US - OSHA SAFETY DATA SHEET

Issue Date 20-Jun-2005 **Revision Date** 29-Apr-2017 **Version** 2

1. IDENTIFICATION OF THE SUBSTANCE/PREPARATION AND OF THE COMPANY/UNDERTAKING

Product identifier

Product Name Megestrol Acetate Oral Suspension, USP 40 mg/mL

Other means of identification

Synonyms Pregna-4,6-diene-3,20-dione, 17-hydroxy-6-methyl-, acetate;
Megestrol acetate

Recommended use of the chemical and restrictions on use

Recommended Use Megestrol acetate oral suspension is indicated for the treatment of anorexia, cachexia, or an unexplained significant weight loss in patients with a diagnosis of acquired immunodeficiency syndrome (AIDS).

Uses advised against Not available.

Details of the supplier of the safety data sheet

Supplier Address
Par Pharmaceutical
1 Ram Ridge Rd
Chestnut Ridge, NY 10977

Emergency telephone number

24 Hour Emergency Phone Number Chemtrec (US):
1-800-424-9300

Emergency Telephone 1-845-425-7100

2. HAZARDS IDENTIFICATION

Classification

Health Hazards
Not classified.

Physical hazards
Not classified.

OSHA Regulatory Status
This product is not considered hazardous by the 2012 OSHA Hazard Communication Standard/Globally Harmonized System of Classification and Labelling of Chemicals (GHS); (29 CFR 1910.1200; Revision 3).

Label elements

Emergency Overview

This mixture is a drug product regulated by the FDA. Within the meaning of the OSHA Hazard Communication Standard [29 CFR 1910.1200]: this mixture is not considered a hazard when used in a manner which is consistent with the labeled directions.

Appearance Suspension **Physical state** Liquid **Odor** Not available

Hazards not otherwise classified (HNOC)
Not available.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Synonyms Pregna-4,6-diene-3,20-dione, 17-hydroxy-6-methyl-,acetate; megestrol acetate

Chemical Name	CAS No.	Weight-%
Megestrol Acetate	595-33-5	<1
Sucrose	57-50-1	2-5
Glycerin	56-81-5	25-30
Water	7732-18-5	60-70

4. FIRST AID MEASURES

First aid measures

General advice Consult a physician. Show this safety data sheet to the doctor in attendance.

Eye contact In case of eye contact, immediately flush eyes with fresh water for at least 15 minutes while holding the eyelids open. Remove contact lenses if worn. Get medical attention if irritation persists.

Skin Contact In case of contact, remove contaminated clothing. Immediately flush skin with copious amounts of water for at least 15 minutes. Obtain medical attention if skin reaction occurs.

Inhalation Inhalation is not an anticipated route for liquid handling. For the intended use, see product label.

Ingestion In case of accidental ingestion, wash out mouth with copious amounts of water. Seek medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Self-protection of the first aider Do not use mouth-to-mouth methods if victim ingested or inhaled the substance; give artificial respiration with the aid of a pocket mask equipped with a one-way valve or another proper respiratory medical device.

Most important symptoms and effects, both acute and delayed

Symptoms The most common adverse events occurring in > 5% of all patients receiving 800mg/20mL of megestrol acetate oral suspension were: nausea, diarrhea, impotence, rash, flatulence, hypertension, and asthenia.

Indication of any immediate medical attention and special treatment needed

Note to physicians Treat symptomatically.

5. FIRE-FIGHTING MEASURES

Suitable extinguishing media
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media None known.

Specific hazards arising from the chemical
Not available.

Hazardous combustion products Not available.

Explosion data
Sensitivity to Mechanical Impact Not available.
Sensitivity to Static Discharge None known.

Protective equipment and precautions for firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures

Personal precautions Avoid excessive contact. Avoid contact with eyes.

Environmental precautions

Environmental precautions See Section 12 for additional ecological information.

Methods and material for containment and cleaning up

Methods for containment Collect and place in a suitable container. Sorbents may be used.

Methods for cleaning up Dispose of in accordance with local, state, and national regulations.

7. HANDLING AND STORAGE

Precautions for safe handling

Advice on safe handling Handle in accordance with good industrial hygiene and safety practice.

Conditions for safe storage, including any incompatibilities

Storage Conditions Store megestrol acetate oral suspension between 15° to 25° C (59° to 77° F) and dispense in a tight container. Protect from heat.

