Guidance Notes on Registration of Pharmaceutical Products Containing a New Chemical or Biological Entity

Version November 2023

Pharmacy and Poisons Board of Hong Kong

Contents

1. Preface 3
2. General requirements 3
3. Additional requirements 3
4. Special Considerations 5
5. Pharmacovigilance requirements 7
6. Imposing sales control on new chemical or biological entity 8
7. Applicability of NCE requirements 8

1. Preface

1.1 The aim of this document is to provide guidance on making application for registration of pharmaceutical products containing a New Chemical or Biological Entity (NCE).

1.2 These Guidance Notes outline the procedures and additional requirements for registration of pharmaceutical products containing NCE. When applying for registration of pharmaceutical products containing NCE, applicants should read these Guidance Notes in conjunction with the <Guidance Notes on Registration of Pharmaceutical Products/Substances>, where applicable.

1.3 The procedures and requirements for registration of advanced therapy products are set out in the <Guidance on Application of Certificate of Drug/Product Registration — Advanced Therapy Products>.

2. General requirements

2.1 You should submit your application for registration of pharmaceutical product via the online Pharmaceutical Registration System 2.0 (PRS 2.0) of Drug Office of the Department of Health at https://www.drugoffice.gov.hk/prs2-ext/client_authentication.jsp together with the documents set out in paragraph 6 of the <Guidance Notes on Registration of Pharmaceutical Products/Substances>.

2.2 The technical requirements for the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Common Technical Document (CTD) Modules for pharmaceutical products apply to the registration of NCE. Applicants are recommended to take reference to the ICH CTD for the presentation and format of the registration dossier.

2.3 All dossiers should be in text searchable Portable Document Format (PDF), with table of contents, hypertext links and bookmarks provided to navigate through PDF documents.

3. Additional requirements

3.1 In addition to the documents set out in paragraph 6 of the <Guidance Notes on Registration of Pharmaceutical Products/Substances>, the following additional documents should also be submitted:

3.1.1 Official evidence of registration approval of the product (e.g. electronic copy and original or certified true copies of Free Sale Certificates / Certificate of a

Pharmaceutical Products) in:

two or more of the following countries: Australia, Austria, Belgium, Brazil, Bulgaria, Canada, China, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Holland, Hungary, Ireland, Italy, Japan, Republic of Korea, Latvia, Lithuania, Luxembourg, Malta, Poland, Portugal, Romania, Singapore, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, UK and USA (Please see paragraph 4 below);

3.1.2 ICH CTD Module 2 (or equivalent). Module 3 and 5 may also be required if appropriate;

3.1.3 Evaluation report(s) on the safety, efficacy and quality of the product signed by expert(s) and the expert's curriculum vitae;

3.1.4 Proposed Risk Management Plan (RMP) and/or Risk Evaluation and Mitigation Strategy (REMS) to be implemented in Hong Kong, taking into account the identified and potential risks of the product, with reference to the RMP and/or REMS as required by the drug regulatory authorities of reference countries as listed in 3.1.1 above;

3.1.5 Proposed package insert of the product. A prescribing information leaflet for healthcare professionals for use in Hong Kong is required;

3.1.6 Risk assessment report of elemental impurities in accordance with ICH Q3D;

3.1.7 Information of any pre-registration importation of the product [e.g. named patient import and clinical trial(s)] in Hong Kong. For clinical trial information, please include clinical trial certificate number, trial site(s), principal investigator, locally reported serious adverse drug reactions, etc.;

3.1.8 A comparison of the therapeutic indications, dosage, warnings / precautions, contraindications or side effects between this application and authorizations for the same product in other countries/regions;

3.1.9 Worldwide registration status of the product;

3.1.10 Any other countries / regions where the product's authorization was refused / suspended / revoked by the competent authorities.

4. Special Considerations

4.1 In the case of applications for registration of NCE that cannot provide the official evidence of registration approval in two or more of the listed countries in paragraph 3.1.1, the applications may also be accepted for evaluation on a case-by-case basis, provided that:

4.1.1 (i) there is a local unmet medical need of the product for public health emergency#, communicable diseases or matters of public health importance in the areas of tuberculosis, emerging and/or re-emerging infectious diseases (e.g. avian influenza, chicken pox, Ebola, COVID-19, etc.) and antimicrobial resistance; and

(ii) the product for the public health emergency#, communicable diseases or matters of public health importance is promulgated by reputable international health agencies on human or veterinary medicines, including the World Health Organization (WHO), World Organisation for Animal Health, etc.;

OR

4.1.2 (i) there is a local unmet medical need of the product for life-threatening or severely-debilitating disease(s);

(ii) the product is approved with orphan drug designation, breakthrough therapy designation, priority review designation, or equivalent, and marketed in any of the listed countries in paragraph 3.1.1; and

(iii) there are local clinical data (e.g. clinical studies, case reports, case series, real-world data, etc.) of the product related to the proposed indication(s) and posology.

