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世界中医药学会联合会

World Federation of Chinese Medicine Societies

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血脂平胶囊临床应用专家共识

Expert consensus on clinical application of Xuezhiping Capsule

世界中联技术报告

Technical report of WFCMS

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前 言

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本文件的起草程序遵守了世界中医药学会联合会发布的SCM 1.1-2021《标准化工作导则 第1部分：标准制修订与发布》。

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引 言

血脂平胶囊是贵州太和制药有限公司自主研发的降脂药物，具有独立知识产权（专利号:202011258094.4），已通过国家局审核获取药品注册证（国药准字 Z20025713），国家基本医疗保险乙类药物（化浊降脂剂，编号：835）。

本文件的制定由世界中医药学会联合会介入心脏病专业委员会发起，组织海内中医、西医及中西医结合心血管病专家，起草了本文件，对血脂平胶囊临床应用形成推荐意见和共识建议。

本文件旨在服务临床医师，为血脂平胶囊临床应用提供参考，促进合理用药，减少用药风险，使更多患者获益。随着临床实践的深入，新的证据不断发现，本共识将不断更新和完善。

本文件的发布机构提请注意，声明符合本文件时，可能涉及到本文件与血脂平胶囊相关的专利的使用。

本文件的发布机构对于该专利的真实性、有效性和范围无任何立场。

该专利持有人已向本文件的发布机构承诺，他愿意同任何申请人在合理且无歧视的条款和条件下，就专利授权许可进行谈判。该专利持有人的声明已在本文件的发布机构备案。相关信息可以通过以下联系方式获得：

专利持有人姓名：贵州太和制药有限公司。

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请注意除上述专利外，本文件的某些内容仍可能涉及专利。本文件的发布机构不承担识别专利的责任。

血脂平胶囊临床应用专家共识

1 范围

本文件给出了血脂平胶囊的临床应用的适应症、剂量和疗程，以及特殊人群用药、不良反应和禁忌症等内容。

本文件适用于适合相关专业领域各类具有法律许可的执业医师使用。

2 规范性引用文件

下列文件中的内容通过文中的规范性引用而构成本文件必不可少的条款。其中，注日期的引用文件，仅该日期对应的版本适用于本文件；不注日期的引用文件，其最新版本（包括所有的修改单）适用于本文件。

GB/T16751.1-2021 中医临床诊疗术语 第2部分：证候

中国国家基本药物目录(2018年版)

中国国家基本医疗保险、工伤保险和生育保险药品目录（2019年版）

诸骏仁,高润霖,赵水平,陆国平,赵冬,李建军.中国成人血脂异常防治指南(2016年修订版)[J].中国循环杂志,2016,31(10):937-953

3 术语和定义

下列术语和定义适用于本文件。

3.1

血脂异常

血浆中低密度脂蛋白胆固醇、胆固醇和（或）甘油三酯水平增高，或是高密度脂蛋白胆固醇水平降低等情况，这种状态会促使动脉粥样硬化的形成。

4 血脂平药物基本信息

4.1 处方来源、药物组成及方解

血脂平胶囊处方来源于贵州苗族民间验方，由徐长卿、山楂、刺梨、绞股蓝四味药物组成。徐长卿，味辛，性温，具有祛风，化湿等功效。山楂，味酸、甘，性微温，可消食健胃，行气散瘀，化浊降脂。刺梨，味甘、酸微涩，性凉，能健胃、消食、滋补，止泻。绞股蓝，味甘、苦，性微寒，有清热、补虚、益气健脾的作用。四药合用，共奏健脾、化痰、祛瘀之效。

4.2 功效主治

活血祛瘀，用于痰瘀互阻引起的血脂异常，临床症见：胸闷、气短、乏力、心悸、头晕等。

5 临床应用建议

5.1 适用疾病类型

5.1.1 血脂平胶囊可以治疗痰瘀互阻证血脂异常患者。[共识建议]

5.1.2 血脂平胶囊可以用于改善痰瘀互阻型血脂异常患者；或在西医常规治疗的基础上，加用血脂平胶囊可以进一步改善血脂异常患者的临床症状。[共识建议]

5.1.3 单独使用血脂平胶囊可以降低血脂异常患者的 TC 水平；或在西医常规治疗的基础上加用血脂平胶囊，进一步降低血脂异常患者的 TC 水平。[共识建议]

5.1.4 在西医常规治疗的基础上加用血脂平胶囊，进一步降低血脂异常患者的 LDL-C 水平。[共识建议]

5.1.5 单独使用血脂平胶囊可以降低血脂异常患者的 TG 水平；或在西医常规治疗的基础上加用血脂平胶囊，进一步降低血脂异常患者的 TG 水平。[共识建议]