Incompatible materials Not available.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Control parameters

Exposure Guidelines This product, as supplied, does not contain any hazardous materials with Occupational Exposure Limits (OEL) established by the region specific regulatory bodies.

Appropriate engineering controls

Engineering Controls The health hazard risks of handling this material are dependent on factors, such as physical form and quantity. Site-specific risk assessments should be conducted to determine the appropriate exposure control measures. Good general ventilation should be used. Ventilation rates should be matched to conditions. If applicable, use process enclosures, local exhaust ventilation, or other engineering controls to maintain airborne levels below recommended exposure limits. If exposure limits have not been established, maintain airborne levels as low as reasonably achievable.

Individual protection measures, such as personal protective equipment

Eye/face protection None required for consumer use. In laboratory, medical or industrial settings, safety glasses with side shields are highly recommended. The use of goggles or full face protection may be required depending on the industrial exposure setting. Contact a health and safety professional for specific information.

Skin and body protection None required for consumer use. In laboratory, medical or industrial settings, gloves and lab coats are recommended. The use of additional personal protective equipment such as

shoe coverings, gauntlets, and hood or head coverings may be necessary. Contact a health and safety professional for specific information.

Respiratory protection None required for consumer use. Respirators may be required for certain laboratory and manufacturing tasks if engineering controls do not maintain airborne concentrations below recommended exposure limits (where applicable) or to an acceptable level (where the exposure limits have not been established). Workplace risk assessments should be completed before specifying and implementing respirator usage. All respirators must conform to specifications for efficiency and performance.

General Hygiene Considerations Always observe good personal hygiene measures, such as washing after handling the material and before eating, drinking, and/or smoking. Routinely wash work clothing and protective equipment.

9. PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Physical state	Liquid		
Appearance	Suspension	**Odor**	Not available.
Color	Milky white	**Odor threshold**	Not available.

Property	**Values**	**Remarks**
pH	3.5 - 4	
Melting point/freezing point	Not applicable/liquid	
Boiling point / boiling range	Approx. 100°C	
Flash point	Not available.	
Evaporation rate	Not available.	
Flammability (solid, gas)	Not available.	
Flammability Limit in Air		
Upper flammability limit:	Not available.	
Lower flammability limit:	Not available.	
Vapor pressure	Not available.	
Vapor density	Not available.	
Specific Gravity	Not available.	
Water solubility	Soluble in water.	
Solubility in other solvents	Not available.	
Partition coefficient	Not available.	
Autoignition temperature	Not available.	
Decomposition temperature	Not available.	
Kinematic viscosity	Not available.	
Dynamic viscosity	Not available.	
Explosive properties	Not available.	
Oxidizing properties	Not available.	

Other Information

Softening point	Not available.
Molecular weight	Not applicable/mixture
VOC Content (%)	Not available.
Density	Not available.
Bulk density	Not available.

10. STABILITY AND REACTIVITY

Reactivity
Stable at normal conditions.

Chemical stability
Stable at ambient temperatures and atmospheric pressures under recommended storage and handling conditions.

Possibility of Hazardous Reactions
None under normal processing.

Hazardous polymerization
Will not occur during normal storage and use conditions.

Conditions to avoid
Not available.

Incompatible materials
Not available.

Hazardous Decomposition Products
None under normal use conditions.

11. TOXICOLOGICAL INFORMATION

Acute toxicity

Chemical Name	Oral LD50	Dermal LD50	Inhalation LC50	Intravenous LD50
Sucrose 57-50-1	= 29700 mg/kg (Rat)	-	-	-
Glycerin 56-81-5	= 12600 mg/kg (Rat)	> 10 g/kg (Rabbit)	> 570 mg/m^3 (Rat) 1 h	-
Water 7732-18-5	> 90 mL/kg (Rat)	-	-	-
Megestrol Acetate 595-33-5	12,600 mg/kg (Rat)	>10,000 mg/kg (Rabbit)	-	-

Information on toxicological effects

Symptoms The most common adverse events occurring in > 5% of all patients receiving 800mg/20mL of megestrol acetate oral suspension were: nausea, diarrhea, impotence, rash, flatulence, hypertension, and asthenia.

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Skin corrosion/irritation Species: Rabbit. Mild skin irritation.

