附件1

阿司匹林肠溶片生物等效性研究技术

指导原则（征求意见稿）

2022年04月

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[二、人体生物等效性研究设计 1](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758625)

[（一）研究类型 1](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758626)

[（二）受试人群 1](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758627)

[（三）给药剂量 1](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758628)

[（四）给药方法 1](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758629)

[（五）血样采集 2](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758630)

[（六）检测物质 2](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758631)

[（七）生物等效性评价 2](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758632)

[（八）其他 2](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758633)

[三、人体生物等效性研究豁免 3](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758634)

[四、参考文献 3](file:///F%3A%5C%E4%B8%AA%E8%8D%AF%E6%8C%87%E5%8D%97%E5%B7%A5%E4%BD%9C%E8%AE%A1%E5%88%92%5C2022%E5%B9%B4%E7%AB%8B%E9%A1%B9%E8%AE%A1%E5%88%92%5C%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E8%AF%B7%E7%A4%BA%5C%E5%85%B3%E4%BA%8E%E5%85%AC%E5%BC%80%E5%BE%81%E6%B1%82%E3%80%8A%E9%98%BF%E5%8F%B8%E5%8C%B9%E6%9E%97%E8%82%A0%E6%BA%B6%E7%89%87%E7%94%9F%E7%89%A9%E7%AD%89%E6%95%88%E6%80%A7%E7%A0%94%E7%A9%B6%E6%8C%87%E5%AF%BC%E5%8E%9F%E5%88%99%EF%BC%88%E5%BE%81%E6%B1%82%E6%84%8F%E8%A7%81%E7%A8%BF%EF%BC%89%E3%80%8B%E6%84%8F%E8%A7%81%E7%9A%84%E8%AF%B7%E7%A4%BA.docx#_Toc100758635)

阿司匹林肠溶片生物等效性研究技术指导原则

一、概述

阿司匹林肠溶片（Aspirin enteric-coated tablets）是一种延迟释放制剂，其主要成份乙酰水杨酸在吸收前、吸收期间和吸收后，转化成其主要代谢产物水杨酸，代谢产物主要经肾脏途径排泄。乙酰水杨酸的消除半衰期很短，水杨酸的消除速率受给药剂量的影响。

阿司匹林肠溶片人体生物等效性研究应符合本指导原则，还应参照《以药动学参数为终点评价指标的化学药物仿制药人体生物等效性研究技术指导原则》、《生物等效性研究的统计学指导原则》等相关指导原则要求。

二、人体生物等效性研究设计

（一）研究类型

可采用两序列、两周期、交叉试验设计，也可采用部分重复交叉设计或完全重复交叉设计，开展单次给药的空腹及餐后人体生物等效性研究。

（二）受试人群

健康受试者。

（三）给药剂量

建议采用申报的规格，单片服用。

（四）给药方法

口服给药。

（五）血样采集

血浆中乙酰水杨酸和水杨酸的达峰时间不同，餐后给药时阿司匹林吸收延迟，建议合理设计样品采集时间点，使其包含吸收、分布及消除相。

（六）检测物质

血浆中的乙酰水杨酸和水杨酸。

（七）生物等效性评价

建议以乙酰水杨酸的Cmax、AUC0-t和AUC0-∞作为生物等效性评价的指标，水杨酸的Cmax、AUC0-t和AUC0-∞用于进一步支持临床疗效的可比性。

若选择两序列、两周期、交叉试验设计，应采用平均生物等效性方法，乙酰水杨酸的Cmax、AUC0-t、AUC0-∞几何均值比值的90%置信区间应在80.00%~125.00%范围内；若采用部分重复交叉设计或完全重复交叉设计，具体统计方法和评价标准参照《高变异药物生物等效性研究技术指导原则》。

（八）其他

1. 良好的采血点设计，将有助于获得有效、可靠的药代动力学参数。

2. 临床试验和分析检测过程中应控制乙酰水杨酸和水杨酸的相互转化，提高乙酰水杨酸和水杨酸检测结果的可靠性，并在资料中提交两种检测物质转化的评估结果。

三、人体生物等效性研究豁免

通常不适用。

四、参考文献

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