et Rhizoma Rhei / Rheum Palmatum / Rheum Officinalis*) – root part (for oral use only):

- Do not use when abdominal pain, nausea or vomiting is present.
- Frequent or prolonged use of this preparation may result in dependence towards the product and ‘imbalanced electrolytes’.
- Please consult a health care practitioner for use beyond 7 days″

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(June 2023 Updates)

There are two (2) amendments for the June 2023 DRGD Updates as follows:

Main Body of DRGD Third Edition, Fourth Revision January 2023

Section E: Post-Registration Process

1. Addition of information, 20.4 New/Additional Indication, Page 58

Appendix of DRGD Third Edition, Fourth Revision January 2023

Appendix 20: Specific Labelling Requirements

2. Addition of new ingredient and safety information, No. 49, Chromium, Page 49

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(June 2023 Updates)

Amendment of Section E: Post-Registration Process

1. Addition of information in 20.4 New/Additional Indication on Page 58 by –

   (a) adding "European Medicines Agency (EMA)" to the list of reference countries in a) Full Evaluation Process.

   (b) adding the statement, "(i) EMA centralised approval is considered as ONE approval." to Note.

Amendment of Appendix 20: Specific Labelling Requirements

2. **Addition of new ingredient 49. Chromium and safety information on page 49** as follows in accordance with Directive No. 7, 2023: *Direktif Berkenaan Penambahan Pernyataan Amaran Bagi Produk Suplemen Kesihatan yang Mengandungi Bahan Aktif Chromium* as decided in DCA Meeting No. 385, which takes effect on 1 July 2023 –

"**49. CHROMIUM**

The following statement shall be included in the label, package insert and Consumer Medication Information Leaflet (RiMUP) for health supplement products containing *Chromium;*

Warning:

Please consult your doctor/pharmacist before using this product. If you are on other medicines, there may be a potential for interactions or side effects.

Reference: Directive No. 7, 2023. *NPRA.600-1/9/13 (25)Jld.1* *Direktif Berkenaan Penambahan Pernyataan Amaran Bagi Produk Suplemen Kesihatan yang Mengandungi Bahan Aktif Chromium"*

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(July 2023 Updates)

There are five (5) amendments for the July 2023 DRGD Updates as follows:

Main Body of DRGD Third Edition, Fourth Revision January 2023

Section B: Product Registration Process

1. Amendment of information, 6.3.3 Registration of For Export Only (FEO) Product, Page 28

Appendix of DRGD Third Edition, Fourth Revision January 2023

Appendix 9: Fees

2. Amendment of information in Table, 3. Charges for Application of Licenses, Page 4

Appendix 20: Specific Labelling Requirements

3. Amendment of existing safety information, No. 51, Clindamycin, Page 51

Appendix 28: Licensing

4. Amendment of information, 2. License Application Form, Page 1
5. Amendment of information, 3. Additional Product List of Licenses for Registered Products, Page 2

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(July 2023 Updates)

Amendment of Section B: Product Registration Process

1. Amendment of information in 6.3.3 Registration of For Export Only (FEO) Product on Page 28 by –

   (a) substituting "declaration letter" with "certificate of declaration" in statement g) (ii).

Amendment of Appendix 9: Fees

2. Amendment of information in Table, 3. Charges for Application of Licenses on Page 4 by –

   (a) deleting the Timeline column.

   (b) adding the phrase, "or until 31 December of the same year" to "1 year" in the Validity column for Manufacturer's, Import and Wholesaler's Licenses.

Amendment of Appendix 20: Specific Labelling Requirements

3. **The specific labelling requirements for existing ingredient, No. 51, Clindamycin on page 51** is amended in accordance with Directive No. 8, 2023: *Direktif untuk semua produk yang mengandungi clindamycin bagi kegunaan sistemik (sediaan oral dan injeksi): Pengemaskinian sisip bungkusan dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) dengan maklumat keselamatan berkaitan risiko Acute Kidney Injury (AKI)* as decided in DCA Meeting No. 386, which takes effect on 1 August 2023 by –

   (a) inserting the following statements:

   "**51. CLINDAMYCIN (ORAL & INJECTION)**

   The following statements shall be included in the package insert and Consumer Medication Information Leaflet (RiMUP) for oral and injection products containing clindamycin;

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(July 2023 Updates)

Package Insert

a) Warnings & Precautions:

Clindamycin is potentially nephrotoxic. Acute kidney injury including acute renal failure has been reported. Therefore, monitoring of renal function should be considered during therapy of patients with pre-existing renal dysfunction or taking concomitant nephrotoxic drugs and monitoring of renal function should be performed if therapy is prolonged.

