

Prepared by Amber Schilling, PharmD
January 15, 20XX

Date: January 15, 20XX

Requestor's Name: Chief of Pharmacy (Dr. XXXX)

Request Classification: General Product Information

Verbatim Request: Why is Fiorinal® a controlled substance in Pennsylvania, but Fioricet® is not?

Interpreted / Detailed Request:

Both agents contain butalbital and caffeine; however, one contains aspirin and the other contains acetaminophen. Why, if both contain butalbital, and neither aspirin nor acetaminophen are controlled, is one controlled in the state of Pennsylvania and the other is not?

Response to Question:

- **Pertinent Background Information**

Fioricet® and Fiorinal® are both on formulary at the US Army Clinic in City X, PA for active duty and veterans. However, one is easier for the pharmacy to dispense because it is not controlled.

- **Pertinent Patient Factors**

If patients have a contraindication to ASA (high bleeding risk, peptic ulcer disease, allergy, etc.), then Fioricet® may be preferred. If patients respond better to the presence of an anti-inflammatory drug for symptom control of their headache, then Fiorinal® may be preferred.

- **Pertinent Medication Factors**

Both Fioricet® and Fiorinal® carry FDA indications for the treatment of tension-type headache. Fiorinal® is a C-III DEA controlled substance; Fioricet® is not a controlled substance in the state of Pennsylvania.

Both Fioricet® and Fiorinal® contain 50 mg butalbital, a barbiturate. Butalbital is considered a non-narcotic, controlled substance in the United States. However, it is not commercially available as a single agent. It is only available in combination with other agents. All available drugs on the market containing butalbital are shown in the table on the next page for reference.

Both Fioricet® and Fiorinal® also contain 40 mg caffeine, a vasoconstrictor and non-controlled substance.

In addition to butalbital and caffeine, Fioricet® contains acetaminophen (APAP; a non-narcotic, non-controlled analgesic).

In addition to butalbital and caffeine, Fiorinal® contains aspirin (acetyl salicylic acid; ASA; a non-narcotic, non-controlled, non-steroidal anti-inflammatory drug [NSAID]).

Thus, the only differing ingredient feature between the two drugs is APAP or ASA. Refer to the **Table**.

Table. Ingredients, DEA Schedule, and FDA labeled indication for Fioricet®, Fiorinal®, and associated products.

Drug	Butalbital	Caffeine	APAP	ASA	Codeine	DEA Schedule*	FDA Labeled Indication
	non-narcotic controlled barbiturate	non-narcotic non-opioid non-controlled vasoconstrictor	non-narcotic non-opioid non-opioid non-controlled analgesic	non-narcotic non-opioid non-controlled non-steroidal anti-inflammatory drug (NSAID) analgesic	narcotic opioid controlled analgesic		
Fioricet®	50 mg	40 mg	325 mg	---	---	---	Tension-type headache
Fiorinal®	50 mg	40 mg	---	325 mg	---	C-III	Tension-type headache
Fioricet®/Codeine	50 mg	40 mg	300 mg 325 mg	---	30 mg	C-III	Tension or muscle contraction headache
Fiorinal®/Codeine #3, Ascomp-Codeine®	50 mg	40 mg	---	325 mg	30 mg	C-III	Tension or muscle contraction headache
Azital® Bupap®	25 mg 50 mg	---	325 mg 300 mg or 325 mg	---	---	---	Tension-type headache

APAP, acetaminophen; ASA, acetyl salicylic acid [aspirin]

*State law is more stringent than federal law in the following states and is where both Fioricet® and Fiorinal® are classified as C-III: Georgia, Maryland, New Mexico, Utah, Illinois, and Rhode Island.

● **Review of Pertinent Literature**

According to the Controlled Substances Act (CSA), section 811(g) (3) (A), exceptions from the DEA scheduling can be made if a drug meets the following requirements:

- One of the active ingredients is a non-narcotic controlled substance; and

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- One of the other active ingredients is a non-scheduled compound.

The minimum ratios of non-controlled substance to controlled substance required for exemption are:

- 70 mg of APAP : 15 mg butalbital
- 188 mg ASA : 15 mg butalbital

The rationale for this exception is that the potential for abuse is decreased when a sufficient amount of a non-narcotic, non-controlled substance is present.

Please note, however, that this exception does not apply in all states. Whenever state law is more stringent than the federal law, the state law must be followed. BOTH Fioricet® and Fiorinal® are classified as Schedule III controlled drugs in the following states:

1. Georgia
2. Maryland
3. New Mexico
4. Utah
5. Illinois
6. Rhode Island

- **Analysis and Synthesis**

In the case of Fioricet® and Fiorinal®, both contain the active ingredient butalbital, which is the non-narcotic controlled substance component according to the CSA exception rule. Both also contain another active ingredient (ASA or APAP) which are both non-scheduled (or non-controlled) compounds.

The minimum decimal ratio of non-controlled to controlled substance to meet the exception requirement are as follows:

$$\text{Minimum Ratio Required for APAP to Butalbital} = \frac{70 \text{ mg APAP}}{15 \text{ mg butalbital}} = \frac{4.67 \text{ mg APAP}}{1 \text{ mg butalbital}}$$

$$\text{Minimum Ratio Required for ASA to Butalbital} = \frac{188 \text{ mg ASA}}{15 \text{ mg butalbital}} = \frac{12.5 \text{ mg ASA}}{1 \text{ mg butalbital}}$$

The actual ratios of non-controlled to controlled substances in Fioricet® and Fiorinal® are as follows:

$$\text{Fioricet} = \frac{325 \text{ mg APAP}}{50 \text{ mg butalbital}} = \frac{6.5 \text{ mg APAP}}{1 \text{ mg butalbital}} > \frac{4.67 \text{ mg APAP}}{1 \text{ mg butalbital}}$$

$$\text{Fiorinal} = \frac{325 \text{ mg ASA}}{50 \text{ mg butalbital}} = \frac{6.5 \text{ mg ASA}}{1 \text{ mg butalbital}} < \frac{12.5 \text{ mg ASA}}{1 \text{ mg butalbital}}$$

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Thus, the ratio of non-controlled to controlled substance in Fioricet® exceeds the minimum requirement but Fiorinal® does not. In other words, Fioricet® contains enough APAP to be considered abuse-deterrent, but Fiorinal® would require nearly twice the amount of ASA to be classified as a non-controlled drug.

References Used:

1. Controlled Substances Schedules.
<https://deaddiversion.usdoj.gov/schedules/schedules.html>
2. Title 21 United States Code Controlled Substances Act. Section 811(g) (3) (A)
<https://uscode.house.gov/view.xhtml%3Bjsessionid=2C85B8DEBFB1BB15A7D31E29A34C3DAA?req=granuleid%3AUSC-prelim-title21&saved=%7CZ3JhbnVsZWlkOIVTQy1wcmVsaW0tdGl0bGUyMS1zZWN0aW9uODAx%7C%7C%7C0%7Cfalse%7Cprelim&edition=prelim>
3. “Fiorinal is a Schedule III controlled drug but Fioricet is not!”
<http://www.pharmacyexam.com/index.cfm/blog/48/fiorinal-is-a-schedule-iii-controlled-drug-but-fioricet-is-not-.cfm>
4. LexiDrug.