5.1.6 单独使用血脂平胶囊可以升高血脂异常患者的 HDL-C 水平；或在西医常规治疗的基础上加用血脂平胶囊，进一步升高血脂异常患者的 HDL-C 水平。[共识建议]

5.2 用法及疗程

胶囊，每粒装 0.3g，口服，一次 2~4 粒，一日 3 次。（共识建议）

现有的血脂平胶囊临床应用研究中，多以 4-8 周为一个疗程。血脂异常为慢性长期伴随疾病，临床研究显示^[2]，在疗程范围内，其降脂效果与使用时间成正相关。目前尚无血脂平胶囊长期使用出现相关不良反应的报告。（共识建议）

6 安全性

6.1 不良反应/不良事件

文献报告显示：李泽荣等^[2]报告临床观察 197 例患者，在常规西药治疗的基础上，联合使用血脂平胶囊治疗未见严重的不良反应。

孔德明等^[3]报告临床观察 30 例患者，治疗组在常规治疗的基础上合用血脂平胶囊，对照组应用常规西药治疗，血脂平治疗组有 2 例患者诉轻微头晕和上腹不适，均不影响治疗，治疗结束后，症状均消失。

国家药物不良反应监测中心显示，2018 年-2022 年间共收到 8 例不良反应报告。少数患者服用本品后可出现恶心、呕吐、胃痛、便秘、头晕等，停药减药后症状均可减轻或消失，未见严重不良事件/不良反应报告（具体见附录 C）。

6.2 禁忌证

尚无妊娠方面的安全性研究，故不建议孕妇应用；也没有严重肝肾功能障碍患者的应用经验，体内药代动力学过程尚不清晰，建议严重肝肾功能不全患者慎用；考虑其组成药物有活血化瘀功效，有出血倾向的患者慎用。（共识建议）。

6.3 联合用药

现有的血脂平胶囊临床研究中，大多数是西医规范化治疗基础上叠加的试验，未见联合使用增加相关不良反应、毒副作用的报告。

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附录 A
(资料性)
血脂平胶囊研究资料

A.1 中医理论基础

现代医学中血脂的概念与古代文献中对于“膏”和“脂”的论述较为相似。膏脂本为水谷，化生精微之后，随津液运行流动，而精微物质又奉心化赤而为血，故津液、血液中均存在膏脂的成分。目前大多数学者都认为，饮食不节，嗜食肥甘厚味、过逸少劳以及情志失调等因素直接或间接影响脏腑，导致人体气血津液运行失调，脂肪代谢紊乱，形成痰凝、湿浊、瘀血等病理产物，这是血脂异常的重要致病因素。脾受胃禀，乃能熏熟五谷，脾胃虚弱，过多的水谷精微不能及时转化和排泄，留而不去，即成痰浊，阻碍脾胃的运化功能，使脾虚更甚。“气为血之帅”“运血者气也”，气盛则血行滑疾，气虚则血流迟缓滞涩可形成瘀血，而瘀血形成后也将导致或加重血脂异常。故中医常常从痰、从瘀论治血脂异常。

血脂平胶囊处方来源于贵州苗族民间验方，由刺梨、徐长卿、绞股蓝、山楂四味药物组成。其中徐长卿、山楂两味药物被《中国药典（2020 版）》收录。徐长卿，味辛，性温，归肝、胃经；具有祛风，化湿等功效。山楂，味酸、甘，性微温，归脾、胃、肝经；可消食健胃，行气散瘀，化浊降脂。刺梨，味甘、酸微涩，性凉，归脾、胃、肾经；有健胃、消食、滋补，止泻的功效。绞股蓝，苦、微，归肺、脾、肾经；具有清热、补虚、益气健脾的功效。四药合用，共奏健脾、化痰、祛瘀之效。

A.2 工艺质控

贺祝英等^[4]报告了血脂平胶囊的化学成分分析结果，包括黄酮类、皂甙类化合物、丹皮酚和 Zn、Mg、Fe 等化学成分，其中丹皮酚是血脂平胶囊的主要成分之一。叶凤等^[5]认为用薄层扫描法测定能较好地定量测定血脂平胶囊中丹皮酚的含量，方法简便准确，可作为血脂平胶囊的控制指标之一。