Serious eye damage/eye irritation Species: Rabbit: Mild irritant.

Sensitization No data found.

Germ cell mutagenicity Micronucleus assay, carried out in rats given a single p.o. dose of 100 mg/kg, CPA induced the maximum increase in the frequency of micronucleated hepatocytes (6.6-fold as compared to controls) when treatment was performed 3 days before partial hepatectomy and cell sampling 2 days later. Under the same experimental conditions the clastogenic potencies of CMA and MGA were 69% and 36% of that of CPA respectively.

In the liver foci assay, p.o. dosing with 100 mg/kg CPA once a week for 6 successive weeks induced, as compared to controls, a significant increase in the number and area of gamma-glutamyltranspeptidase-positive foci. At the same dosage schedule the tumor-initiating activity of CMA and MGA was 7- to 10-fold lower than that of CPA. These findings suggest that the 1,2 alpha-methylene group, present in CPA but absent in both CMA and MGA, favors the activation to a reactive species and/or hinders the biotransformation to non-toxic metabolites.

The synthetic progestin cyproterone acetate has been recently shown to elicit DNA repair synthesis in cultured rat hepatocytes and to form adducts with rat hepatocyte DNA in vitro and in vivo. In the present study /investigators/ have examined the genotoxic potential of the structural analogues of cyproterone acetate, chlormadinone acetate and megestrol acetate in rat liver cells. Cyproterone acetate strongly induced DNA repair synthesis in

hepatocyte cultures from females but not from males. In contrast, chlormadinone acetate and megestrol acetate (2-50 uM) did not detectably increase repair synthesis in cultured hepatocytes from either gender. chlormadinone acetate and megestrol acetate, however, caused the formation of DNA adducts detectable by the 32P-postlabelling technique. At a concentration of 30 uM, between 30 and 50 adducts/10(9) nucleotides were found with megestrol acetate and chlormadinone acetate in cultured hepatocytes of female rats, and between 5 and 20 adducts/10(9) nucleotides in hepatocytes from female rats. Chlormadinone acetate and megestrol acetate also induced low levels of DNA adducts in vivo.

When female rats were treated with 100 mg/kg of chlormadinone acetate or megestrol acetate per os, the adduct levels were 2 and 10 adducts/10 nucleotides respectively. The results indicate that both chlormadinone acetate and megestrol acetate show some genotoxicity at rat liver cells, which is, however, much lower than that for cyproterone acetate. Our findings further suggest that the high genotoxicity of cyproterone acetate is associated with the presence of the 1,2 alpha-methylene group, which is absent in chlormadinone acetate and megestrol acetate.

Carcinogenicity

Female beagles receiving megestrol acetate dosages of 0.01, 0.1, or 0.25 mg/kg daily for 7 years, both benign and malignant breast tumors occurred. No tumors were reported in female monkeys receiving megestrol acetate dosages of 0.01, 0.1, or 0.5 mg/kg daily for 10 years. Pituitary tumors were observed in female rats receiving megestrol acetate dosages of 3.9 or 10 mg/kg daily for 2 years.

Chemical Name	ACGIH	IARC	NTP	OSHA
Megestrol Acetate 595-33-5		Group 2B		X

Reproductive toxicity

Reproduction studies in female rats using megestrol acetate dosages of 0.05-12.5 mg/kg daily (lower than the recommended (13.3 mg/kg daily) dosages in humans) have revealed evidence of impaired fertility in male offspring of mothers receiving megestrol acetate; similar results were obtained in dogs.

Micro doses (1.5 ug/rat/day) of megestrol acetate (6-methyl-17beta-acetoxypregna-4,6-diene-3,20 dione) were administered to 16 rats for 1 year to determine the effect on the genital organs and female fertility. No noteworthy ponderal or histologic effect of the genital organs or the pituitary was observed. However, uterus glycogen concentration and alkaline phosphatase activity were greatly reduced (versus controls, p.05 and p.01, respectively) while glucose-6-phosphate and lactic dehydrogenase activities increased significantly (versus controls, p.01).

In the fertility performance test, 86% of the 14 controls showed positive mating compared with 50% for the treated group. By Day 10 of pregnancy many of the fetuses in the treated group were in the process of resorption. The factors contributing to pregnancy failure were inhibition of mating, implantation failure and fetal resorption.