b) Adverse Effects/ Undesirable Effects:

Renal and urinary disorders
Frequency 'not known': Acute kidney injury

Consumer Medication Information Leaflet (RiMUP)

a) Before you use [product name]:

Before you start to use it
Tell your doctor if you have any of the following conditions to help him or her decide if <product name> is suitable for you:

- you suffer from problems with kidneys

Taking other medicines

Tell your doctor if you are taking any other medicines.

b) Side effects:

If you develop decreased urine output, fluid retention causing swelling in your legs, ankles or feet, shortness of breath or nausea you should contact your doctor immediately.

LIST OF UPDATES FOR

DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD) THIRD EDITION, FIFTH REVISION JULY 2023

(July 2023 Updates)

Reference: Directive No. 8, 2023. ***NPRA.600-1/9/13 (26)Jld.1*** *Direktif untuk semua produk yang mengandungi clindamycin bagi kegunaan sistemik (sediaan oral dan injeksi): Pengemaskinian sisip bungkusan dan Risalah Maklumat Ubat Untuk Pengguna (RiMUP) dengan maklumat keselamatan berkaitan risiko Acute Kidney Injury (AKI)"*

Amendment of Appendix 28: Licensing

4. Amendment of information in 2. License Application Form on Page 1 by –

(a) substituting the following paragraph,

"Applications must be submitted with the following supporting documents:

a) A copy of Company/ Business Registration Certificate
b) A copy of Business License (Local Authority) for business premises or store (if any)
c) A copy of the Applicant's/ License Holder's Identity Card
d) A copy of the License Holder's Type A License (This document is necessary if products manufactured/ imported/ wholesaled are Scheduled Poison A products or any other products that require a Pharmacist)
e) A copy of previous license (For renewal application only)"

with the following paragraph,

"Applications must be submitted with the following supporting documents:

a) A copy of Company/ Business Registration Certificate
b) A copy of the License Holder's Identity Card/Passport (if foreigner). Copy of Identity Card/Passport and Type A License (wholesale) must belong to the same License Holder if the application involves Scheduled Poison A products
c) A copy of Business License (Local Authority) for business premises
d) A copy of Business License (Local Authority) for store (if any). All the stores must be in the same state as the business/ manufacturing premise. Exception is only for Selangor and Wilayah Persekutuan Kuala Lumpur
e) A copy of the License Holder's Type A License (wholesale). This document is necessary if products manufactured/ imported/ wholesaled are Scheduled Poison A products or any other products that require a Pharmacist
f) For renewal application, documents (c) to (e) together with a copy of previous Manufacturer's, Import and Wholesaler's License shall be submitted"

(b) adding the statement, “Application for Government Agencies shall be submitted using the ‘Application for Licence for Registered Product for Government Agencies’ form, which can be downloaded from the NPRA website.” after “The processing fee shall not be refundable. The processing fee of an application for a Manufacturer’s License is RM 1,000.00 and RM 500.00 for an Import License or a Wholesaler’s License.”

(c) substituting the statement, “Each license is valid for **one (1) year** or until 31 December, whichever earlier.” with “Timeline for license approval is within 4 working days upon complete and satisfactory application. Hardcopy of license will be generated after the license has been approved. Each license is valid for one (1) year or until 31 December of the same year.”

(d) adding the statement, “For more information on licensing, please refer to Guideline on Application of Manufacturer’s, Import and Wholesaler’s Licenses for Registered Products, which can be downloaded from the NPRA website.”

5. Amendment of information in 3. Additional Product List of Licenses for Registered Products on Page 2 by –

(a) substituting the word, “License” with “Manufacturer’s License/ Import License” in “Application of Additional Product List of a License is required when there is:”.

(b) deleting “or c) Omission of registered products from the product list issued together with the Manufacturer’s License or Import License.” in “Application of Additional Product List of a License is required when there is:”.

(c) substituting the phrase, “a copy of approval letter from the Authority (The Authority’s meeting result)” with “a copy of approval from the Drug Control Authority (DCA)” in “When submitting the application for Additional Product List of License for Registered Products, a copy of the current Manufacturer’s License/ Import License and a copy of approval letter from the Authority (The Authority’s meeting result) shall be provided as supporting documents.”.

(d) adding the statement, “Application for Government Agencies shall be submitted using the ‘Application for Additional Product List of Licence for Registered Product for Government Agency’ form, which can be downloaded from the NPRA website.”