A.3 药理研究

现代药理学研究证实：方中刺梨含足量的微量元素及总黄酮等成分，能降低血清中血脂、过氧化脂质水平，减少脂质过氧化物对 LDL 的损伤^[6]；徐长卿中挥发油成分丰富，以丹皮酚为著，能够抑制脂肪细胞分化及脂滴形成，具有较强的调脂作用；同时能增加冠脉血流量，减少心肌细胞功能损伤^[7-10]；绞股蓝主要活性成分绞股蓝总皂苷具有降低血脂、保护血管内皮细胞活性、防治动脉粥样硬化的作用^[11,12]；山楂可以抑制胆固醇合成酶，抑制脂肪吸收，促进脂质的排泄，具有活血化瘀、降血脂及降压作用^[13,14]。

聂红等^[15]观察了血脂平胶囊对正常小鼠血清胆固醇及血脂异常大鼠病理模型的影响，结果显示血脂平胶囊可使正常小鼠血清 TC 较给药前下降 $35.62 \pm 0.3\%$ ；可降低血脂异常大鼠 TC、TG、LDL-C，升高 HDL-C。

申强等^[16]构建金黄地鼠血脂异常模型，实验显示血脂平胶囊可通过上调模型组过氧化物酶体增殖物激活受体 α (PPAR- α) 表达，进而调节细胞中的脂肪酸代谢，促进胆固醇 7-羟化酶 (CYP7A1) 的 mRNA 及蛋白表达，起到降低 TC 的作用。同时，血脂平胶囊通过下调胆固醇调节元件结合蛋白 1c (SREBP-1c) 表达，降低其下游的乙酰辅酶 A 羧化酶 (ACC1) 表达以达到调节血脂的目的，对于 ACC1 的调节作用优于阿托伐他汀。血脂平胶囊合用半量阿托伐他汀时，与单独应用常规剂量阿托伐他汀的药效相当甚至更优。

A. 4 非临床安全性研究

小鼠每日经口给药 30g/kg(合生药量 120g/kg)，此剂量相当于临床正常剂量的 500 倍，连续给药 7 天，小鼠行为活动及摄食正常，毛光泽，未见任何毒性反应，亦无死亡发生。

大鼠每日经口给药 6g/kg，此剂量相当于临床正常剂量的 100 倍，连续给药 60 天，未见大鼠出现外观及行为异常变化，体重、外周血象、肝肾及各脏器系数，均无显著变化，未见毒性反应。

附录 B
(资料性)
临床问题清单

本文件研制过程中共形成 9 个临床问题（表 B.1）。

表 B.1 临床问题清单

序号	临床问题
1	血脂平胶囊适用于什么证型的血脂异常患者？
2	血脂平胶囊能否缓解血脂异常（痰瘀互阻证）患者胸闷、气短、乏力、心悸、头晕等临床症状？
3	血脂平胶囊是否有利于降低血脂异常患者 TC 的水平？
4	血脂平胶囊是否有利于降低血脂异常患者 TG 的水平？
5	血脂平胶囊是否能降低血脂异常患者 LDL-C 的水平？
6	血脂平胶囊是否能升高血脂异常患者 HDL-C 的水平？
7	血脂平胶囊是否存在明确注意事项，如用药(配伍) 禁忌、特殊人群用药及其他临床用药注意事项？
8	血脂平胶囊常见不良反应有哪些？出现不良反应时应如何应对？
9	长期服用血脂平胶囊的安全性如何？

附录 C
(资料性)
共识建议概要表

本文件采用国际公认的 GRADE 系统进行证据等级评价, 采用德尔菲法与名义组法相结合, 主要考虑六个方面的因素: 证据质量、临床疗效、安全性、经济性、患者可接受性及其他。对于有循证医学证据的适应症, 根据证据等级, 形成“推荐意见”; 对于目前文献不充分, 具有临床适应症的, 经专家讨论, 形成“共识建议”。

本文件通过文献检索、证据等级评价、德尔菲法问卷及名义组法专家讨论, 最终专家讨论形成共识。血脂平胶囊临床应用文献相对较少, 本文以“共识建议”为最终呈现形式, 共 13 条共识建议 (表 C.1)。

