The China Food and Drug Administration pushes forward on conditional approval and compassionate use of new drugs

January 2018

Hogan Lovells

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On December 20, 2017, the China Food and Drug Administration ("**CFDA**") released two draft documents for public comment:

(1) *Conditional Approval for Urgently Needed Drugs Technical Guidance* (the "**Draft Conditional Approval Guidance**"); and

(2) *Compassionate Use of Clinical Trial Drugs Administrative Measures* (the "**Draft Compassionate Use Measures**" and, together with the Draft Conditional Approval Guidance, the "**Draft CFDA Documents**").

The Draft Conditional Approval Guidance provides rules on the early use of new drugs where there is a pressing clinical need in China to treat patients in a critical clinical condition. As the name of the document suggests, the marketing of these drugs on the Chinese market is permitted on the basis of a conditional approval.

The Draft Compassionate Use Measures regulate the administration of clinical trial drugs to patients who are not enrolled in clinical trials in China, but who have an urgent need.

General principles: the State Council's Opinion

On October 10, 2017, the State Council issued a policy document that encouraged extended access to clinical trial drugs and the conditional approval of new drugs: the *Opinion on Deepening Review and Approval System to Encourage Drug and Medical Device Innovation* (the "**Opinion**"). This set in place the policy basis and support for the new rules.

The Opinion referred for the first time to the conditional marketing of new drugs that are urgently needed for the treatment of life-threatening diseases when no other effective treatment is available, or for public health purposes. Under the Opinion, use in such circumstances is subject to two pre-conditions:

(a) the efficacy of the drug is capable of confirmation through early and mid-stage clinical trials; and

(b) the predictability of its clinical value.

The Opinion can be seen as an innovation in the field of drug administration, although given its nature as a policy document, it does not carry binding legal force: the Draft CFDA Documents represent the Chinese legislator's attempt to transpose the general principles contained in the Opinion into legislation.

Draft Conditional Approval Guidance

What are the requirements for the grant of the conditional approval?

The Draft Conditional Approval Guidance regulates the commercialization, by way of conditional approval, of innovative drugs (including traditional Chinese medicine, chemical drugs and innovative biological drugs) that treat severe and life-threatening diseases or so-called orphan diseases, when no other effective therapy is in place. This is only possible under one of the following circumstances:

(a) a surrogate clinical endpoint or intermediate clinical endpoint indicates a high likelihood that the innovative drug has both efficacy and clinical value;

(b) data from the early or mid-stage clinical trials reasonably predicts or indicates clinical benefits and obvious advantages over other available therapies (in this case, confirmatory clinical trials must be completed after the conditional approval is granted); or

(c) in relation to the treatment of orphan diseases, the drug has already been granted marketing authorization in an overseas jurisdiction.

How can the conditional approval be obtained?

Foreign drug manufacturers may file a normal drug marketing application with the CFDA and specify in the application that they intend to seek conditional approval for the marketing of the drug. Applicants are permitted to apply for preliminary discussions with the CFDA on the possibility of obtaining conditional approval and the related requirements. The Center for Drug Evaluation under the CFDA (the "**CDE**") is in charge of the technical review of applications, and can hold expert consultation meetings to discuss technical issues as needed.

The applicant can use foreign clinical trial data to support a conditional approval application in China. But additional race and/or ethnicity difference studies must be performed as soon as possible after a conditional approval has been granted.

Can the conditional approval be revoked?

The CFDA can revoke a conditional approval in the following circumstances:

(a) clinical trials fail to confirm the intended clinical benefits of the drug;

(b) other evidence shows that the use of the drug is not safe or effective;

(c) after having obtained conditional approval, the applicant fails to duly perform the required clinical trials; or

(d) the applicant uses false or misleading promotional materials when marketing the new drug subject to conditional approval.

Our comments

The Draft Conditional Approval Guidance represents a meaningful step towards the implementation of a conditional drug approval system in China. However, the text of the Draft Conditional Approval Guidance could be improved. In our view the main issues are as follows:

(a) there is no exhaustive definition of the "conditions" that may be attached to the granting of approval; in particular, if anything else may be required in addition to completing the prescribed clinical trials following the granting of conditional approval (for instance, any ongoing reporting obligations that could be imposed on the applicant or any other party after obtaining conditional approval); if these are made too onerous, it could discourage drug development companies from taking this route; and

(b) in contrast to the Draft Compassionate Use Measures where there is a defined timetable, there is no clear timeframe within which the CFDA review and approval process must be completed, and thus there is a lack of certainty as to whether a conditional approval application can be processed reasonably quickly; and there is no indication as to whether a conditional approval application will be prioritized compared to other drug registration applications; this is a factor of critical importance, considering the inherent urgent nature of a conditional drug approval (by definition, it is being sought for drugs that are needed urgently by patients suffering from a critical clinical condition).

Draft Compassionate Use Measures

Who is eligible to gain access to the compassionate use of new drugs?

Patients treated in a facility that hosts clinical trials in China may be in urgent need of drugs used in the clinical trials, but may have failed to enrol in the clinical trials. Under the Draft Compassionate Use Measures, these patients may exceptionally be granted access to the clinical trial drugs by way of compassionate use.

More specifically, approval for compassionate use can be granted to patients that meet the following requirements:

(a) they are patients of medical institutions at which clinical trials are being performed for the drugs;

(b) they urgently need the clinical trial drugs to treat a serious or life-threatening disease that could have serious implications for their quality of their life, when no other effective therapies are available; and

(c) they cannot obtain the clinical trial drugs by participating in clinical trials, because:

(i) they do not meet the requirements for the enrolment to the clinical trial (i.e. the protocol);

(ii) they are physically unable to participate in the clinical trials due to their location or time constraints; or

(iii) the clinical trials have been completed, the drugs have not been marketed on the Chinese market, but available clinical data preliminarily indicate the efficacy and safety of the drugs.

How can approval for compassionate use be obtained?

Foreign drug manufacturers may file an application with the CDE to obtain approval for the compassionate use of clinical trial drugs. The CDE must take a decision within 30 days of receiving the application, taking into consideration the requirements listed above and whether compassionate use will hinder R&D and the registration process in relation to the drug undergoing clinical trials in China.

In addition to approval from the CDE, physicians would need to perform a risk-benefit assessment on the drug intended for compassionate use and confirm that the benefits outweigh the risks, and obtain informed consent from the patient concerned. This may be a delicate judgment for a Physician to make.

Data generated from compassionate use can be used as supporting documentation to evidence the safety of the drug undergoing clinical trials and be presented to the CFDA when applying for drug registration.

Our comments

The Draft Compassionate Use Measures should be welcomed as an important legal development, as they potentially grant patients suffering from critical conditions access to experimental treatments, and show a more caring approach to modern healthcare in China. However (as is the case for the Draft Conditional Approval Guidance), certain aspects of the Draft Compassionate Use Measures appear to be incomplete or unclear and could be improved. For instance, it should be confirmed whether a single patient can seek to obtain approval (rather than a group or category of patients with similar conditions), and how long such approval remains effective once it is obtained.

Conclusion

The Draft CFDA Documents may presage the promulgation of new legislation that applies the conditional approval and compassionate use mechanisms to medical devices (a possibility that is expressly mentioned in the Opinion), another development to be welcomed, provided that adequate patient safeguards are put in place at the same time.

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