4.2 Applicants are required additionally to provide the followings:

4.2.1 justification for non-compliance with paragraph 3.1.1 above, with documentary evidence showing that the product fulfils requirements stated at paragraph 4.1.1 or 4.1.2;

4.2.2 (i) an assessment report on safety and efficacy of the product to be prepared by a local expert with fellowship or equivalent qualification and he/she has at least 5 years of experience in the field relevant to the product;

(ii) for applications under circumstances stated in paragraph 4.1.2, the assessment report by the local expert should also include a review of the global and local epidemiology of the disease(s), international and local

treatment paradigms of the disease(s), local unmet medical need of the disease(s), how the product could address the local unmet medical need, and safety and efficacy of the product; and

(iii) for applications under circumstances stated in paragraph 4.1.2, the expert should submit evaluation report(s) on the local clinical data of the product related to the proposed indication(s) and posology (e.g. clinical studies, case reports, case series, real-world data, etc.);

4.2.3 for applications under circumstances stated in paragraph 4.1.2,

(i) assessment report(s), post-authorization requirement(s), and licensing condition(s) issued and imposed by the drug regulatory authority which granted the approval of the product in paragraph 4.1.2 (ii);

(ii) periodic safety update report(s), summary safety report(s), or equivalent, if available; and

(iii) post-registration development plan (e.g. global regulatory planning of the product, planned and ongoing efficacy and safety studies, local clinical studies, real-world evidence studies).

Public health emergency refers to the occasion as specified in section 8(5) of the Prevention and Control of disease Ordinance (Cap. 599).

An application which does not fulfill the requirements stated in paragraph 4.1 may be refused during screening. However, the refusal does not preclude an application for registration under the requirements stated in paragraph 3.

5. Pharmacovigilance requirements

5.1 The applicant will be required to comply with the following pharmacovigilance requirements upon registration of the pharmaceutical product:

5.1.1 report all serious adverse drug reactions[1] of the product occurring in Hong Kong; any actions[2] taken by overseas health authorities, any changes of the manufacturer or manufacturing process, and any product recalls to Drug Office within a prescribed time frame; *(same requirement as generic product)*

5.1.2 document any product defect; *(same requirement as generic product)*

5.1.3 implementation of the proposed RMP[3];

5.1.4 submit all final reports of all planned, on-going or future clinical studies of the product for reassessment at the same time when the reports are submitted to the drug regulatory authorities of reference countries. A summary of the conclusion of the clinical studies and the proposed follow-up actions should also be provided. Inform the Drug Office of the actions of any regulatory actions taken by the relevant drug regulatory authorities in view of the result of the clinical studies of the product as soon as possible, and in any event no later than 72 hours after the actions have been taken;

5.1.5 submit periodic safety update reports (PSUR), or their equivalents[4], of the product every 6 months for the first 2 years, and then annually for the following 3 years after the registration is approved, or at a frequency as specified by the Drug Office.

---

[1] For applications under circumstances stated in 4.1.2, the applicant is also required to report unexpected adverse drug reactions of the product occurring in Hong Kong.

[2] For applications under circumstances stated in 4.1.2, the applicant is required to report any actions taken by overseas health authorities, including withdrawal or refusal of applications.

[3] For applications under circumstances stated in 4.1.2, the proposed RMP should be updated in accordance with the global RMP when the latter is modified and implemented in the reference country.

[4] For applications under circumstances stated in 4.1.2, the PSUR or summary safety report, or equivalent should be submitted every 6 months.

6. Imposing sales control on new chemical or biological entity

6.1 In general, when an application for registration of a pharmaceutical product containing NCE is approved by the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances: Certification of Clinical Trial/Medicinal Test) Committee ("the Committee"), the product can be registered once appropriate sales control has been imposed by the enactment of legislative amendment to the Pharmacy and Poisons Regulations, subject to any conditions the Committee thinks fit to impose. The certificate of registration will then be issued subject to payment of registration fee.

6.2 To facilitate timely registration of pharmaceutical product containing NCE, the Pharmacy and Poisons Board determined that with effect from June 2018, once an application of the concerned product is submitted and accepted for evaluation, or is listed in public medical assistance programme, the legislative amendment procedures to impose appropriate sales control would be commenced unless it is necessary to seek advice (e.g. if the sale control is subject to the indications or dosage of the product to be approved) from the Committee in advance.

7. Applicability of NCE requirements

7.1 These Guidance Notes may also be applicable to application of registration of pharmaceutical products when no reference products have been previously registered in Hong Kong, or pharmaceutical products having any one of the following properties:

- New combination of active ingredients
- New indication(s)
- New dosing regimen
- New route of administration
- New strength
- New dosage form

7.2 The Drug Office would consider whether an application for registration of pharmaceutical product is subject to the requirements specified in these Guidance Notes on a case-by-case basis.