表 C.1 血脂平胶囊共识建议表

共识建议	共识条目	结论
共识建议 1	血脂平胶囊适用于中医痰瘀互阻证候的血脂异常患者。	建议
共识建议 2.1	单独服用血脂平胶囊可以改善痰瘀互阻型血脂异常患者的中医证候。	建议
共识建议 2.2	在西医常规治疗的基础上, 加用血脂平胶囊可以进一步改善血脂异常患者的临床症状。	建议
共识建议 3.1	单独服用血脂平胶囊可以降低血脂异常患者的 TC 水平。	建议
共识建议 3.2	在西医常规治疗的基础上, 加用血脂平胶囊可以进一步降低血脂异常患者的 TC 水平。	建议
共识建议 4.1	单独服用血脂平胶囊可以降低血脂异常患者的 TG 水平。	建议
共识建议 4.2	在西医常规治疗的基础上, 加用血脂平胶囊可以进一步降低血脂异常患者的 TG 水平。	建议
共识建议 5	在西医常规治疗的基础上, 加用血脂平胶囊可以进一步降低血脂异常患者的 LDL-C 水平。	建议
共识建议 6.1	单独服用血脂平胶囊可升高血脂异常患者的 HDL-C 水平。	建议
共识建议 6.2	在西医常规治疗的基础上, 加用血脂平胶囊可以进一步升高血脂异常患者的 HDL-C 水平。	建议
共识建议 7	孕妇、严重肝肾功能不全、存在严重出血倾向或对本药物成分过敏者禁用。	建议
共识建议 8	个别患者服药期间可能出现头晕、上腹不适、腹泻, 可通过减量或停药来缓解。	建议
共识建议 9	本药物性味较为温和, 若无不良反应, 符合适应症的患者可在医生指导下规律服用。	建议

附录 D
(规范性附录)
疾病诊断要点

血脂异常诊断要点：参考《中国成人血脂异常防治指南（2016 年修订版）》^[4]中的相关诊断标准：连续 2 次空腹 12 小时以上检测血清总胆固醇（Total cholesterol, TC） $\geq 6.2\text{mmol/L}$ ，或甘油三酯（Triglyceride, TG） $\geq 2.3\text{mmol/L}$ ，或低密度脂蛋白胆固醇（Low density lipoprotein cholesterol, LDL-C） $\geq 4.1\text{mmol/L}$ ，或高密度脂蛋白胆固醇（High-density lipoprotein cholesterol, HDL-C） $\leq 1.0\text{mmol/L}$ 。
符合以上任意一项则诊断为血脂异常。

附录 E
(资料性附录)
国家药物不良反应监测中心报告

中国国家药物不良反应监测中心出具的血脂平胶囊报告见表 E.1。

表 E.1 国家药物不良反应监测中心报告

序号	编号	生产批号	不良反 应 名 称	累及系统	停药减药后反应 是否减轻或消失	年度
1	XZP-2020-001	20100902	恶心	胃肠疾病	是	2020
2	XZP-2020-002	20200902	便秘	胃肠疾病	是	
3	XZPJN-2021-01	20191106	心慌; 恶心	胃肠疾病	是	2021
4	XZPJN-2021-02	202001001	恶心; 呕吐	胃肠疾病	是	
5	XZPJN-2021-03	20210201	双下肢水肿	全身整体疾病	是	
6	XZPJN-2021-04	20200901	头晕	神经疾病	是	
7	XZPJN-2021-05	20210701	皮疹	皮肤及皮肤附件疾病	是	
8	XZPJN-2022-001	20220101002	胃痛	胃肠疾病	是	2022

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Forward

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Introduction

Xue Zhi Ping Capsule is a lipid-lowering drug independently developed by Guizhou Taihe Pharmaceutical Co., Ltd., with independent intellectual property rights (patent No.202011258094.4) . It has been approved by the National Bureau of Medicine and obtained the drug registration certificate (National medical approval number Z20025713) and the national basic medical insurance Class B drug (turbidimetric lipid-lowering agent, number: 835).

The formulation of this document was initiated by the Interventional cardiology of the World Federation of Chinese Medicine Societies. Experts of cardiovascular diseases of traditional Chinese medicine, western medicine and integrated traditional Chinese and Western medicine in China were organized to draft this document and provide recommendations and consensus suggestions for the clinical application of Xue Zhi Ping Capsule.

This document aims to serve clinicians, provide reference for the clinical application of Xue Zhi Ping Capsule, promote rational drug use, reduce drug use risk, and benefit more patients. With the deepening of clinical practice and the discovery of new evidence, this consensus will be constantly updated and improved.

The issuing institution of this document draws attention to the possibility that the declaration of compliance with this document may involve the use of patents related to Xueping capsules in this document.

The issuing authority of this document takes no position on the authenticity, validity, or scope of the patent.

The patent holder has promised to the issuing authority of this document that he is willing to negotiate with any applicant for the license of the patent on reasonable and non-discriminatory terms and conditions. The patent holder's declaration has been filed with the issuing authority of this document. Relevant information can be obtained at:

Name of patent holder: Guizhou Taihe Pharmaceutical Co., LTD.

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Please note that in addition to the patents mentioned above, certain elements of this document may refer to patents. The issuing institution of this document assumes no responsibility for the identification of patents.

Expert consensus on the clinical application of Xue Zhi Ping Capsule

1 Scope

This document gives the indications, dosage and course of clinical application of Xue Zhi Ping Capsule, as well as the use of special populations, adverse reactions and contraindications.