The effect of the oral administration of megestrol acetate (MA; 17 alpha-acetoxy-6-dehydro-6-methylprogesterone) for 30 days at a dose of 40 mg/kg body weight/day on the genital organs and fertility of male rats was studied. MA had no effect on spermatogenesis or the fertility of the animals. However, the weights of the genital organs were significantly reduced (p less than .05) and pituitary gonadotropin levels were significantly increased (p less than .01). These alterations were reversed after cessation of treatment. Although MA and testosterone propionate each increase seminal vesicle weight, their combined administration significantly decreased seminal vesicle and ventral prostate weight (p less than .01). The significance of the results is discussed.

STOT - single exposure

Not classified.

STOT - repeated exposure

Not classified.

Target Organ Effects

Not available.

Neurological effects	Not available.
Aspiration hazard	Due to the physical form of the product, it is not an aspiration hazard.

12. ECOLOGICAL INFORMATION

Ecotoxicity
Not available for formulation.

Persistence and degradability
Not available for formulation.

Bioaccumulation
Not available for formulation.

Mobility
Not available for formulation.

Other adverse effects
Not available for formulation.

13. DISPOSAL CONSIDERATIONS

Waste treatment methods

Disposal of wastes	Disposal should be in accordance with applicable regional, national and local laws and regulations.
Contaminated packaging	Disposal should be in accordance with applicable regional, national and local laws and regulations.
US EPA Waste Number	Not available.
California Hazardous Waste Codes	This product does not contain substances that are listed with the State of California as a hazardous waste.

14. TRANSPORT INFORMATION

DOT	Not regulated.
TDG	Not regulated.
MEX	Not regulated.
ICAO (air)	Not regulated.
IATA	Not regulated.
IMDG	Not regulated.
RID	Not regulated.
ADR	Not regulated.
ADN	Not regulated.

15. REGULATORY INFORMATION

International Inventories

TSCA	Does not comply
DSL/NDSL	Complies
EINECS/ELINCS	Complies
ENCS	Does not comply
IECSC	Does not comply
KECL	Does not comply
PICCS	Does not comply
AICS	Complies

Legend:

TSCA - United States Toxic Substances Control Act Section 8(b) Inventory
DSL/NDSL - Canadian Domestic Substances List/Non-Domestic Substances List
EINECS/ELINCS - European Inventory of Existing Chemical Substances/European List of Notified Chemical Substances
ENCS - Japan Existing and New Chemical Substances
IECSC - China Inventory of Existing Chemical Substances
KECL - Korean Existing and Evaluated Chemical Substances
PICCS - Philippines Inventory of Chemicals and Chemical Substances
AICS - Australian Inventory of Chemical Substances

US Federal Regulations

SARA 313

Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372.

SARA 311/312 Hazard Categories

Acute health hazard	Yes
Chronic Health Hazard	Yes
Fire hazard	No
Sudden release of pressure hazard	No
Reactive Hazard	No

CWA (Clean Water Act)

This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42).

CERCLA

This material, as supplied, does not contain any substances regulated as hazardous substances under the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) (40 CFR 302) or the Superfund Amendments and Reauthorization Act (SARA) (40 CFR 355). There may be specific reporting requirements at the local, regional, or state level pertaining to releases of this material.

US State Regulations

California Proposition 65

This product contains the following Proposition 65 chemicals.

Chemical Name	California Proposition 65
Megestrol Acetate - 595-33-5	Carcinogen Developmental

U.S. State Right-to-Know Regulations

This product may contain substances regulated by state right-to-know regulations.

Chemical Name	New Jersey	Massachusetts	Pennsylvania
Sucrose 57-50-1		X	X
Glycerin 56-81-5	X	X	X
Megestrol Acetate 595-33-5		X	

16. OTHER INFORMATION

Prepared By	IES Engineers
Issue Date	20-Jun-2005
Revision Date	29-Apr-2017
Revision Note	Formatted to the new 2012 GHS Standard.

Disclaimer

This SDS is intended to provide a summary of our knowledge and guidance regarding the use of this material. It is not meant to be an all-inclusive document on worldwide hazard communications regulations. This information is offered in good faith. Each user of this material needs to evaluate the conditions of use and design the appropriate mechanisms to prevent employee exposures, property damage or release to the environment.

End of Safety Data Sheet