This document is applicable to all types of licensed medical practitioners in relevant fields.

2 Normative References

The contents of the following documents constitute essential provisions of this document by normative reference in the text. Where a reference document is dated, only the version corresponding to that date applies to this document; Undated reference documents, the latest version of which (including all amendments) apply to this document.

GB/T16751.1-2021 Clinical diagnosis and treatment terms of traditional Chinese medicine part 2: Syndromes

China National Essential Medicine List (2018 edition)

Drug list of China's National Basic medical Insurance, Work-related Injury Insurance and Maternity Insurance (2019 edition)

Zhu Junren, GAO Runlin, ZHAO Pingli, LU Guoping, ZHAO Dong, LI Jianjun. Chinese guidelines for the prevention and treatment of dyslipidemia in adults (2016 revision)[J]. Chinese Journal of Circulation, 2016, 31(10):937-953

3 Terms and Definitions

The following terms and definitions apply to this document.

3.1

Dyslipidemia

Elevated plasma levels of low-density lipoprotein cholesterol, cholesterol and/or triglycerides, or decreased levels of high-density lipoprotein cholesterol, which contribute to the formation of atherosclerosis.

4 Basic Information of Xue Zhi Ping Capsule Components

4.1 Prescription Source, Composition and Formula Explanation

The prescription of Xue Zhi Ping Capsule derives from the folk and experience-based prescription of Miao nationality in Guizhou, and is composed of four ingredients including Xu Chang Qing, Hawthorn, Rosa roxburghii and Gynostemma pentaphyllum. Pungent in flavour and warm in property, Xu Changqing has the effects of expelling wind and eliminating dampness. Hawthorn sour, sweet in flavour and slightly warm in property, can invigorate stomach to promote digestion, promote qi circulation to dissipate blood stasis, as well as resolve turbidity and lower lipid. ,Commonly sweet, acid, and slightly astringent in flavour, and mild cool in property, rosa roxburghii can invigorate stomach to promote digestion, tonify and arrest diarrhea. Gynostemma pentaphyllum, sweet and bitter in flavour, is slightly cold in property, and has the functions of clearing heat, tonifying deficiency, reinforcing qi and invigorating the spleen. The combination of the four ingredients has the effects of invigorating the spleen, eliminating phlegm and removing stasis.

4.2 Efficacy and Indications

Xue Zhi Ping capsule has effects of activating blood circulation and eliminating phlegm, and is commonly used for dyslipidemia caused by retention of phlegm and stasis. Clinical symptoms include chest tightness, shortness of breath, fatigue, palpitation, dizziness and so on.

5 Suggestions for Clinical Application

5.1 Applicable Disease Types

5.1.1 Xue Zhi Ping Capsule can treat dyslipidemia (phlegm and stasis retention pattern). (Consensus Suggestion)

5.1.2 Xue Zhi Ping Capsule can be used to improve the clinical symptoms of patients with dyslipidemia (phlegm and stasis retention pattern); or Xue Zhi Ping combined with conventional treatment of western medicine can further improve the clinical symptoms of patients with dyslipidemia. (Consensus Suggestion)

5.1.3 Using Xue Zhi Ping Capsule individually can lower TC level of patients with dyslipidemia; or Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further lower TC level of patients with dyslipidemia. (Consensus Suggestion)

5.1.4 Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further lower LDL-C level of patients with dyslipidemia. (Consensus Suggestion)

5.1.5 Using Xue Zhi Ping Capsule individually can lower TG level of patients with dyslipidemia; or Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further lower TG level of patients with dyslipidemia. (Consensus Suggestion)

5.1.6 Using Xue Zhi Ping Capsule individually can increase HDL-C level in patients with dyslipidemia; or Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further increase HDL-C level of patients with dyslipidemia. (Consensus Suggestion)

5.2 Usage and Course of Treatment

Capsule form, 0.3g per capsule, taken orally and 2~4 capsules once, 3 times a day. (Consensus Suggestion)

In the existing clinical application research of Xue Zhi Ping Capsule, 4-8 weeks is usually a course of treatment. Dyslipidemia is a chronic long-term concomitant disease. And clinical studies have shown that ^[2], within the course of treatment, the lipid-lowering effect of Xue Zhi Ping Capsule is positively correlated with the use time. At present, there is no report of adverse reactions caused by long-term use of Xue Zhi Ping Capsule. (Consensus Suggestion)

6 Safety

6.1 Adverse Reactions/Adverse Events

In Li Zerong's study ^[2], it was reported that no serious adverse reactions were observed in clinical practice with Xue Zhi Ping Capsule combined with conventional treatment of western medicine which involved in 197 patients..

In Kong Deming's study which involved 30 patients, the treatment group received Xue Zhi Ping Capsule combined with conventional treatment of western medicine, while the control group received conventional treatment of western medicine only. In treatment group, two patients complained of slight dizziness and epigastric discomfort, which did not affect the treatment. After the treatment, symptoms of discomfort disappeared.

According to the National Center for Adverse Drug Reaction Monitoring, adverse reactions were reported in 8 cases from 2018 to 2022. A few patients may have nausea, vomiting, stomachache, constipation, dizziness, etc. after taking Xue Zhi Ping Capsule. When stop or reduce medication, the discomfort symptoms can be alleviated or disappeared, and no serious adverse events/adverse reactions are reported (see Annex C for details).

6.2 Contraindication

There is no safety study of Xue Zhi Ping Capsule in pregnancy, so it is not recommended for pregnant women. And there is no application experience in patients with severe hepatic and renal dysfunction, besides, the pharmacokinetic process in vivo is still unclear, so it is recommended to use it with caution in patients with severe hepatic and renal dysfunction. Considering that the ingredients in Xue Zhi Ping Capsule have the effect of promoting blood circulation and removing stasis, therefore, patients with bleeding tendency should use with caution. (Consensus Suggestion).

6.3 Drug Combination

In the existing clinical studies of Xue Zhi Ping Capsule, most included trials which use Xue Zhi Ping Capsule and conventional treatment of western medicine. No relative adverse reactions and toxic and side effects induced by combination use were reported.

Annex A
(Informative)
Research data of Xue Zhi Ping Capsule

A.1 Theoretical Basis of Traditional Chinese Medicine

The concept of blood lipid in modern medicine is similar to the description of “Gao”(ointment) and “Zhi” (fat) in ancient literature. Gao and Zhi come from Shui Gu (drink and food) originally, after being transported and transformed into refined essence, they flow with body fluids and transformed into red blood under the action of the heart. Therefore, Gao and Zhi exist in body fluids and blood. At present, most scholars believe that factors such as persistent improper diet, preference to greasy, sweet and thick flavour food, excessive idleness and less work, and emotional imbalance will affect *zang-fu* organs directly or indirectly, eventually resulting in disorder flow of Qi, blood and body fluid, disturbance of fat metabolism, and pathological products such as phlegm, dampness and blood stasis, which are important pathogenic factors of dyslipidemia. Under the assistance effect of stomach, the spleen can decompose grains. When the spleen and stomach are weak, excessive Shui Gu and refined essence can not be transformed and excreted in time, the retention, therefore, will become phlegm and turbidity, which hinders the transportation and transformation function of the spleen and stomach and makes spleen deficiency worse. Since “Qi commands blood circulation” and “Qi transports blood”, when *qi* is abundant, blood circulation will be slippery and quick, while when *qi* is deficient, blood flow will be slow, stagnant and lead to blood stasis, which will result in or aggravate dyslipidemia. Therefore, traditional Chinese medicine often views dyslipidemia from the perspective of phlegm and stasis.

Xue Zhi Ping Capsule comes from the folk and experience-based prescription of Miao nationality in Guizhou, which is composed of four ingredients including *rosa roxburghii*, Xu Changqing, *gynostemma pentaphyllum* and hawthorn. Among them, Xu Changqing and hawthorn (山楂) are included in Chinese Pharmacopoeia (2020 Edition). Pungent in flavour and warm in property, Xu Changqing has entry into liver meridian and stomach meridian, and can expel wind and eliminate dampness. Hawthorn, sour, sweet in flavour and slightly warm in property, has entry into spleen meridian, stomach meridian and liver meridian. Its effects include invigorating stomach to promote digestion, promoting qi circulation to dissipate blood stasis, as well as resolving turbidity and lower lipid. *Rosa roxburghii*, is commonly sweet, acid, and slightly astringent

in flavour, and its property is mild cool. It has entry into spleen meridian, stomach meridian and kidney meridian, and can invigorate stomach to promote digestion, tonify and arrest diarrhea. *Gynostemma pentaphyllum*, sweet and bitter in flavour, is slightly cold in property and has entry into lung meridian, spleen meridian and kidney meridian. The functions include clearing heat, tonifying deficiency, reinforcing qi and invigorating the spleen. The combination of the four ingredients has the effects of invigorating spleen, eliminating phlegm and removing stasis.

A.2 Quality Control on Pharmaceutical Technology

He Zhuying et al. [4] reported the analysis results of chemical components of Xue Zhi Ping Capsule, which include flavonoids, soap II compounds, paeonol, Zn, Mg, Fe and so on, among which paeonol is one of the main constituents of Xue Zhi Ping Capsule. Ye Feng et al. [5] thought that as a simple and accurate method, TLC scanning can be used to quantitatively measure the content of paeonol in Xue Zhi Ping Capsule. It can act as one of the quality control indexes of Xue Zhi Ping Capsule.

A.3 Pharmacological Research

Modern pharmacological studies have confirmed that sufficient trace elements and total flavonoids contained in *rosa roxburghii* can lower the levels of blood lipid and lipid peroxide in serum and reduce the damage of lipid peroxide to LDL [6]. The volatile oil in Xu Chang Qing is abundant, among which the paeonol represents most. It can inhibit adipocyte differentiation and lipid droplet formation, and has a strong lipid-regulating effect. At the same time, it can increase coronary blood flow and reduce myocardial cell function damage [7-10]. *Gynostemma pentaphyllum* total saponins, the main active component of *Gynostemma pentaphyllum*, can lower blood lipid level, protect vascular endothelial cell activity, and prevent and treat atherosclerosis [11, 12]. Hawthorn can inhibit cholesterol synthase and fat absorption, promote lipid excretion, and have the functions of promoting blood circulation, removing stasis, reducing blood lipid and blood pressure [13, 14].

Nie Hong et al. [15] observed the effect of Xue Zhi Ping Capsule on serum cholesterol in normal mice and pathological model of dyslipidemia mice. The results showed that the serum TC in normal mice decreased by $35.62 \pm 0.3\%$ compared with that before Xue Zhi Ping Capsule administration. It could also reduce TC, TG and LDL-C and increase HDL-C in dyslipidemia mice model.

Shen Qiang et al. [16] established a model of dyslipidemia in mesocricetus auratus. Experiments showed that Xue Zhi Ping Capsule can regulate the metabolism of fatty acids in cells, promote the mRNA and protein expression of cholesterol 7-hydroxylase (CYP7A1), and play a role in reducing TC by up-regulating the expression of peroxisome proliferator activated receptor α (PPAR- α) in model group. At the same time, by down-regulating the expression of cholesterol regulatory element-binding protein 1c (SREBP-1c) and lowering the expression of acetyl-CoA carboxylase (ACC1) downstream, Xue Zhi Ping Capsule can regulate blood lipids, and its regulatory effect on ACC1 is better than that of atorvastatin. When combined with half dose of atorvastatin, the efficacy of Xue Zhi Ping Capsule is equivalent or even better than that of conventional dose of atorvastatin alone.

A.4 Non-clinical Safety Studies

Medicine were given to mice 30g/kg (equivalent to 120g/kg of unrefined herbs) orally every day, which was equal to 500 times the normal clinical dose. After 7 days of continuous administration, with shiny hair, the behavior and eating of mice were also normal. No toxic reaction was observed, and no death occurred.

Medicine was were given to mice (equivalent to 100 times the normal clinical dose) 6g/kg orally every day and after 60 days of continuous administration, there was no abnormal change in rats' appearance and behavior. Also no significant change appeared in body weight, peripheral blood hemogram, liver, kidney and other organ coefficients. No toxic reaction was observed.

Annex B
(Informative Materials)
List of Clinical Problems

A total of 9 clinical questions were formed during the development of this document (Table B.1).

Table B.1 List of Clinical Problems

Number	Clinical Problems
1	What pattern type of dyslipidemia patients is Xue Zhi Ping Capsule suitable for?
2	Can Xue Zhi Ping Capsule relieve chest tightness, shortness of breath, fatigue, palpitation, dizziness and other clinical symptoms of patients with dyslipidemia (phlegm and stasis retention pattern)?
3	Is Xue Zhi Ping Capsule beneficial to lower TC level in patients with dyslipidemia?
4	Is Xue Zhi Ping Capsule beneficial to lower TG level in patients with dyslipidemia?
5	Can Xue Zhi Ping Capsule lower LDL-C level in patients with dyslipidemia?
6	Can Xue Zhi Ping Capsule increase HDL-C level in patients with dyslipidemia?
7	Is there any clear precautions for Xue Zhi Ping Capsule, such as medication (compatibility) contraindication, medication for special groups and other clinical medication precautions?
8	What are and how to deal with the common adverse reactions of Xue Zhi Ping Capsule?
9	How about the safety of taking Xue Zhi Ping Capsule for a long time?

Annex C

(Normative Materials)

Summary of Consensus Suggestions

This consensus adopts the internationally-recognized Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the evidence, and combines Delphi method with nominal group method, mainly considering six factors including evidence quality, clinical effectiveness, safety, economy, patient acceptability and others. For indications with evidence-based medicine evidence, “Recommendations” are formed according to the level of evidence; for those clinical indications which can not be supported by sufficient studies, “Consensus Suggestions” are formed after experts discussion.

Consensus is finally reached after retrieving literature, evaluating evidence level, collecting Delphi questionnaire, conducting nominal group and expert discussion. There are relatively few literature on clinical application of Xue Zhi Ping Capsule, therefore, “Consensus Suggestions” are presented. A total of 13 Consensus Suggestions are shown (Table C.1).

Table C.1 Summary of Consensus Suggestions for Xue Zhi Ping Capsule

Consensus Proposal	Consensus Item	Recommended or not
Consensus Suggestion 1	Xue Zhi Ping Capsule is suitable for patients with dyslipidemia (phlegm and stasis retention pattern in traditional Chinese medicine).	Yes
Consensus Suggestion 2.1	Taking Xue Zhi Ping Capsule individually can improve the syndrome of patients with dyslipidemia (phlegm and stasis retention pattern in traditional Chinese medicine).	Yes
Consensus Suggestion 2.2	Xue Zhi Ping Capsule combined with conventional treatment of western medicine, can further improve the clinical symptoms of patients with dyslipidemia.	Yes
Consensus Suggestion 3.1	Taking Xue Zhi Ping Capsule individually can lower TC level in patients with dyslipidemia.	Yes
Consensus Suggestion 3.2	Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further lower TC level of patients with dyslipidemia.	Yes

Consensus Suggestion 4.1	Taking Xue Zhi Ping Capsule individually can lower TG level in patients with dyslipidemia.	Yes
Consensus Suggestion 4.2	Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further lower TG level of patients with dyslipidemia.	Yes
Consensus Suggestion 5	Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further lower the LDL-C level of patients with dyslipidemia.	Yes
Consensus Suggestion 6.1	Taking Xue Zhi Ping Capsule individually can increase HDL-C level in patients with dyslipidemia.	Yes
Consensus Suggestion 6.2	Xue Zhi Ping Capsule combined with conventional treatment of western medicine can further increase the HDL-C level of patients with dyslipidemia.	Yes
Consensus Suggestion 7	Pregnant women, patients who with severe liver and kidney insufficiency and severe bleeding tendency or allergic to the ingredients of Xue Zhi Ping Capsule are prohibited to take.	Yes
Consensus Suggestion 8	Some patients may have discomfort symptoms including dizziness, epigastric discomfort and diarrhea during taking Xue Zhi Ping Capsule, which can be alleviated by reducing or stopping medication.	Yes
Consensus Recommendation 9	Xue Zhi Ping Capsule is mild in flavour and property, so patients who meet the indications can take regularly under the guidance of doctors if no adverse reactions are observed.	Yes

Annex D
(Normative)
Key points of disease diagnosis

Diagnostic points of dyslipidemia: Refer to the relevant diagnostic criteria in the *Guidelines for Prevention and Treatment of Dyslipidemia in Chinese Adults (Revised Edition in 2016)* ^[1]: Serum Total cholesterol (TC) ≥ 6.2 mmol/L, or Triglyceride (TG) ≥ 2.3 mmol/L, or Low density lipoprotein cholesterol (LDL-C) ≥ 4.1 mmol/L, or High-density lipoprotein cholesterol (HDL-C) ≤ 1.0 mmol/L detected on fasting for more than 12 hours for two consecutive times.

If any one of the above criteria is met, it will be diagnosed as dyslipidemia.

Annex E
(Informative)
Report from National Center for Adverse Drug Reaction Monitoring

A report on Xue Zhi Ping Capsule from the Chinese National Center for Adverse Drug Reaction Monitoring is provided in Table E.1.

Table E.1 Report from National Center for Adverse Drug Reaction Monitoring

No.	Numbering	Production batch number	Adverse reaction	Involved system	Whether the reaction is alleviated or disappeared after drug withdrawal or reduction	Year
1	XZP-2020-001	20100902	Nausea	Gastrointestinal diseases	Yes	2020
2	XZP-2020-002	20200902	Constipation	Gastrointestinal diseases	Yes	
3	XZPJN-2021-01	20191106	Palpitation; Nausea	Gastrointestinal diseases	Yes	2021
4	XZPJN-2021-02	202001001	Nausea; Vomiting	Gastrointestinal diseases	Yes	
5	XZPJN-2021-03	20210201	Edema of both lower limbs	Systemic diseases	Yes	
6	XZPJN-2021-04	20200901	Dizziness	Neurological diseases	Yes	
7	XZPJN-2021-05	20210701	Skin rash	Diseases of skin and skin accessories	Yes	
8	XZPJN-2022-001	20220101002	Stomachache	Gastrointestinal diseases	Yes	2022

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